1. PHILADELPHIA CHROMOSOME POSITIVE *DE NOVO* AML OR BLAST PHASE CML? CASE REPORT AND LITERATURE REVIEW

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Abstract

Background. The *BCR::ABL1* translocation and the accompanying Philadelphia chromosome represents the first mutation which defined a disease, chronic myeloid leukemia. It also represents the first druggable target for which a specific compound was developed and accepted in current clinic practice, imatinib. Despite these, there are still areas in which the diagnosis and the best treatment sequence still needs investigation. One such context is the diagnosis and management of *BCR::ABL1* positive myeloid neoplasms with ≥20% blasts, more specifically the differentiation between myeloid blast phase chronic myeloid leukemia and *BCR::ABL1* positive acute myeloid leukemia. In this paper we present our recent experience with a *BCR::ABL1* positive myeloid neoplasms with ≥20% blasts.

Case report

A 57-year-old, male patient, presented to our department to further investigate complete blood count (CBC) abnormalities. The clinical exam and the history of the patient were unremarkable, except for mild hepatomegaly: 1-2 cm below costal margin measured by palpation. The local CBC and blood lab tests revealed leukocytosis (WBC= 98500/μL), with basophilia (BA= 3.7%, 3645/μL) moderate anemia (Hgb= 10.3 g/dL) and mild thrombocytopenia (PLT= 72000/μL) and an elevated LDH 1075 U/L. During the initial presentation the patient presented a syncope episode for which he underwent a CT examination. The CT scan excluded a central nervous system or venous thromboembolism causes for the syncope, however revealed hepato- and splenomegaly: 15 cm, respectively, 12 cm.

Bone marrow aspirate was performed revealing a hypercellular marrow consisting of 80% myeloid cells: 40% myeloblasts, and 40% myeloid precursors (8% promyelocytes, 5% myelocytes, 10% metamyelocytes, 3% unsegmented granulocytes). Flow cytometry revealed 43% $CD34^+$ myeloid precursors with aberrant $CD9^+$ and $CD123^+$ expression. Cytogenetic

analysis revealed complex translocations involving chromosomes 6, 9 and 22 with 12 trisomy leading to the formation of the Philadelphia chromosome in 100% of analyzed metaphases (Figure 1). The final karyotype was: 47,XY,t(6,9,22)(6pter->6q21::q11.2->qter;9pter->9q34::6q21->6qter;22pter->q11.2::9q34->9qter),+12[21]. RT-PCR identified the p210 *BCR::ABL1* mRNA isotype, with negative *NPM1* and *FLT3*-ITD mutations.

Conclusion. Differentiating myeloid BP-CML and AML with *BCR::ABL1* translocation is an important step in evaluating each patient with ≥20% myeloid bone marrow blasts with *BCR::ABL1* translocation. This process is facilitated by local protocols which guide diagnostic testing prioritization in a limited resource situation, while also differentiating between myeloid BP-CML and *BCR::ABL1*+ AML, therefore providing the therapeutic options for each patient.

2. ACUTE MYELOID LEUKEMIA – THE CHARACTERISTICS OF THE PATIENTS DIAGNOSED AND TREATED IN THE HEMATOLOGY CLINIC OF CRAIOVA. RESULTS.

Authors: Ionela Rotaru, Doriana Duta, Luminita Ocroteala, Mihail Badea, Amelia Gaman, Ana Maria Patrascu, Janina Georgiana Goanta

Hematology Clinic of Craiova

Background:

Acute myeloid leukemia is the most severe hematologic malignancy, with different treatment approaches, according to intensive chemotherapy eligibility, therefore with different therapeutic targets: curability versus non-curative treatment.

Purpose: to analyze our activity regarding acute leukemia patients and the challenges we face and to inform the hematologist community about them.

Material and methods:

Between 01/01/2020 and 06/30/2022 a number of 112 acute myeloid leukemia patients were diagnosed in the Hematology Clinic of Craiova. 19,64% of patients were younger than 60, therefore eligible for intensive chemotherapy. Morphologic, immunophenotype and citogenetics analysis was performed for all newly diagnosed patients. Molecular analysis was only performed for 40.9% of patients. All patients eligible for intensive chemotherapy were tested for FLT3 mutation and 13.63% were positive. Allogeneic stem cell transplant was indicated for 8 patients: 3 FLT3 positive, 2 failing to complete remission after the first induction, 2 MRD positive and 1 blastic myelofibrosis phase patient.

HLA typing identified only one sibling donor and allogeneic stem cell tranplant was performed.

Results:

The majority of cases were diagnosed in patients in their 60s and 70s (69 patients), with the minimun age being 18 and the maximum 86. The dominant morphologic types were M1 and M4 (40 patients). Sex ratio nearly 1:1, 59 men and 53 women.

Out of the 112 diagnosed patients, 16 received intensive chemotherapy and 90 hipomethilant agents treatment. 31 patients were alive in June 2022: 5 patients with intensive chemotherapy induction and 26 over 60 years old, with hipomethylant agents treatment. The main death

causes were: sistemic infection with multi-organ failure, vital hemorrhage and progressive disease.

Conclusion:

In our clinic, the majority of cases were diagnosed in patients noneligible for intensive chemotherapy. Although our analysis was performed at the same time as the Covid 19 pandemic, the annual median number of new cases was around 50, similar to the prepandemic period. Sterile rooms and continous blood supportive treatment, on time and in proper amount, remain the main obstacles for us in these frail patients' caretaking.

3. ACUTE LEUKEMIAS WITH UNFAVORABLE PROGNOSIS

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Abstract Text:

Introduction:

Acute leukemia is a clonal, malignant disease characterized by the accumulation of abnormal blast cells, mainly in the bone marrow, and inhibition of normal hematopoiesis. Acute leukemia is a pathology that requires emergency diagnosis and can be associated with a poor prognosis.

Objectives and Methods: There will be presented 6 cases of acute leukemia with associated pathology, with unfavorable prognosis.

Results:

Case 1: The 38-year-old female, with no known history, was diagnosed in December 2021 with acute promyelocytic leukemia - a high-risk form, for which chemotherapy was initiated. During the evolution, the patient installs massive supratentorial hemorrhagic stroke. Emergency decompression neurosurgery was performed, which revealed a ruptured arterio-venous malformation, which led to death.

Case 2: Another 38-year-old female, with grade III obesity, diagnosed in March 2022 with acute myelomonocytic leukemia FLT3 TKD positive - hyperleukocytic form, for which standard chemotherapy and FLT3 inhibitor was initiated. During the evolution, the patient associated left cephalic vein thrombosis, complicated with PE in the segmental and subsegmental arteries, splenic infarction, bilateral central retinal vein thrombosis - hemorrhagic form and subsequent cerebellar hemorrhagic stroke, which led to death.

Case 3: 44-year-old patient, chronic ethanol user and smoker, diagnosed in June 2022 with acute lymphoblastic B cell leukemia, with severe pancytopenia at diagnosis, for whom specific chemotherapeutic treatment was initiated, and during post-chemotherapy aplasia presented positive blood cultures with E. Coli and Candida Tropicalis, with unfortunate evolution, despite the broad-spectrum antibiotic and antifungal treatment.

Case 4: A 66-year-old female, with no significant history, diagnosed in February 2020 with acute myelomonocytic leukemia after CMMoL, for which therapy with hypomethylating agent was administered, and a BCL2 inhibitor was added. The patient had initial favorable response to treatment. In January 2022, the patient associated SARCOV2 infection with severe thrombocytopenia, with the appearance of severe GI bleeding, which led to death.

Case 5: A 64-year-old female, initially diagnosed in 2011 with MDS-RAEB2, for whom she received treatment with a hypomethylating agent, with a partial hematological response, with persistent thrombocytopenia. In June 2022, the patient was hospitalized with extensive cutaneous mucosal hemorrhagic syndrome, and investigations revealed a transformation into acute leukemia- AML FAB 4 with hyperleukocytosis, high risk, with the presence of del (11) (q23) and positive FLT3 ITD mutation. During evolution, the patient installs cerebellar hemorrhagic stroke, which led to death.

Case 6: A 54-year-old female, known with Spondylitis on immunosuppressive treatment, was diagnosed in December 2021 with acute myeloblastic leukemia-AML FAB2, post myelodysplastic syndrome, for which standard induction treatment was initiated, followed by period of severe aplasia, during which she presents Clostridium Difficile infection, SARS-COV2 infection, positive blood cultures with E. Coli for which she received broad-spectrum antibiotic treatment and antiviral treatment. Due to severe thrombocytopenia, the patient has severe GI bleeding. During the hospitalization the patient also presented an internal jugular vein thrombosis associated with the insertion of the central venous catheter. The patient's evolution was unfavourable.

Conclusion: Acute leukemia is a high-risk malignancy that can be associated with other conditions which influence the patient's outcome.

4. BLINATUMOMAB THERAPY IN ACUTE LYMPHOBLASTIC LEUKEMIA: REAL-LIFE EXPERIENCE - FUNDENI CLINICAL INSTITUTE

Mihaela Cirstea[1,2] , Alexandra Ghiaur[1] , Bogdan Ionescu[1], Camelia Stancioaca[1] , Roxana Hîrjan [1] , Alexandru Bardas [1,2], Simona Costache[1], Codruta Popa [1 ,2], Camelia Dobrea[1,2], Cerasela Jardan[1,2], Mihaela Dragomir[1] , AureliaTatic[1,2], Daniel Coriu [1,2]

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Despite advances in recent years, the treatment of acute lymphoblastic leukemia (ALL) in adults remains a challenge. The introduction of new monoclonal antibodies in the treatment of ALL have improved the response rate and overall survival. Blinatumomab is a C19/CD3 bispecific antibody indicated in relapsed-refractory CD 19-positive B- cell ALL and in cases of ALL with positive minimal residual disease.

Objective of the study: evaluating the response rate and overall survival of patients with B-ALL treated with Blinatumomab. A retrospective study on a cohort of 62 patients diagnosed with ALL at the Center of Hematology and Bone Marrow Transplantation of Fundeni Institute between January 2020 and June 2022. The studied group included 16 patients with refractory/relapsed B-ALL treated with Blinatumomab from 2016 to 2022.

Laboratory methods: morphology, flow-cytometry, cytogenetic / FISH studies, identification of molecular abnormalities: E2A-PBX1 - t(1;19)(q23;p13), MLL-AF4 - t(4;11)(q21;q23), BCR-ABL p190 - t(9;22)(q34;q11), BCR-ABL p210 - t(9;22)(q34;q11), TEL-AML1 - t(12;21)(p13;q22), SIL-TAL 1 - del(1)(p32;p32).
Statistical analysis: performed with dedicated software - SPSS 20.0, Excell.

Results: the study group of 16 cases of B-cell ALL treated with Blinatumomab included 12 cases of relapsed/ refractory ALL and 4 cases of ALL with positive minimal residual disease. The median age of the relapsed / refractory ALL group was 30.6 years (range: 18-48 years). The rate of complete remission was 31.25% (5 patients) after treatment with Blinatumomab. Allotransplantation with HSC was performed in 5 cases (31.25%). In 31% of cases therapy with blinatumomab was used as a bridge to allogeneic transplant with HSC.

Conclusions: Blinatumomab therapy as a bridge to allogeneic transplant with HSC improved survival rate in relapsed/refractory ALL.

5. INDUCTION THERAPY FOR NEWLY DIAGNOSED FLT3 AML - A UNICENTRIC RETROSPECTIVE ANALYSIS

Maria-Camelia Stancioaica, AureliaTatic, B. Ionescu, Roxana Hirjan, Alexandra Ghiaur, Mihaela Carstea, A. Bardas, Ana Mihail, D. Coriu

According to literature, 30% of newly diagnosed AML carries an FLT3 mutation. Patients with FLT3-ITD mutations tend to have a particularly unfavorable prognosis, with an increased risk of relapse and shorter overall survival. In Romania, starting December 2019, the treatment includes addition of FLT3 inhibitor to standard chemotherapy. A number of 25 patients with FLT3-ITD AML were observed for a period of ~ 30 months. Through the analysis of each case, we followed: clinical-biological characteristics at diagnosis, the patients tolerance to the drug, the evaluation of short- and long-term complications, achievement of complete remission and the management related to the allograft. For a better understanding of disease evolution, we tried to reach at a correlation between the patients clinic and molecular markers using genomic evaluation (NGS).

6. OUTCOME OF RELAPSED/REFRACTORY FLT3- MUTATED ACUTE MYELOID LEUKEMIA IN THE GILTERITINIB ERA: A UNICENTRIC RETROSPECTIVE ANALYSIS OF 9 MONTHS

Roxana Hîrjan, Aurelia Tatic, Bogdan Ionescu, Camelia Stăncioaica, Alexandra Ghiaur, Mihaela Cîrstea, Alexandru Bardaș, Mihail Matei, Cristina Constantin, Daniel Coriu

Gilteritinib is a tirosin kinase FMS-like inhibitor (FLT3) approved by EMA in October 2019 and reimbursed in Romania in March 2022. Patients with FLT3 mutated acute myeloid leukemia are high risk and this mutation is associated with drug resistance and high risk of relapse. In Romania, Gilteritinib is approved in monotherapy, in relapsed/refractory disease after the presence of the biomarker FLT3 is confirmed. In Fundeni Clinical Institute we have treated six patients with Gilteritinib 120mg once-daily dose from December 2021 through September 2022. A complete morphological remission was achieved in four out of six treated patients.

7. EARLY-DEATH IN ACUTE PROMYELOCYTIC LEUKEMIA: CASE SERIES AND LITERATURE REVIEW

Alexandra Ghiaur1, Bogdan Ionescu1, Aurelia Tatic1,2, Mihaela Cirstea1,2, Camelia Stancioaica1, Roxana Hirjan1, Cristina Constantin1, Alina Tudosescu1, Didona Vasilache1, Cerasela Jardan1,Anca Gheorghe1, Mihaela Dragomir1, Daniel Coriu1,2 1

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The survival of patients with acute promyelocytic leukemia (APL) has improved over the past four decades due to utilization of targeted agents and advances in supportive care.Through a literature review, the probability of cure is around 80% for high-risk disease and even higher for low/intermediate risk APL. Nowadays, the most important challenges for hematologist remain preventing early mortality and approach of high-risk patients. Depending on what source of information is used: clinical trial vs real-world data , early-death in APL varies widely between 9.6% and as high as 60%. Immediate access to ATRA and best supportive care (transfussion, antibiotics, corticotherapy) could result in preventable death via thrombohemorrhagic complication, infections and differentiation syndrome

8. ACUTE LEUKEMIA TREATMENT IN THE ELDERLY- A CONTINUOUS CHALLENGE

Dr. Cristina Negotei, Conf Dr. Berbec Nicoleta, Conf Dr Colita Andrei, Dr Iuliana Mitu, Dr Sincean Bogdan, Dr Coles Elena, Dr Stanca Oana, Prof. Dr Anca Roxana Lupu

Coltea Clinical Hospital

Acute leukemias represent a heterogeneous group of disorders of the hematopoietic stem cell, characterized by proliferation and accumulation of a population of immature clonal cells, associated with a bone marrow failure syndrome. The new international guidelines recommend categorizing acute leukemias based on their cytogenetic and molecular profile.

The thesis consists of a sample of 82 patients, with clinical and paraclinical investigations orienting the diagnosis towards an acute myeloproliferative/ lymphoproliferative syndrome, collected from 2019 to 2022, taken place in Coltea Clinical Hospital. The sample is composed by 38 females and 44 males, aged over 65 years old. The distribution of de novo acute leukemia (48,78%) vs secondary acute leukemia (51,21%) was homogenous in this case. Over 90% of patients presented at the diagnosis a series of serious comorbidities, the majority of them being cardiovascular in nature. More than half of the patients (54,8%) benefited from new therapies with hypomethylating drugs. This kind of therapy is frequently used in the treatment of the patients with a high risk score and in those not eligible for intensive chemotherapy, having better overall response rates and a better quality of life. Overall survival at 9 months was 25 % for the patients treated with hypomethylating agents.

The main objective of this research is identifying a prognostic model, based on biological features of acute leukemia, with predictive value regarding the therapeutical response, in order to ensure a better adapted therapy for the risk category of each patient, to raise the efficiency of the treatments and to reduce as much as possible the toxicities related to therapy.

9. PERSONALIZED APPROACH TO ACUTE MYELOID LEUKEMIA IN THE ELDERLY PATIENT

Prof. Dr. Ana Maria Vladareanu

Acute myeloid leukemia is a rare hematological disease that mostly affects the elderly, with a median age of onset of more than 65 years. The prognosis is often poor, with a 5-year survival rate of less than 5%.

This poor prognosis is caused by both patient- and disease-related particularities. A poor performance status, significant comorbidities, and decreased functional reserves are all patient-related factors. As a result, the elderly have a lower tolerance for intense chemotherapy than younger ones. Unfavorable cytogenetics and the expression of genes that confer treatment resistance are examples of disease-related variables (multidrug resistance-1 gene). The complex karyotype is observed in the majority of older people, but favorable findings, such as t (8;21) and inv (16)/t (16;16), are uncommon, accounting for fewer than 5%. Secondary AML is also more common in these patients, resulting in treatment resistance. It can develop as a result of myelodysplastic syndromes, myeloproliferative neoplasms, or as a consequence of chemotherapy for other neoplasms.

According to the National Comprehensive Cancer Network Guidelines, the treatment strategy must be adapted to the performance status, cytogenetic risk, molecular exam, and prior chemotherapy of hematological disorders. Intensive chemotherapy, molecularly targeted therapy (FLT3, IDH1, and IDH2 inhibitors), anti-CD33 monoclonal antibodies, Venetoclax, and hypomethylating agents are among the treatment possibilities.

Hematopoietic stem cell transplantation is recommended for acute myeloid leukemia patients with intermediate and high risk. However, elderly patients are rarely transplanted due to toxicity concerns. Reduced-intensity regimens make possible the transplantation of these patients while decreasing toxicity and ensuring effective engraftment.

In conclusion, despite advances in therapy, many patient- and disease-related particularities lead to a poor prognosis in the elderly.

10. CONSIDERATIONS AND FIRST-LINE TREATMENT STRATEGIES FOR DIFFUSE LARGE B CELL LYMPHOMA

Dr. Luminita Ocroteala1, hematology senior physician, Dr. Luiza Gica2, Dr. Gabriela Diana Baluta2

hematology senior physician, hematology resident physician, Hematology Clinic Craiova

Fortunately, effective therapies are available for many, but not for all patients with diffuse large cell lymphoma, because 30% to 50% of them relapse, thus the necessity of improvements in first-line therapy options for newly diagnosed patients. The addition of immunotherapy to the DLBCL therapeutic arsenal is ready to define a new standard of care in first-line treatment. Furthermore, the early integration of these new agents, when the immune status of the host is still preserved, might significantly change the way we approach the initial management of this condition.

11. GENOTYPIC AND PHENOTYPIC ALTERATIONS OF NATURAL KILLER CELLS IN THE SETTING OF ACUTE MYELOID LEUKEMIA

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Introduction: Natural killer (NK) cells are innate lymphoid cells (ILCs) with a distinct and important role in mediating the destruction of malignant cells, in setting such as acute myeloid leukemia (AML) or chronic myeloid leukemia (CML). Phenotypically, 3 types of functional NK cells have been described, based on their expression of CD56, CD94, CD16 and CD57 antigens and were named immature, mature and hypermature. They differ in terms of cytokine secretion, cell trafficking and cytotoxic activity. NKs elicit antitumor responses based on signals derived from their activating or inhibitory receptors and, even though they present multiple receptor classes, killer immunoglobulin-like receptors (KIR) stand out as the most heterogeneous and diverse group. Studies have reported that tumor immune evasive mechanisms lead to upregulation of inhibitory KIRs (iKIRs) and downregulation of the activating KIR (aKIRs) to ensure leukemic cell survival and disease progression. Objectives: Our study explored the distribution of NK cell subpopulations in the setting of AML. We analyzed the expression of the main iKIR associated with tumor progression and immune evasion (CD158a, CD158b and CD158e1), as well as the expression of NKG2A, another potent inhibitory receptor associated with tumor cell survival. In addition, we evaluated the KIR genotypes in our AML group to search for potential discrepancies in individual genes, as well as to classify them in the larger A (inhibitory) and B (activating) haplotypes. Materials and Methods: Fresh bone marrow samples from patients admitted to the Regional Institute of Oncology (Iasi, Romania) and newly diagnosed with AML (n = 12) were obtained. The subjects were investigated by multiparameter flow cytometry for NK phenotypes and by PCR-SSP for KIR genotype evaluation. As phenotype control, we used peripheral blood samples from 15 volunteers. The genotype control population was comprised of 98 volunteers from the National Registry of Stem Cell Donors. Statistical analysis was performed with the GraphPad Prism 8.0.1 TM software and IBM SPSS TM. For phenotype analysis, parametric t-test and nonparametric Mann Whitney test were applied to evaluate data distribution. Pearson's and Spearman's correlation coefficients were used to assess associations between measured variables. For the genotype analysis, Fisher's exact test was utilized to calculate the difference between the allelic groups. Results: An impaired distribution of NK and T cells were observed in the AML population (r= - 0.78; ***p =

0.0005), as well as a phenotypic shift from the mature to the immature stage of development. Moreover, upregulation of CD158a, a key iKIR, in early stages of maturation, can suggest an efficient immune evasion mechanism of the tumor cells (*p = 0.03). Lastly, characterization of the KIR genotype showed a lower incidence of KIR2DS3 in AML NK cells compared to the control group (*p = 0.02), which further suggests that lack of this receptor might favor an impaired anti-tumor response in AML.

Conclusions: Detection of NK and KIR receptor alterations in AML can lead to further insight in our ability to understand the mechanisms of immune evasion, predict tumor progression and devise new and better therapeutic options. Key words: NK, KIR, NKG2A, flow cytometry, genotyping

12. EPSTEIN-BARR VIRUS-RELATED POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE (EBV-PTLD) IN THE SETTING OF ALLOGENEIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA

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Allogeneic stem cell transplant (allo-HSCT) is used for a wide range of malignant hemopathies, in certain types of hematological disorders being the only curative option. Following this procedure the patients can develop multiple complications which can be life-threatening. One example is lymphoproliferative disease related to Epstein-Barr virus (EBV-PTLD), in which more frequently the cell of origin is the B lymphocyte. Even though it's a rare disease, EBV-PTLD is a serious condition and it increases the morbidity and mortality in this setting. Before the year 2000 almost 85% of the cases evolved to exitus but since the introduction of Rituximab the prognosis of the patients improved. Studies have shown that the mortality rate remains high with almost one third of the cases performing poorly.

We bring to your attention the case of a 30 years old female patient which was diagnosed in may 2019 in our clinic, at the Regional Institute of Oncology Iași, with Acute Myeloid Leukemia NPM1 positive. Given the presence of NPM1 mutation the case is considered to have a good prognostic based on WHO classification. In this conditions the patient underwent standard chemo induction "3+7" with Cytarabine and Idarubicin followed by consolidation treatment with Cytarabine. The evaluation post chemotherapy showed that the patient has obtained complete response and the minimal residual disease (MRD) was negative (assessed by flow-cytometry and molecular biology). She remained in complete response for 1 year. In October 2020 the scheduled check-up reveals that the disease has relapsed. It was mandatory to administer a new line of chemotherapy which was a success. The patient achieved the second complete response with negative MRD. In this context she underwent conditioning chemotherapy Flu160/Mel140 followed by allo-HSCT from MUD 10/10. For GVHD prophylaxis PCT Cy/MMF/Tacro was used. We must note that there was a mismatch regarding the viral serology between the donor (EBV, CMV negative) and the patient (EBV, CMV positive). In the 90th day after the allo-HSCT procedure, the patient shows signs of high temperature with lymph node enlargement in the cervical, submandibular and retro-auricular area as well as right tonsil hypertrophy. Based on this we performed radiographic

assessments (CT scan), molecular biology tests (PCR for EBV), flow-cytometry from peripheral blood and a biopsy from a lymph node. The results point to a lymphoproliferative disease associated with the Epstein-Barr virus. Treatment with Rituximab is started right away and the results are favourable as the adenopathies disappear altogether with the associated symptoms. Regarding the underlying haematological disease it remains in complete remission (MRD negative) at 18 months from the allo-HSCT.

Discussion:

Patients who undergo allo-HSCT can develop numerous complications, some involving viral reactivation, which can increase the morbidity and mortality. In this case, a young female patient with Acute Myeloid Leukemia received a stem cell graft from an unrelated donor (10/10). In the literature there are studies which show that the EBV-PTLD occurs more often in cases where there is a viral serology mismatch. Surprisingly the administration of Cyclophosphamide as GVHD prophylaxis is a protective factor regarding the reactivation of EBV. We must mention the fact that in order to establish the diagnosis of certainty it is needed to perform a FISH exam to reveal the EBV-encoded RNA. We consider that the fact that we managed to establish the diagnosis in a timely manner after the first symptom (6 days), with the help of the laboratory findings, and we have started the Rituximab early on, the chances of a good outcome improved drastically. The patient had a good response and after 18 months from allo-HSCT she is in complete remission.

Keywords: Allogeneic Stem-Cell Tranplant, Acute Myeloid Leukemia, Epstein-Barr Virus, Epstein-Barr virus-related post-transplant lymphoproliferative disease, Rituximab

13. MYELODYSPLASTIC SYNDROMES: COMPARISON OF PROGNOSTIC SCORING SYSTEMS IN THE IDENTIFICATION OF HIGH-RISK PATIENTS

Dr. Mihai Lapadat

INTRODUCTION: Myelodysplastic syndromes are a heterogeneous group of clonal disorders of hematopoietic stem cells characterized by progressive cytopenia and risk of transformation into acute myeloid leukemia. As a result, a series of prognostic scores have been developed that classify patients with myelodysplastic syndrome into two main risk categories: low risk and high risk. High-risk patients benefit from targeted therapies, while low-risk patients benefit only from symptomatic and supportive treatment. OBJECTIVE: A comparison of the efficiency of the three prognostic scores for myelodysplastic syndrome: IPSS, IPSS-R, and WPSS in identifying high-risk patients who may benefit from targeted treatments (hypomethylating agents, standard cytostatic treatment). METHODS: Fifty-three patients who were diagnosed with myelodysplastic syndrome in the Hematology department of the Colțea Clinical Hospital. The criteria of inclusion were represented by age over 18 years, definitive diagnosis of myelodysplastic syndrome based on the histopathological and immunohistochemical examination of the bone marrow biopsy, and performing cytogenetic analysis at diagnosis. Epidemiological, laboratory data and data related to the duration of evolution, the time of transformation to acute myeloid leukemia, and death were collected. Three prognostic scores were calculated for the patients: IPSS, IPSS-R, and WPSS. The three

scores were directly compared. The median survival of the groups of patients and the leukemic transformation rate based on the prognostic scores were calculated. Statistical analysis was used to assess the prognostic value of the scores and Kaplan-Meier curves were constructed for overall survival and leukemia-free survival. RESULTS: Following patient classification, two groups of patients resulted: low-risk (36 patients according to IPSS, 22 patients according to IPSS-R, and 24 patients according to WPSS) and high-risk respectively (17 patients according to IPSS, 31 patients according to IPSS-R and 29 patients according to WPSS). IPSS low-risk patients were reclassified as low- or intermediate-risk according to IPSS and WPSS, while intermediate-2- and high-risk patients were reclassified as high- and very high-risk patients according to IPSS and WPSS. A particular category was represented by patients with IPSS-intermediate-1 risk (24 patients), who were inconsistently reclassified as IPSS-R-low (1 patient), intermediate (9 patients), high (10 patients), and very high-risk (4 patients), respectively as WPSS-low (3 patients), intermediate (9 patients) and high-risk (12 patients). Moreover, among the 14 patients reclassified as high- or very high-risk patients using the IPSS-R, respectively the 12 patients reclassified as high-risk patients using the WPSS score, 8 patients underwent leukemic transformation. The median overall survival within the cohort was 15 months. The IPSS-R and WPSS were more effective in classifying the low- and high-risk groups reported to the median survival of the two groups. The overall leukemic transformation rate in the group was 37.7% (20/53 patients), with a median leukemia-free survival of 4.5 months. A strong relationship was identified between IPSS-R classification and the risk of leukemic progression. CONCLUSION: Both the WPSS and particularly the IPSS-R scoring proved to be superior to the IPSS scoring regarding the identification of high-risk patients. As the therapeutic approach is based on risk assessment at diagnosis, the superior efficiency of the IPSS-R and WPSS scoring leads to a more efficient classification of patients, which further on has a positive impact on the treatment options for the patients and ultimately on patient survival.

FRIDAY - OCTOBER 7th, 2022

Oral presentations session LMNH I / CLL

1. IBRUTINIB, SEVEN YEARS OF REAL LIFE EXPERIENCE IN TREATING CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): AN ASSESSMENT OF A COHORT OF PATIENTS TREATED IN IRO IASI

Catalin Danaila1,2, Angela Dascalescu1,2, Cosmin Minciuna2, Gabriela Dorohoi2, Elena Albu1,2, Alexandru Gluvacov2, Alina Dascalu2 , Ion Antohe2, Amalia Titianu2 , Elena Dolachi-Pelin, et al 1. Universitatea de Medicina si Farmacie GrT Popa Iasi 2. Institutul Regional de Oncologie Iasi

Chronic lymphocytic leukemia (CLL) is the most common leukemia in Western countries and is increasing in prevalence with the prolonged survival observed with introduction of novel combinations and targeted treatments. Complete response (CR) and negativity of minimal residual disease (MRD) in CLL is associated with improved progression-free and overall survival for some therapies, and several prognostic factors can predict treatment outcomes. Ibrutinib, a once-daily Bruton's tyrosine kinase inhibitor, represent a targeted therapy with significant progression-free survival (PFS) and overall survival (OS) benefit in multiple randomized phase 3 studies versus established therapies in patients (pts) with previously untreated and relapsed chronic lymphocytic leukemia/small lymphocytic

lymphoma (CLL/SLL). Extended long-term follow-up data for the patients treated in IRO Iaşi are reported. Ibrutinib use has rapidly become standard of care for relapsed CLL patients, as well as for many frontline high-risk or older patients. But the treatment is associated with adverse events such atrial fibrillation (AF), bleeding, and infection and patients had to discontinue the treatment. Data from real-world use of ibrutinib indicate that these toxicities may limit ibrutinib use. Trying to give an image of real life experience in treating CLL patients with ibrutinib, we conducted a retrospective updating assessment to evaluate efficacity and safety of ibrutinib in a cohort of 100 CLL patients treated off-study in Hematology department of IRO Iasi between December 2015 and September 2022.
Keywords : Chronic Lymphocytic Leukemia, B Cell Receptor, Bruton Tyrozine kinase, Ibrutinib

2. BRENTUXIMAB VEDOTIN IN FIRST LINE TREATMENT FOR NEWLY DIAGNOSED ADVANCED STAGE HODGKIN LYMPHOMA- FUNDENI CLINICAL INSTITUTE EXPERIENCE DURING PANDEMIC WITH CORMONAVIRUS

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Background: ABVD was used widely starting 2007 for treatment of newly diagnosed Hodgkin's Lymphoma patients. It was the less toxic chemotherapy regimen available for Hodgkin's Lymphoma patients, reason why fast become " standard of care".

Although progress was made with the new regimen, the prognosis of advanced disease patients remains unfavourable despite using chemotherapy and radiotherapy .

Brentuximab-vedorin represents a conjugate between drug- monoclonal antibody approved and reimbursed for first line treatment of newly diagnosed advanced stage Hodgkin's Lymphoma patients in association with AVD chemotherapy (doxorubicin, dacarbazine and vinblastine).

Methods:There were evaluated all the newly diagnosed patients admitted in Fundeni Clinical Institute with advanced stage Hodgkin's Lymphoma during the Coronavirus Pandemic, between march 2020 and march 2022. These patients were treated with AVD plus brentuximab-vedotin for 6 cycles. The treatment response was evaluated, but also the toxicities and the adverse reactions. We used primary prophylaxis with granulocytes colony stimulating factors due to the increased risk of developing febrile neutropenia.

Conclusions: The response to the treatment was better compared to standard treatment, like in the reported clinical trials. There were also evaluated the toxicities to the treatment with brentuximab vedotin. The most frequent was neuropathy, but most of the patients were able to finish treatment and it resolved when treatment was finished.

- Overall Survival with Brentuximab Vedotin in Stage III or IV Hodgkin's Lymphoma

Stephen M. Ansell, M.D., Ph.D., John Radford, M.D., Joseph M. Connors, M.D., Monika Długosz-Danecka, M.D., Ph.D., et al., for the ECHELON-1 Study Group[*]
https://www.nejm.org/doi/full/10.1056/NEJMoa2206125

- German Hodgkin Study Group website : https://en.ghsg.org/
- Comparison of first-line chemotherapy including escalated BEACOPP versus chemotherapy including ABVD for people with early unfavourable or advanced stage Hodgkin lymphoma, Nicole Skoetz [1], Andrea Will [1], Ina Monsef [1], Corinne Brillant [1], Andreas Engert [2], Bastian von Tresckow [2] https://pubmed.ncbi.nlm.nih.gov/28541603/

- Safety and efficacy of brentuximab vedotin in patients with Hodgkin lymphoma or systemic anaplastic large cell lymphoma Christos Vaklavas and Andres Forero-Torres

3. INVESTIGATION OF MOLECULAR MECHANISMS INVOLVED IN HEPATITIS B VIRUS ASSOCIATED B-CELL NON-HODGKIN LYMPHOMA (B-NHL)

Mihaela Uta

Non-Hodgkin lymphoma (NHL) is a heterogeneous disease, ranked as the 7th most common cancer worldwide. Despite the etiologic heterogeneity among NHL subtypes, epidemiological studies have shown an increased risk of developing B-cell lymphomas in patients with chronic hepatitis B virus (HBV) infection, including DLBCL and FL subtypes. Survival of DLBCL patients with HBV infection is low compared to uninfected DLBCL patients and DLBCL-HBV younger patients seem to have a more advanced disease with a worse outcome. However, the mechanistic relationship between HBV infection and lymphoid cancer is not known. In this context, the current study aims to investigate the ability of lymphocytes to sustain productive HBV replication and modulation of cellular signaling pathways by HBV in lymphocytes, such as the ER stress and unfolded protein response, activation of inflammation and upregulation of mutagenic enzymes. GRP78, IRE1α, and ATF6 protein expression levels are over-expressed in B cells positive for HBV-specific markers, as well as the expression of spliced XBP1 mRNA; these may indicate that splicing activity of XBP1 mRNA possibly occurs in response to the ER stress induced by the HBV presence in these cells. Moreover, the expression levels of mutagenic enzymes APOBEC3 deaminase family were upregulated in B lymphocytes exposed to HBV. To investigate whether expression of APOBEC3 proteins is correlated with inhibitory effect of viral DNA synthesis and/or oncogenic role, viral markers will be analyzed in correlation with the expression of the enzymes.

4. TREATMENT OPTIONS IN THE RELAPSED/ REFRACTORY SETTING, IN PATIENTS WITH PERIPHERAL T CELL LYMPHOMA WITH T HELPER FOLLICULAR PHENOTYPE

Authors: Alexandru Bardas, Camelia Dobrea, Sorina Badelita, Didona Vasilache, Alina Dimcea, Adina Stemate, Miruna Elena Tirnovan, Stambole Steliana, Daniel Coriu

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The 2016 Who Classification of Tumours of Haematopoietic and Lymphoid Tissues introduces a novel lymphoma category, that of T cell lymphomas arising from a T helper cell. Under the umbrella of T-cell lymphomas with T-follicular helper phenotype (TFH) are the fallowing three entities: angioimmunoblastic T-cell lymphoma (AITL), the most studied/known of the three, follicular T-cell lymphoma, and nodal peripheral T cell lymphoma (PTCL) with a TFH phenotype. [1]

Histopathologically, angioimmunoblastic lymphoma is defined by the presence of interfollicular polymorphous infiltrate, proliferation of high endothelial venules and/or expanded follicular dendritic cell meshwork [2] and the presence of EBV+ large B immunoblasts. These findings are not seen in the other two entities but immunohistochemically they share a similar profile: CD3 positive, CD4 positive and the presence of two, ideally three of the fallowing markers: PD-1, CXCL13, BCL6, CD10 and ICOS. [3]

Also, the three lymphomas share a common mutational landscape with frequent recurrent mutations seen in the TET2, RHOA, DNMT3A and IDH2 genes. [3]

Usually, AITL has a poor prognosis with a median survival of 32% at 5 years [5]. In the case of follicular T-cell lymphoma and nodal peripheral T cell lymphoma (PTCL) with a TFH phenotype, because of the rarity of these lymphomas, the aspects of optimal treatment and prognosis are not well understood at the moment.

The treatment of patients with PTCL in the relapsed/ refractory setting (THF phenotype lymphomas included) generally involves two approaches regarding the choice of treatment. First, the choice between multi agent chemotherapy versus single agent treatment and second, deciding if the patient is eligible or not for stem cell transplant (be it autologous or allogeneic). The protocols used to treat these patients generally involved a combination of different chemotherapy agents and platinum salts (for example DHAP, GDP, GemOx or ICE protocol). The monotherapy approach involves treatment with specific antineoplastic agents like histone deacetylase inhibitors (belinostat, romidepsin), brentuximab vedotin, pralatrexate (folate analog antimetabolite) or lenalidomide (immunomodulatory drug).

Recent trails have shown a clear beneficial activity in combining specific antineoplastic agents in the patients. For example, the combination of romidepsin and lenalidomide has shown to be especially active in patients with AITL [6]. Also encouraging results have been seen in the case of combining romidepsin with lenalidomide and carfilzomib [7]. This paper shows the results and the treatment used in some of our patients in the Fundeni Clinical Institute, Hematology and Bone Marrow Transplant Center.

5. CLASSICAL HODGKIN LYMPHOMA – PAPPILAR THYROID CARCINOMA, SIMULTANEOUS DIAGNOSIS IN A NEWLY DIAGNOSED PATIENT

Authors: Ionela Rotaru, Ana Maria Patrascu, Janina Goanta, Carmen Ionelia Popa, Ramona Ingrid Corbeanu, Rodica Vaduva, Bianca Popa

Hematology Clinic of Craiova

Background

Hodgkin lymphoma represent nearly 10% of lymphoma and is the lymphoproliferation with the highest rate of curability. Thyroid pappilar carcinoma is the most frequent thyroid

malignancy, representing almost 90% of thyroid cancers. The molecular mechanism wich binds these two malignancies is still unknown. Risk factors also differ and there are only a few cases of simultaneous diagnosis published.

Case report

We present the following case: a 33 year old male patient complaining about B symptoms and severe dyspnoea. Clinical exam revealed systemic lymphadenopathy. The laterocervical lymph node biopsy with histopathological and immunohistochemical exams confirms the classical Hodgkin lymphoma, nodular sclerosis type. The PET CT exam, performed in order to establish the disease extention, shows a positive thyroid tumor mass (SUV 32,34), 1,8/1,3 cm in diameter. The patient received 6 ABVD cycles and complete remission was induced. The final PET CT evaluation shows the persistence of the positive thyroid tumor mass (SUV 28,95). Total thyroidectomy was performed and the histopathological and immunohistochemical exams confirm the thyroid pappilar carcinoma. The patient received radioiodine therapy and hormone replacement therapy with favorable outcome.

Conclusion

Although the high risk for thyroid carcinoma after radiotherapy in Hodgkin lymphoma patients is well known, the simultaneous diagnosis in still an extremely rare situation. The thyroid carcinoma was diagnosed accidentally, when the imaging investigation was performed in order to establish the disease extension in a new case of classical Hodgkin lymphoma.

6. AGGRESSIVE EXTRANODAL NON-HODGKIN'S LYMHOMAS: EPIDEMIOLOGICAL CHARACTERISTICS AND CAUSES OF LATE DIAGNOSIS

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Introduction: Non-Hodgkin lymphomas are a heterogeneous group of malignant tumors of B-, T- and, more rarely, of NK-cell origin that can primarily affect any organ and tissue that contains lymphoid cells. There is a clear increase in the incidence of NHL by approximately 80% more than at the beginning of the 70s. Annually, around 287k new cases of NHL are diagnosed in the world. Aggressive lymphomas are a heterogeneous group of malignant tumors that reflect clinical, biological and pathological diversity. They refer to those subtypes that grow quickly (proliferation index KI-67 > 40%) and would often be lethal in a few months without appropriate therapy. The tumor originally from the extranodal tissue is called primary extranodal lymphoma (ENL), its incidence being constantly increasing. The primary extranodal localizations of NHL represent 30-48%, the Waldeyer lymphatic ring being affected more frequently (19-21%), followed by the gastrointestinal tract (17-19%) and the spleen (4-6%). In other organs and tissues (soft tissues, skin, bones, pleura, lung tissue, central nervous system, orbit, mammary gland, ovary, body of the uterus, prostate, etc.) NHL rarely develops (from 0.8 to 3-4%). Researchers observed that patients with primary extranodal NHL tend to present at a lower stage than those with primary lymph node disease, the same phenomenon was also noted in the Republic of Moldova, but the number of patients presenting in stages III-IV continues to remain increased. So, the predominantly late diagnosis of patients with aggressive, extranodal non-Hodgkin's Lymphoma leads to the increase of morbidity indices for the able-bodied population as well as to the increase of the

level of disability that constitutes a current problem of Clinical Hematology. Objectives: Study of the incidence of aggressive, extranodal non-Hodgkin lymphomas and the causes of their late detection. Materials and methods: The following methods were used for the research: epidemiological method, descriptive statistics method, comparative method, clinical-analytical method. The type of non-Hodgkin lymphoma was identified according to the criteria of the International Classification of Tumors of Hematopoietic and Lymphoid Tissue revised by the WHO in 2016. Histological, immunohistochemical, flow cytometry examinations were used to confirm the diagnosis. Results: Making a comparative analysis between the years 2020 and 2021, within the Hematology Department of the Oncological Institute, it is confirmed for the year 2020 – 469 primary patients diagnosed with hemoblastosis, of which 145 (30.9%) new cases confirmed by NHL. For 2021, there is a clear increase in the number of patients primarily diagnosed with hemoblastosis - 584, of which 180(30,82%) were new cases of NHL. In 2020 there were 62 cases of extranodal NHL (42%), and in 2021 the number of cases is slightly increasing - 81 cases (45%). According to research, it was observed that the most frequently affected locations of NHL are: Stomach - 32.3%, Nasopharynx - 13.2%, Palatine tonsils - 10.1%, Soft tissues - 7.7% and Skin - 7.7 %. In the Republic of Moldova, the lymphoblastic variant predominates - 55.5%, followed by DLBCL – 33,3%, then T-cell – 7,07%. Although the worldwide trend that patients with primary extranodal NHL tend to present at a lower stage than those with primary nodal disease is also maintained in the Republic of Moldova, the number of those presenting at advanced stages continues to remain increased. So, 35% of the patients are registered in stage I, followed by those in stage IV which constitute - 31%, in stage II - 29.3% and respectively stage III - 4.7%. The average age at the time of diagnosis of NHL was 60 years, with a slight predominance of the female sex (male-female ratio 1:1.27). The period from the onset of the disease to the first visit to the doctor was 6.3 months, and the period until the confirmation of the diagnosis was 5.9 months. The most common causes of late diagnosis are late referral of the patient to the doctor, as well as confusion of the diagnosis by other doctors, often treating the disease as an inflammatory/reactive process and redirecting the patient to the hematologist after several attempts of treatment with anti-inflammatory/ antibiotic therapy, which ultimately leads to an increase in the number of patients detected in stages III-IV. Conclusions: Non-Hodgkin's lymphomas are an important part of the structure of hemoblastoses, their incidence having an increasing trend in recent years. Although the diagnosis of NHL does not involve great impediments, patients are often diagnosed in the late stages of the disease, either because of their delayed referral to the doctor, or because of the incorrect establishment of the diagnosis by the primary doctors, which is a current problem of medicine, that requires efforts and greater financial means to solve it.

7. "INVOLVEMENT OF IMMUNOHISTOCHEMICAL AND HIGH-PERFORMANCE IMAGING INVESTIGATIONS IN THE THERAPEUTIC DECISION THAT LEADS TO THE CURING OF MALIGNANT HODGKIN'S LYMPHOMA" PhD:

Lebedenco Mihaela

Abstract: • Objectives: Follow-up of clinical evolution and response to treatment in Hodgkin's Lymphomas. • Material and methods: Comparative study (retrospective and prospective) of two groups of patients with Hodgkin's Lymphoma - Group 1 - with favorable evolution; Group 2 – refractory/relapsed/partial remission cases. • Results: Creation of a panel regarding correct staging, identification of histological subtype and response to

treatment. • Conclusions: Evaluation of the response to treatment and the degree of metabolic activity of the lesions described on CT by means of the PET-CT examination in the two examined groups.

SATURDAY - OCTOBER 8th, 2022

Oral Presentations Session BONE MARROW TRANSPLANT

1. THE ACTIVITY OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TRANSPLANTATION CENTER OF COLȚEA CLINICAL HOSPITAL BUCHAREST

Andrei Coliță, Cecilia Ghimici, Raluca Manolache, Doina Barbu, Florentina Grădinaru, Prof. Dr. Anca Roxana Lupu Hematology Department,

Colțea Hospital, Bucharest The Bone Marrow Transplantation Compartment of the Colțea Clinical Hospital was accredited in April 2013 and has been operating within the National Program for Transplantation of Organs, Tissues and Cells of Human Origin since 2014. The first transplant was performed in December 2013 with own funds, the rest after obtaining funding from the National Program. To date, peripheral hematopoietic stem cells have been collected from 157 patients and 7 healthy family donors. Peripheral stem cells were collected by apheresis, initially at the Fundeni Clinical Institute (the first 2 cases) and later in our department. The mobilization regimes were different depending on the diagnosis as follows: - Multiple myeloma/plasma cell leukemia - cyclophosphamide combined with filgrastim or filgrastim monotherapy - Hodgkin's or non-Hodgkin's lymphomas - regimens such as DHAP, IGEV or Etoposide associated with filgrastim or pegfilgrastim or monotherapy with filgrastim. In a case of NHL, with an allergy to filgrastim, the mobilization was performed with the IGEV regimen without the addition of growth factor, but with the addition of Plerixafor the evening before apheresis. - Healthy family donors - filgrastim In cases treated with multiple lines of chemotherapy and/or radiotherapy with unsatisfactory mobilization at the first attempt, Plerixafor was associated. The number of CD34 cells harvested/apheresis ranged from 2.014 to 19.3 x 106/kg. The cryopreservation of the grafts was performed in the Stem Cell Bank of the Fundeni Clinical Institute. Transplant procedures consisted of 151 autotransplants and 6 allogeneic transplants from matched related donors. Autotransplantation procedures were performed in patients with: - Multiple myeloma – 75 cases, leukemia with plasma cells – 1 case. Among the patients with multiple myeloma, 7 performed 2 autotransplant procedures (6 cases with a 2nd transplant following relapse, 1 case with a high-risk cytogenetic profile – tandem procedure) - Hodgkin lymphoma – 40 cases - Non-Hodgkin's lymphoma – 35 cases (13 – large B cell, 14 - mantle cell, 2 – large B cell with cerebral involvement, 1- plasmablastic, 5 – T cell) - Epiphyseal germinal tumor - 1 case The conditioning regimes were represented by: - Multiple myeloma – MLF200/MLF140 - Lymphoma- BEAM, LEAM, CLV, BeEAM, TEAM. Allotransplantation procedures were performed in patients with: - Acute lymphoblastic leukemia – 1 allotransplant from a related donor - Acute myeloid leukemia – 4 allotransplants from a related donor, 1 haplotransplant Conditioning regimes were represented by Clo/Bu, Flu/Mel, TT/Flu/Mel. The infused grafts had cellularity between 2.57 and 19.3x 106 CD34+ cells/kg, and the median duration of grafting was 11 days for neutrophils and 14.5 days for platelets in cases with autotransplantation and 19 and 28 days respectively in cases with allograft. The follow-up

duration of the cases varies between 0.5 and 93 months. Transplant-related mortality was 2%. Of the 148 transplanted patients, 114 are alive.

2. HEMATOPOIETIC STEM CELL TRANSPLANTATION ACTIVITY WITHIN THE EMERGENCY UNIVERSITY HOSPITAL BUCHAREST

Horia Bumbea[1,2], Georgiana Ene[1], Dan Sebastian Soare[1], Ana-Maria Costache[1,2], Delia Soare[1,2], Daniela Diaconescu[1,2], Daniel Iordache[2]

[1] Bone Marrow Transplant Unit, University Emergency Hospital Bucharest

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Autologous hematopoietic stem cell transplantation (autoHSCT) represents an important step in consolidating and maintaining the response of hematologic malignancies after initial treatment. Among hematological diseases, multiple myeloma is the most common disease that benefits from stem cell transplantation. Within the Department of Bone Marrow Transplantation - UEHB, in the last year there has been an increase in the number of autologous transplants performed, as well as hematopoietic stem cell apheresis both for local patients and for patients referred to our center.

In 2021, a total of 21 autoHSCT were performed, and in the first 3 quarters of 2022, 23 autoHSCT were performed. Thus, compared to last year, this year the department's activity increased by 2 autoHSCT in the first quarter, 2 autoHSCT in the second quarter, and by 3 autoHSCT in the third quarter. Among patients who received autoHSCT in 2022, a total of 15 patients with multiple myeloma and 6 patients with non-Hodgkin's lymphomas. Regarding hematopoietic stem cell harvesting, 45 peripheral mononuclear cell apheresis were performed throughout 2021, and during the first 3 quarters of 2022 also 45 peripheral mononuclear cell apheresis were performed.

One of the problems in the management of patients undergoing hematopoietic HSCT is viral reactivation. The prevalence of viral reactivations, among patients undergoing autoHSCT, is higher in patients with lymphomas compared to patients diagnosed with multiple myeloma, especially CMV reactivations. Within our department, since the initiation of our activity in 2018, 5 patients with CMV reactivation and 3 patients with HHV6 reactivation have been diagnosed.

Regarding further development of the activities within the UEHB Bone Marrow Transplant Department, we plan to implement local viral screening for viruses: CMV, EBV, HHV6/7, Parvovirus B19 through quantitative RT-PCR and the next step in patient treatment is to start allogeneic HSCT and cellular therapies.

3. HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HEMATOLOGIC MALIGNACIES – SINGLE CENTER EXPERIENCE

Autori : Angela Dascalescu1,2, Ion Antohe1,2, Elena Dolachi-Pelin. Roxana Dumitru, Cătălin Danaila1,2.

1. Universitatea de Medicină Şi Farmacie "Grigore T. Popa", Iaşi, Departament Hematologie
2. Institutul Regional de Oncologie Iaşi, Clinica de Hematologie

Introduction: HSCT is standard of care for consolidation therapy in different hematologic malignacies. The aim of this presentation is to share our five years experience in hematologic malignancies transplantation. Our experience is based on 173 transplant procedures, 138 autotransplant and 35 allotransplant in : multiple myeloma - 76 patients, non Hodgkin lymphoma – 38 patients, Hodgkin lymphoma -28 patients, acute myeloid leukemia – 20 patients, acute lymphoblatic leukemia – 9 patients, myelodisplastic syndrome – 2 patients. We present mangement of early complications in first 30 days after transplant: infections, bleeding, cardiac failure, renal failure, acute respiratory failure, engraftement syndrome, venooclusive disease. We also noted transplant related mortality, late complications, duration of response, posttransplant survival.

4. IMPLEMENTATION OF CAR-T THERAPIES IN FUNDENI CLINICAL INSTITUTE

autori: Alina D.Tanase, Oana Craciun, Laura Stefan, Lavinia Lipan, Andra Stoica, Alexandra Ichim, Codruta Popa, Dana Tomescu, Madalina Berbecel, Adriana Dulamea, Elena Marin , Daniel Coriu, Anca Colita

Cell therapies represent a new area of treatment, which uses the immune system's ability to recognize and destroy tumor cells. CAR-T therapy consists in the manufacture of a chimeric antigen receptor that is represented by a synthetic transmembrane protein, located on the surface of immune cells (T lymphocytes). These are genetically reprogrammed in vitro, in order to easily identify and attach to target tumor cells, independent of MHC. The first products approved by the EMA were in 2018, in Romania, the product Tisagenlecleucel (Kymriah) was approved for adult patients with relapsed/refractory Acute Lymphoblastic Leukemia in children and adults up to 25 years old, for refractory large B-cell Malignant Non-Hodgkin Lymphoma or relapsed, after at least 2 lines of therapy, and, starting with May 2022, the indication of the therapy was extended for the treatment of adult patients with refractory or relapsed follicular lymphoma after two or more lines of systemic therapy. In the adult Bone Marrow Transplantation Unit of the Fundeni Clinical Institute, starting from January 2022, 4 CAR-T procedures were performed on patients diagnosed with refractory or relapsed large B cell Non-Hodgkin Lymphoma. Disease status before administration of CAR-T cells: two were in disease progression, one patient met the criteria of stable disease and one patient had a complete metabolic response to the PET-CT evaluation. During the administration of the CAR-T product, two of the patients presented CRS grade I, one of which required the administration of two doses of Tocilizumab, one patient presented CRS grade II, with the administration of four doses of Tocilizumab, and one patient did not present specific complications of CAR-T therapy. One patient presented thrombosis at the level of

the catheter installed on the left internal jugular vein, and another at the level of the left axillary vein. One patient died of disease progression less than 3 months after CAR-T therapy, one patient is in disease progression, another has a complete metabolic response and one patient is to be investigated. T-lymphocyte harvests were performed for 2 other candidates, in order to perform the CAR-T procedure, a female patient and another male patient. Another 2 patients received a favorable opinion for the collection of T lymphocytes until August 2022. Conclusions: CAR-T therapy represented a real revolution in the management of adult patients with refractory/relapsed large B-cell Malignant Non-Hodgkin Lymphoma, after several therapeutic lines, considerably increasing their survival. Although we can signal some positive effects on the evolution of the disease, the experience of the Fundeni Bone Marrow Transplant Clinic is small, the procedure being approved and recently implemented in Romania. We will continue to monitor the clinical-biological status of the patients and formulate conclusions after accumulating a corresponding number of treated cases.

5. MONITORING OF CIRCULATING CAR T CELLS BY FLOW CYTOMETRY FOLLOWING TISAGENLECLEUCEL

Delia Codruta Popa, Anca Gheorghe, Catalin Serban, Raluca Suciu, Valeria Gabriela Tica, Horia Sandu, Alina Tanase, Anca Colita, Daniel Coriu Fundeni Clinical Institute

For decades, cancer treatment foundations included surgery, chemotherapy, and radiation. These continue to be critical mainstays of treatment, but new categories of treatment have recently been approved by the Food and Drug Administration (FDA) like imatinib and trastuzumab targeted therapies. Recently, CAR T-cell therapies have been approved by FDA for the treatment of blood cancers, including lymphomas, some forms of leukemia, and multiple myeloma. This year, we started the CAR T cell therapy at Fundeni Clinical Institute, and so far we have treated seven patients (four adults and three children). All patients received Tisagenlecleucel in the Cell Therapy Unit, adults with about 3.5x108 cells/kg body, and children with about 2.8x106 cells/kg body. A flow cytometry panel was designed using a commercial CD19 CAR Detection Reagent (Miltenyi Biotec, Bergisch Gladbach, Germany). We used BD Multitest™ 6-color TBNK reagent with BD Trucount™ to identify and determine the percentages and absolute counts of T, B, and natural killer (NK) cells, as well as the CD4 and CD8 subpopulations of T cells in peripheral blood. We observed a peak in CAR T-cell percentage between 6-9 days after infusion. The mean proportion of CD4 or CD8 in CAR T cells and CD4 or CD8 in T cells did not significantly differ. We observed an inverted CD4:CD8 ratio, which was 0.21 for CAR T cells and 0.48 for all T cells. The cellular kinetics of CAR T cell subpopulations following tisagenlecleucel treatment identified the effector memory and central memory subsets to be higher and the others, like naïve and T EMRA subsets to be lower. Routine monitoring of CAR T-cell subpopulations could be helpful to predict the occurrence and severity of cytokine release syndrome or neurotoxicity and exclude the differential diagnosis.

Oral Presentations Session – MULTIPLE MYELOMA

1. THE IMPACT OF CHROMOSOME 1Q ABNORMALITIES ON THE EVOLUTION AND RESPONSE TO TREATMENT IN MULTIPLE MYELOMA

Sinziana Barbu 2, Sorina Badelita 2 , Cerasela Jardan 1, 2, Ruxandra Irimia 1, 2, Diana Preda 2, Andreea Jercan 2, Loredana Cirlan 2, Larisa Zidaru 2, Daniel Coriu 1, 2

1- "Carol Davila" University of Medicine and Pharmacy
2- Fundeni Clinical Institute

Multiple myeloma is a relatively rare disease, representing 1-2% of all cancers and approximately 17% of hematological malignancies. Also, myeloma is a very heterogeneous disease, and can have different evolution from one patient to another. The prognosis of patients with multiple myeloma is influenced by multiple factors related both to the patient and the disease. Among the characteristics of the disease, the one that impacts mostly the evolution is the cytogenetic risk.

The evolution of patients with multiple myeloma (both PFS and OS) has seen a significant improvement in recent years, due to access on new therapies. However, there remains a subgroup of patients with suboptimal results .

R-ISS staging does not include the chromosome 1q abnormalities, which have become a very important prognostic marker.

This retrospective study, carried out on a group of patients diagnosed and treated in Fundeni Clinical Institute between August 2020 and August 2022, aims to analyze the evolution and response to treatment in patients with newly diagnosed or refractory/relapsed multiple myeloma and who also have associated chromosome 1q abnormalities.

2. DETECTION OF GENOMIC ALTERATIONS BY MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION IN MULTIPLE MYELOMA

Mihaela Popescu[1], Cristina Mambet[2,3], Viola Popov[1], Felicia Mihai[1], Oana Patrinoiu[1], Lilia Matei[3], Coralia Bleotu[3], Carmen Cristina Diaconu[3], Anca Roxana Lupu [2,4]

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Introduction: Multiple myeloma (MM) is a genetically heterogeneous hematologic malignancy, most of patients carrying chromosomal translocations that involve the immunoglobulin heavy chain locus, hyperdiploidy, copy number variations (CNVs), or recurrent somatic mutations. Cytogenetic abnormalities represent the most important prognostic factor in MM, being currently detected by interphase fluorescence in situ

hybridization (iFISH). However, iFISH is an expensive and laborious method, and it is not able to identify amplifications/deletions smaller than 20–50 kb. Multiplex ligation-dependent probe amplification (MLPA) has emerged as a useful tool for determining CNVs of up to 50 genomic DNA sequences in a single reaction.

Aim: To apply MLPA for detection of CNVs in malignant plasma cells obtained from MM patients.

Material and methods: Purified bone marrow CD138+ cells were obtained by imunomagnetic separation from 40 patients with newly diagnosed or relapsed MM. After DNA extraction, SALSA MLPA Probemix P425-B2 Multiple Myeloma (MRC-Holland) kit was used for CNV detection in 46 chromosomal regions and target genes of prognostic relevance in MM.

Results: All except two patients harbored at least one CNV. Seven patients (17.5%) with multiple genetic lesions presented some anomalies only in a cellular fraction, suggesting the existence of subclones. Chromosome 1q gains (one additional copy of 1q) or amplifications (two or more extra copies of 1q) represented the most frequently detected genetic aberrations (53.6%). Out of 40 patients, 11 (27.5%) presented combined 5q, 9 and 15q amplifications, suggestive for hyperdiploidy. Deletions at 17p13.1 affecting *TP53* tumour suppressor gene were found only in 4 patients (10%). Interestingly, partial *TP53* gene amplifications were observed in 7 patients (17.5%) and their impact on gene expression requires further investigations.

Conclusions: MLPA is able to provide useful information about genomic alterations in MM that could improve prognostic assesment and guide therapy.

3. PLASMABLASTIC MYELOMA AND HEMOPHAGOCYTIC SYNDROME A RARE ASSOCIATION WITH A POOR PROGNOSIS

Dr Ioana Teodorescu, Dr Eliza Tapelea, Dr Cristina Laura Predescu, Dr Alexandru Dontu, Dr Gabriela Borsaru

Plasmablastic myeloma is a rare form of multiple mieloma and is associated with a poor prognosis.The hemophagocitic syndrome is an agressive disorder due to the phagocytosis of celular elements by bone marrow derived macrophages. The associoation of this two disorders goes with theworst outcome.We present here a case of a 50 years old woman who presented with pancitopenia and hepatosplenomegaly and with suspicion of maligne hemopathy. The clinical examination and imagistic CT mostred semnificativ a splenomegaly long axis 16 cm and liver of 20.5 cm cranio-caudal right lobe . The hemogram monstred pancitopenya and left deviation of leucocitary formula.The biochimical showed tumoral lisis syndrome with high level of uric acid and azotate retention, hepatocitolisis, high level of LDH, without monoclonal protein or kappa, lambda chain , HIV negativeThe most important investigation ;the bone marrow aspirate fallowed by flowcitometry identified 40% myelomatoase plasmocites (positiv for MUM1, aberant positiv for CD68/KP1,CD 38+, ,CD 138+, CD 117+, CD 56+, CD 33+, cylgk+ , CD19-, CD20-, cylg , MPO-) and bone marrow biopsy revealed plasmablastic myeloma with hemophagocitic syndrome.The pacient have received high dose corticotherapy with proteosome inhibitor and ciclophosphamide.Despide the treatment applied, the patient had a rapid progresion of multiple organ dysfunction syndrome, and eventualy exitus.

Oral Presentations Session SMPC

1. THROMBOSIS IN IMMUNE THROMBOCYTOPENIA : AN INTRIGUING ASSOCIATION

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One of the most frequent complication in immune thrombocytopenic purpura is the bleeding manifestation. Despite the small thromocyte count, these patients have a higher risk of arterial/venous thrombotic events during their lifetime, compared to general population. Some of the risk factors are due to the ITP itself and the treatment given, while other risk factors are dependent on the patient's health and habits.

I am going to present the case of a 75 years old man who during a preoperative check-up for relapsed meningioma was diagnosed with ITP. Despite the low thrombocyte count at diagnosis (Tr= 20 000mmc) the patient did not complain of any bleeding history. By the time corticotherapy was elected without favorable evolution of the case. For this reason second line treatment with thrombopoietin receptor agonist was given, with better results, the patient being able to have the surgery (Tr= 175 000mmc). The initial response was transitory, one week after the surgery the patient's thromocyte count was 21 000mmc, overlapped with a right superior lobar artery thrombosis. Making the right therapeutic decision for these patients is difficult, also because you have to keep a balance between the hemoragic risk and the thrombotic one.

2. COMPARATIVE CHARACTERIZATION OF THE EFFICACY OF INTERFERON ALFA TREATMENT IN MYELOFIBROSIS PRIMARY AND ESSENTIAL THROMBOCYTHEMIA.

Nina Sghibneva-Bobeico[1,2], Vasile Musteaţa[1,2], Maria Robu[1,2], Dumitriţa Urescu[2], Igor Vinogradov[1,2], Victor Munteanu[1], Cristina Dudnic[1], Lidia Jalbă [1], Ala Dorogan [1].

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Introduction: Primary myelofibrosis (PM) and essential thrombocythemia (ET) are part of Ph-negative myeloproliferative neoplasms. A particular characteristic of these processes is the presence of clinical hematological features and similar pathogenetic aspects. For a long time, there was the opinion that PM and TE are neoplasms of older adults. But several publications recently appeared about confirmed diagnoses in young people and children. This is because medical services have become more available to the population, and there is a more attentive attitude toward health. Despite numerous studies in the field of myeloproliferative tumors, the etiology is unclear. The PM incidence is 1.0, and in TE 1-1.4 at 100000 population, average age of 60 years.

Objectives: Retrospective analysis of cases in the last 3 years treated with interferon alfa in the Oncological Institute of the Republic of Moldova to evaluate the hematological response and a

cardiovascular complications.

Material and Methods: Currently, in the Republic of Moldova, 450 patients with MP and 176 with TE are taken into account by the hematologists of the IMSP Oncological Institute. The type of myeloproliferative neoplasm was distinguished according to the 2018 revision of the WHO classification of hematopoietic and lymphoid tissue tumors. PM and ET were diagnosed histologically by bone marrow examination and molecular-genetic examination of peripheral blood. 16 cases of MP and 17 cases of TE were analyzed, which received the treatment with interferon alfa and antiplatelet agents in the last 3 years.

Results: The average age of patients with PD was 38, and those with TE – were 39 years. Treatment was suspended in 33.3% of cases with MP. 16.7% of patients discontinued therapy for personal reasons, and the other 16.7% – due to drug intolerance. From the group of patients with

TE, therapy was suspended in only 17.64% cases. In 16.7% of patients with MP, recently included in treatment with alpha interferon, a tendency towards normalization of the blood count was observed. Interferon therapy combined with hydroxyurea occurs in 8.3%. In 8.3% of cases, stabilization of the tumor process took place for 2 years. In the group of patients with TE, the normalization of the blood count was found in 64,7% of cases. It is necessary to mention that one patient discontinued treatment with interferon after the normalization of the blood count. In 17.64% of cases of interferon treatment, the number of platelet remains within the limits of 500-700x 10^9/l, with a tendency to increase when treatment is stopped. For 3 years, no thrombotic or hemorrhagic complications were recorded.

Conclusions: Analysis of the data obtained reveals that interferon alpha may be used in the treatment of myeloproliferative neoplasms, especially in young patients or in cases of intolerance to other antineoplastic agents.

3. CHRONIC MYELOID LEUKEMIA: TREATMENT DISCONTINUATION OUTCOMES IN PATIENTS WITH COMPLETE MOLECULAR RESPONSES

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Introduction: Chronic myeloid leukemia (CML) is a relatively frequent chronic myeloproliferative neoplasm within the structure of morbidity by hematological malignancies with primary bone marrow involvement, being characterized in the latest phases by a relapsing course, sizable disease burden and unfavorable prognosis. Tyrosine kinase inhibitors (TKIs) improved considerably the results of management of CML patients and approached the patients' life expectancy to that of population. However, TKIs discontinuation studies are associated with controversial outcomes in terms of maintenance of complete hematological and molecular responses. Aim of the study: The assessment of short- and long-term results of treatment discontinuation in CML patients with complete molecular responses. Material and methods: This prospective study enrolled 22 patients with chronic phase of CML, managed at the Oncologic Institute from Moldova between 2017–2022. The

age range was 29–73 years (average age – 45.8 years). Fourteen (63.6%) patients were less than 50 years old. The male/female ratio was 1:1.2. CML cases were diagnosed by cytological, cytogenetic and molecular examinations of the bone marrow and peripheral blood. The type of hematologic malignancy was identified according to the Revised 2018 WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues. The quantitative real-time PCR was used in order to detemine the expression of the BCR-ABL chimeric gene p210 and p190 transcripts while proceeding CML diagnosis. Five transcription products (b2a2, b3a2, b2a3, b3a3 si e1a2) were analyzed by the application of the quantitative PCR test. The real-time quantitative PCR revealed the wide range of BCR-ABL p210 transcript: 21.84–100% IS. In 7 (31.8%) cases the initial rate of BCR-ABL p210-positive blood cells was less than 50%. Only 2 (9.1%) patients also proved to be positive for BCR-ABL p190 transcript. The study was related to the ambulatory and hospitalized care. TKIs were used as a front-line therapy in the newly diagnosed CML patients and in cases of relapses. Results: Complete molecular responses were achieved in 15 (68.2%) cases under imatinib therapy and in 7 (31.8%) cases under the therapy with 2nd generation TKIs. The therapy with TKIs was stopped due to the different reasons in all patients after the achievement of complete molecular response. Two (9.1%) patients discontinued the TKIs treatment due to the pregnancy. The pregnancy in these 2 females with complete molecular responses resulted in the healthy newborns. The molecular relapses developed in 6 (27.3%) patients, including one postpartum female. There were no subsequent hematological relapses. The initial BCR-ABL p210 transcript expression exceeded 50% in all patients with molecular relapses. One (4.5%) of them was positive for BCR-ABL p190 transcript at diagnosis. The duration of complete molecular response ranged between 2.5-26 months in relapsed patients. The range of BCR-ABL p210 transcript in the relapsed cases was 0.002-0.56%. These patients obtained the 2nd complete molecular responses after restarting the treatment with TKIs at a higher dosage or generation. The relapsed patients did not develop the 2nd molecular relapse. All patients are alive. The ECOG-WHO score is 0-1 in all cases. The patients continue their daily activities. Conclusions: TKIs discontinuation may be recommended as a management option in CML patients with chronic phase, complete molecular responses and low initial expression rates of BCR-ABL p210 and p190 transcripts. CML patients with minor molecular relapses may achieve the 2nd complete molecular responses after restarting TKIs therapy with the increased dosage or newer generation.

Key words: chronic myeloid leukemia, tyrosine kinase inhibitors, complete molecular responses, treatment discontinuation, molecular relapses.

4. COLD AGGLUTININ DISEASE – DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN THE CLINICAL SETTING

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ABSTRACT

Cold agglutinin disease (CAD) is a rare form of autoimmune hemolytic anemia (AIHA), in which IgM specific antibodies cause the agglutination of red blood cells (RBCs) at temperatures < 37°C and activate the classical pathway of complement leading to

extravascular hemolysis, C3b-coated RBCs are phagocytosed by the macrophages of the reticuloendothelial system (predominantly in the liver). Up to date there are two clinical-pathologic entities recognized as distinct with different therapeutic implications: cold agglutinin disease and cold agglutinin syndrome (CAS). Primary CAD is recognised as clonal B-cell lymphoproliferative disorder of the bone marrow, clinical and imagistic evidence of associated malignancy. CAS arises in the setting of an underlying disorder such as infection, autoimmune disease or malignancy (non-Hodgkin lymphoma or other malignant process). The diagnosis of CAD is often delayed due to the unpredictable clinical course. In spite of the current therapeutic options which are directed at the pathogenic B cells or the complement system, the low response rates and frequent relapses lead to challenges regarding the management of this disease.

5. LATE-ONSET HEMATOLOGICAL COMPLICATIONS OF COVID-19

L. Petrov1, Laura Urian2

1. Finas Medical medical center, Cardiomed Medical Center Cluj

2. “Ion Chiricuta” Oncological Institute Cluj Coronavirus disease 19 (COVID-19) pandemic had spread rapidly with devastating consequences world wide. The mortality rate ranges from 3% to 5%, while approximately 80% of patients hospitalized with COVID-19 and 60% of those admitted to intensive care units survive. Older people and those with comorbidities are at increased risk of death and complications from COVID-19. COVID-19 survivors might experience multiple organ impairment with a significant impact on their quality of life post recovery. Although it is well known that the disease primarily manifests as a respiratory tract infection, several studies have demonstrated that it should be considered multisystemic disease including cardiovascular impairment, respiratory illness, gastrointestinal disorders, neurological symptoms, as well as hematopoietic and immune system dysregulation. The multisystemic aspects of acute COVID-19 have been throughly evaluated, however, the long-therm complications are still an underexplored area. Long (haul)-COVID is used to describe the ongoing effects of COVID-19, wich possibly encompastes different entities: postintensive care syndrome, postviral fatigue syndrome and long-therm COVID-19 syndrome. COVID-19 induced coagulopathy is an immunothrombotic state that appears to be more prothrombotic than hemoragic. SARS-CoV2 invades endothelial cells directly and induces a suitable environment for the migration and aggregation of immune cells via negative regulation of the ACE-2 receptor activity and angiotensin II accumulation. Proinflammatory and procoagulant cytokine release and endothelial injury lead to the subsequent activation of coagulation cascade, inpaired fibrinolysis and thrombine generation, and modification of hemostatic environment. The hyperinflammation response induces endothelitis but is not clear how long endotelitis can persist in the convalescent phase of disease. Epidemiological data examining the risk of thrombosis post-hospital discharge are limited, but the overall risk is similar to that of patients hospitalized with acute medical illnesses. Standard tools for VTE risk assessment should be used to identity patients at high risk for thrombosis in the post-acute period (active cancer, immobility, age, high body mass index, recent thrauma, thrombophilia, surgery, familial history of VTE, elevated D-dimer levels). Late-onset thrombocytopenia and hemolytic anemia related to immune system dysregulation are a rare manifestation post COVID-19. Other hematologic autoimmune disorders include Evans syndrome, autoimmune neutropenia and thrombotic thrombocytopenic purpura. Antiphospholipide antibodies, where detected in 52% of patients. SARS-CoV2 can cause potential breakdown of hematopoietic stem cell differentiation. The SARS-CoV2-RNA enters ex vivo in primary hematopoietic

stem cells inducing the formation of defective megakaryocytic and erythroid cells. The renin-angiotensin system imbalance induced by SARS-CoV2 could potentially promote in vivo leukemo-genesis through several mecanisms. The role of hematologists is essential in terms of multidisciplinary approach of long COVID-19.

THURSDAY - OCTOBER 6th, 2022

POSTERS SESSION

1. THE IMPORTANCE OF FLT3-ITD AND NPM1 MUTATIONS IN THE MOLECULAR DIAGNOSIS OF ACUTE LEUKEMIA

Silvia Aposteanu[1], Mihaela Dragomir[1], Onda-Tabita Calugaru[2], Cerasela Jardan[1,2], Ana-Maria Mihalache[1], Georgiana Stoica[1], Daniel Coriu[1,2]

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2- "Carol Davila" University of Medicine and Pharmacy, Bucharest

Introduction: Acute Leukemias with tandem internal duplication of the FLT3 gene (FLT3-ITD), associate a reserved prognosis and an unfavorable evolution, despite targeted therapy. The coexistence of the NPM1 mutation improves the prognosis of the disease. The purpose of this study is to demonstrate the importance of molecular techniques with high sensitivity and specificity in the detection of FLT3-ITD and NPM1 mutations.

Material and Methods: The study included patients diagnosed with Acute Leukemia between 2021-2022, that were tested for detection of FLT3-ITD and NPM1 mutations using PCR (detection limit 10^{-2}). Sanger sequencing method was performed for 5 patients to confirm FLT3-ITD mutation (fragment analysis, with a detection limit of 10^{-5}).

Results: FLT3-ITD mutation was detected in 55 patients at the onset of Acute Leukemia. In their case, the NPM1 gene mutation was detected in 1 sample. Although the PCR technique is an important tool in detection of these mutations, the gold standard is represented by Sanger sequencing, which is also used in the detection of minimal residual disease (allelic ratio).

Conclusions and discussions: FLT3-ITD mutation is a dynamic mutation, with high transcriptional variability. For its detection, high-sensitivity techniques are needed (Sanger method). Because FLT3-ITD and NPM1 mutations are modified at a small-scale, cytogenetic and immunophenotyping techniques are limited.

2. THE IMPORTANCE OF HSA-MIR-4328 GENE MUTATIONS IN ACUTE PROMYELOCYTIC LEUKEMIA

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2 – Fundeni Clinical Institute – Hematology Department

Introduction: miRNAs are involved in pathogenesis of neoplastic syndromes by silencing target genes. As previously shown, hsa-mir-4328 is downregulated in Acute Promyelocytic Leukemia (APL).

Purpose and objectives: The study aims to identify the somatic mutations of the hsa-mir-4328 gene that caused its downregulation in APL and their localization in key regions of the mature miRNA structure.

Material and methods: The study included 40 subjects: the patient group (20 people at the onset of LAP, as well as in remission and relapse) and the control group (20 apparently healthy patients). High Resolution Melting (HRM) was used for genotyping.

Results: As hsa-mir-4328 has not been studied before, a structure design of the coding region was performed to better understand the impact of somatic mutations on the mature miRNA. Following HRM, 5 mutant genotypes were identified, different from the wild-type (WT) genes.

Conclusions and discussion: Due to the major deviation of the mutant genotypic curves compared to WT, the existence of major mutations (probably insertions/deletions) can be assumed. If these mutations are located in the seed region of the gene, attachment to exon 3 of the RARA gene is no longer possible, and therefore overexpression of the target gene occurs. Also, frameshift mutations, or substitutions that change the nucleotide sequence of the seed region, can produce a completely different mature miRNA that may have tropism for another gene. To test these hypotheses, sequencing of the entire gene is required.

3. CHROMOSOMAL INSTABILITY IN ACUTE MYELOID LEUKEMIA

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INTRODUCTION

Chromosomal instability (CIN) represents a complex category of cytogenetic abnormalities, found in malignant diseases with poor prognosis, as a result of therapeutic resistance and rapid progression of the disease.

Recent studies have shown that CIN is involved in the etiology, progression and relapse of AML, regardless the type of the disease (de novo, secondary or therapy-related AML).

MECHANISMS AND CYTOGENETIC ASPECTS OF CIN

THE EXPERIENCE OF THE CYTOGENETICS LABORATORY, FUNDENI CLINICAL INSTITUTE

Chromosomal instability occurs as a result of the segregation errors, during mitosis, and causes structural and numerical chromosomal abnormalities.

In patients diagnosed with hematological malignancies, especially in AML, various chromosomal rearrangements have been described, which occur in the process of chromoanagenesis, that is characterized by fragmentation of the chromosomes, abnormal reunions of the fragments, loss or amplification of some chromosomal fragments. Another mechanism of chromosomal instability is the accelerated process of telomere shortening, which is likened to double-stranded breaks in the DNA molecule and constitutes a trigger for the repair process, leading to fusion of the chromosome ends and to formation of dicentric chromosomes, triads or tetrads.

The effects of these mechanisms of chromosomal instability have been noticed during the cytogenetic examination, in patients diagnosed with AML and investigated in the Hematology and Bone Marrow Transplant Center of Fundeni Clinical Institute. We will present two cases of patients diagnosed with acute myeloid leukemia, with particularities in regard with the etiology and cytogenetic findings, with significant impact on the evolution and prognosis of the disease.

CONCLUSIONS

Although the genetic mechanisms and etiopathogenetic implications of this heterogeneous category of cytogenetic abnormalities are not yet known, chromosomal instability is an open chapter that deserves the attention of the specialists, because of its incontestable role in cancer biology and, in particular, in the evolution and prognosis of hematological malignances.

4. PROGNOSTIC VALUE OF GENETIC ABNORMALITIES ASSED WITH MLPA TECHNIQUE ON ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS

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Key word: Acute lymphoblastic leukemia, Multiplex Ligation-dependent Probe Amplification Acute Lymphoblastic Leukemia represents a more rare hematological malingancy on adult population compared to children but with poorer survival rate of approximately 40% at 5 years. There are a lot of prognostic factors regarding ALL: age, clinical presentation, WBC count, chromosomal abnormalities, therapeutic results. MLPA technique is used to assess the number of copies of IKAROS genes family zinc finger 1 (IKZF1), PAX5, ETV6, RB1, BTG1, EBF1, CDKN2A/2B, CRLF2. The goal of our study is to identify abnormalities of these genes and prognosis of adult ALL patients. Material and method: We evaluated 17 patients diagnosed with ALL at Hematology Departament of Regional Institute of Oncology Iasi between 2017 and 2021. We performed DNA extraction following MLPA protocol. Statistical data analysis was assessed with IBM SPSS version 20. Results: We identified genic abnormalities at 38 of 45 patients. 56,6 % presented with deletions and 43.4 % duplications. The most frequent deletion was CDKN2A/2B (41,20 %), followed by IKZF1 (27,40%), PAX5 (13,5), RB1 (10,30%), ETV6 and JAK2 (6,75%). 31.4 % of patients present at least 2 deletions. Conclusions: The type and proportion of number of genes copies were similar with results previous published. Certains proportion of genes copies can be used for prognostic purpose in ALL patients.

4. VIRAL HEPATITIS B AND C AND LYMPHOMA

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Background. The Republic of Moldova is a country that is endemic for Hepatitis B and C infections. Both of these viruses are reportedly related to the pathogenesis of lymphoma and specific clinical and pathological features. Various local studies have shown conflicting results, with some countries, like Canada and USA, revealing no associations between viral hepatitis and lymphoma, whereas a significant connection has been reported in countries with higher rates of infection, like South Korea, Italy, and China. Considering the potential importance of regional variability in the subject matter, we have decided to conduct a local study in order to analyze lymphoma patients with viral hepatitis infections in the Republic of Moldova.

Methods. The study included 129 (64 (49.6%) men and 65 (50.4%) women) new patients with malignant lymphoma (aged over 18 years) in the Hematology Department of the Oncological Institute, Chisinau. Presence of hepatitis B and hepatitis C infections was based on positive AgHBs and Anti-HCV assays, respectively. Patients with and without viral hepatitis were evaluated and compared based on clinical and histopathological features. Mann-Whitney test, Fisher's exact test and logistic regression were used for statistical analyses.

Results. The association of malignant lymphomas with viral hepatitis was appreciated in 37 (28.7%) patients: 15 (11.6%) patients were diagnosed with hepatitis B, 21 (16.3%) patients with hepatitis C and 1 patient (0.78%) was positive for both viral hepatitis. The majority of subjects with viral hepatitis were over 60 years old (62.2%), presented with stage III or IV (81%), with B symptoms (54.1%), normal lactate dehydrogenase (58.3%) and minimal extranodal involvement (either none or only one site, 78.4%). The most common lymphoma subtypes were diffuse large B-cell lymphoma (64.9%) and marginal zone lymphoma (8.1%), whereas other subtypes were less frequent.

Conclusion. We have determined a high prevalence of hepatitis B and C viruses in lymphoma patients when compared to the reported prevalence in the general population; however, we were not able to find any specific clinical or histological features significantly related to hepatitis B or C infections in Moldovan lymphoma patients. Nevertheless, we believe these findings to be significant, since high prevalence of viral hepatitis serves as potential evidence for its involvement in lymphomagenesis, and underlines the need for further epidemiological studies involving a larger number of patients.

5. FREQUENCY OF RELAPSES IN PATIENTS WITH HODGKIN'S LYMPHOMA, STAGES I-II, IN THE REPUBLIC OF MOLDOVA

Aliona Golub, Maria Robu, Sanda Buruiană, Victor Tomacinschii, Vasile Musteață, Maria Popescu, Natalia Sporîș, Cristina Catan, Veronica Finciuc Hematology Discipline, Department of Internal Medicine, "Nicolae Testemițanu"

State University of Medicine and Pharmacy, Chisinau, Republic of Moldova Introduction: Hodgkin's lymphoma is a malignant lymphoproliferative process of B cell origin. Although the cure potential of patients with local stages of HL is high, relapses may develop in 10-15%

of cases. The development of relapses has a negative influence on the prognosis and life expectancy of patients with HL. Material and methods: In order to determine the frequency of relapses, the clinical-morphological aspects were studied in 506 patients aged between 18-84 (197 men, 309 women) with the classical form of Hodgkin's lymphoma, stages I and II, with complete remissions after the first-line treatment, who underwent treatment and were monitored in the Hematology Department of the Oncology Institute of the Republic of Moldova between 1990 and 2018. Results and discussions: Out of 506 patients with HLc, stages I and II, with complete remissions who were followed up, relapses were found in 99 cases, which constitutes 19.6%. The frequency of relapses was higher in patients aged 41-50 years (25.0%), in cases of HLc type with lymphocyte depletion (28.6%), the presence of signs of general intoxication (31.8%), primary involvement of the axillary (35.7%), supraclavicular (23.1%) and mediastinal lymph nodes (18.4%), large tumor sizes (more than 5 cm - 26.2%), the presence of lymphopenia in the peripheral blood test (66.4%), when achieving complete remission after RT (53.5%). Conclusions: Determining the recurrence frequency will contribute to the identification of the prognostic factors, the local stages of LH and the individualization of treatment tactics.

6. CLINICAL APPLICATION OF HALP SCORE IN THE DETERMINATION OF NODAL NON-HODGKIN LYMPHOMA PROGNOSIS.

Authors: Tomacinschii Victor1,2, Sanda Buruiana1, Robu Maria1; 1. Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova 2. Institute of Oncology, Chisinau, Republic of Moldova.

INTRODUCTION: Non-Hodgkin’s lymphomas (NHL) are hematopoietic tumors that develop from the malignant proliferation of the lymphatic tissue. The onset of NHL can occur in any organ and tissue, at the same time the most frequent localization is represented by the primary involvement of the lymph nodes (52-70%). The hemoglobin, albumin, lymphocytes, and platelets compose a score (HALP score), have recently been evaluated to predict the prognosis of cancer patients. However, there are limited reports of the use of HALP score in the determination of survival prognosis with non-Hodgkin lymphoma. OBJECTIVE: This study aims to appreciate the usefulness of the HALP score in the determination of overall survival (OS) characteristics in patients with nodal non-Hodgkin’s lymphomas. MATERIAL AND METHODS: To confirm the hypothesis, a retrospective study was provided including 57 patients diagnosed with nodal NHL in the Oncology Institute of the Republic of Moldova. The HALP score was calculated using formula: hemoglobin (g/L) × albumin (g/L) × lymphocytes (%) / platelets (/L). RESULTS: Of the patients enrolled in study 35 (61.4 %) were female. The mean age of the patients was of 59,09 years (range 22-83 years). Most of the patients were diagnosed in generalized stages: stage III - 16 (28,1%), stage IV - 30 (52,6%). Localized stages being found in 19,3%: stage I - 3 (5,3%), stage II – 8 (14,0%). Peripheral lymph nodes were the most common area of the primary involvement - 37 (64.91%), seconded by onset in the mediastinum - 14 (24.56%), abdominal lymph nodes being involved in 6 (10.52%). Aggressive lymphomas were diagnosed in 45 cases (78.9%), and indolent lymphomas in 12 patients (21.1%). On receiver operating characteristic curve (ROC) analysis, the predictive ability of the HALP score to envisage the risk of unfavorable events was significant (p= 0.038; AUC:0.685). The cut-off value based on ROC was 583,5. As result, we observed that in case of aggressive NHLs HALP patients with a low HALP score have a shorter period of OS: median OS-13(±4,4) months compared with the group of

patients with high HALP score where the median OS was not reached, p=0,049. In contrast, in indolent lymphomas, HALP score failed to show significant differences in survival between groups of patients with high or low HALP score(p=0,081). CONCLUSIONS: The HALP score, appears to be a valuable tool in determining the prognosis of patients with nodal NHL. A low HALP score was associated with lower OS rates - 13(±4,4) months in case of aggressive NHLs. (p=0,049). However, in case of indolent NHLs HALP score failed to perform as a useful prognostic score in the estimation of OS. Keywords: Non-Hodgkin lymphoma; HALP score; prognosis.

7. DIAGNOSIS CHALLENGES AND PARTICULARITIES OF A T-LGLL ASSOCIATED WITH NEUROENDOCRINE TUMOR

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Introduction:T-LGLL is a chronic and indolent lymphoproliferative disorder of the clonal CD3+ CD8+ cytotoxic T lymphocytes usually associated with autoimmunne disorders and cytopenias. Aproximatively 40% of the patients diagnosed wtih T-LGLL have been found to express STAT3 mutation, a known regulator gene of oncogenesis. The treatment of choice is immunosuppresion as a first-line therapy with methotrexate, cyclophosphamide or cyclosporin A; however, the rate of response is low (under 40%), with a high relapse probability. Objectives: This poster aims to highlight the particularities and therapeutical challenges found in S.D, a 34-year-old female, diagnosed in October 2019 with T-LGLL STAT3+, manifested by repeated infectious episodes and neutropenia. Materials and Methods: First hospitalisation in our service was in February 2022, when she was admitted for severe abdominal symptoms; biologically, she displayed leukopenia with grade IV neutropenia, cytolysis and cholestasis. Due to her increased digestive tract manifestations, she is suspected of an inflammatory bowel disease, which was confirmed by imagistic, biochemical and investigations, as well as multiple biopsies. The results certifiy the occurrence of the second neoplasm: the well-differentiated neuroendocrine tumor NET-G1. Second neoplasms can be found in around 5% of patients with LGL. The initial treatment consisted of immunosuppresive therapy: MTX 10mg/m2, reduced to 5mg/m2 due to the toxicity and adverse reactions and further switched to Ciclosporin A 1mg/m2/12h. Conclusions: This poster presents a rare case of a second neoplasm developed in a patient with T-LGLL STAT3+ and inflamatory bowel disease. Keywords: T-LGLL, NET-G1, STAT3+

8. IMMUNE MEDIATED-THROMBOTIC THROMBOCYTOPENIC PURPURA IN A PACIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA- CASE REPORT.

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Thrombotic thrombocytopenic purpura (TTP) is a life- threatening disease that can be related to various causes mainly autoimmune disorders or antineoplastic drugs. The TTP cases in

patients diagnosed with acute lymphoblastic leukemia (ALL) are very rare. Few cases of tyrosine kinase inhibitors associated secondary TTP have been reported in literature. On the other side thrombotic thrombocytopenic purpura has been rarely reported as an complication of severe COVID-19 infection. This poster describe a rare case of a 48-year-old ALL patient in treatment with dasatinib, that was recently infected with Sars-cov 2 virus, who was diagnosed with thrombotic thrombocytopenic purpura in our department.

9. THROMBOTIC COMPLICATIONS IN CHRONIC MYELOPROLIFERATIVE DISORDERS

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University of Medicine and Pharmacy „Victor Babeş", Timişoara, Department of Hematology, Timisoara

Background. Thrombotic complications are major cause of morbidity and mortality in patients with myeloproliferative disorders. The incidence of thrombotic events in myeloproliferative disorders does not correlate significantly with gender or platelet counts, but rather with age and a history of cardiovascular disease and/or thromboembolic events. Low-dose aspirin significantly reduce the risk of thrombotic complications in polycythemia vera (PV) patients, and is used in essential thrombocythaemia (ET). Hydroxyureea, interferon-α and anagrelide and are currently used treatments.

Aim. We performed a retrospective study on a group of patients with myeloproliferative disorders, especially TE, classified according to WHO 2008 guidelines on treatment response and complications occurring in these patients.

Methods. We retrospectively studied 180 patients, 78 (43,4%) male and 102 (56,6%) female with a median age of 60 years (35-85) that were hospitalized in the Hematology Clinic between 2011-2020. Thrombosis at diagnosis were present in 65/180 patients. Median platelet count was 792 x 10^9 / L (600-2103 x 10^9 / L), splenomegaly was present in 78 (43,3%) patients, and fibrosis in 58 (32,2%) patients. Patients were treated with Hydroxyureea (HU) 70 patients (38,8%), 72 (40%) patients received anagrelide, 43 (23,80%) patients received interferon-α. Low dose aspirin were used in Polycytemia vera and in Thrombocytemia essential (ET).

Results. Hemoglobin level and platelet count was similar in the 2 groups of patients (group of patients who received only HU and the group of patients who received anagrelide, interferon). The number of *leukocytes* in the blood and platelet count was correlated with thrombosis at the time of diagnosis. In the study group it was found following risk factors: Hypertension 35%, smoking 22%, obesity(19%), diabetes mellitus 8%. Also, the investigation of thrombotic markers revealed: JAK2 mutation 47%, elevated homocystein level 10%, Factor VIII elevation 12%, Protein S deficiency 10%, Factor V Leiden mutation 10%, Fibrinogen 17%, antiphospholipid antibody syndrome 8%, Lupus anticoagulans 5%, Factor IX elevation 4%, AT III deficiency 2%, Protein C deficiency 7%, prothrombin mutation 2%. Thrombotic events consisted of 36 arterial thrombosis (16 coronary disease, 14 stroke, 6 intestinal infarct) and 32 venous thromboses (22 deep and 6 splanchnic vein thrombosis, 4 cerebral sinus thrombosis).

Conclusion. There is an increased incidence of thrombotic events in myeloproliferative

diseases. They are influenced by the presence of thrombogenic risk factors and thrombotic markers.

10. CHRONIC LYMPHOCYTIC LEUKEMIA WITH LEUKOCYTOCLASTIC VASCULITIS - REMISSION AFTER INITIATION OF BTK INHIBITOR - CASE REPORT

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2. Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Abstract Text:

Introduction:

Recent years have made progress in treating patients with chronic lymphocytic leukemia.

Objectives:

It is presented the case of a 72-year-old patient with chronic lymphocytic leukemia (CLL), type 2 diabetes and leukocytoclastic vasculitis who obtained a haematological response to Ibrutinib therapy, with the disappearance of skin lesions.

Methods:

The 72-year-old patient with type 2 diabetes presents to the Colentina Hematology Department in July 2021 for generalized lymphadenopathy and disseminated skin lesions. He do clinical and imaging examination (CT scan) and blood tests, as well as skin biopsy of disseminated skin lesions with the appearance of leukemides. The diagnosis of hematological disease was established after completion of peripheral blood flow cytometry, detection of mutations in the TP 53 gene, FISH analysis for the detection of 17p13 deletion and somatic hypermutation of IGHV (DNA).

Results:

Diagnosis was chronic lymphocytic leukemia high risk with presence of gene TP 53 heterozygous mutation, with no 17p13 deletion and IGHV status without mutations. Skin biopsy reveals histopathological diagnosis of leukocytoclastic vasculitis. He starts Ibrutinib therapy: 420 mg/day oral.

After a month of treatment it is noticed the disappearance of skin lesions, marked decrease in lymphadenopathy but an increase in the absolute number of lymphocytes in the peripheral blood. He continue the treatment with Ibrutinib 420 mg/day, with good tolerance.

In July 2022 the lymphoproliferative disease is under control, without anemia or thrombocytopenia and no skin lesions.

Conclusion:

By controlling the disease we can offer a good quality of life to patients with high risk CLL.

11. STUDY UPON THE INCIDENCE OF COMPLICATIONS IN PATIENTS WITH HEMOPHILIA A AND B IN ROMANIA

Authors: Pătrașcu AM*, Goanță J*, Văduva A*, Popa C**, Rotaru I*
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Introduction Hemophilia is a rare congenital recessive x-linked disorder caused by the deficiency of coagulation factor VIII and IX, with an incidence of 1 in 10,000 newborns. Clinically, it is characterized by multiple bleeding episodes at the level of joints and other tissues, which in time causes the destruction of articular cartilage with joint deformity, muscle atrophy and soft-tissues contractures. The severity of the bleedings correlates with the degree of deficiency of factor VIII or IX.

Aim This study aims to determine the incidence of complications, the severity, and the type of treatment in patients with hemophilia A and B, in order to improve the therapeutical algorithm of this condition.

Material and methods A questionnaire through the Survio online platform (available at https://www.survio.com /ro/) was distributed either directly or with the help of the National Hemophilia Association to patients aged between 18 and 65 years with type A and B hemophilia. The collected data were processed using Microsoft Excel to facilitate their display and comparison.

Results Among the 66 cases included, 57 cases had severe hemophilia (48 type A and 9 type B) and 9 cases had moderate hemophilia (8 type A and 1 type B). Concerning the therapeutic protocol, 28 patients were receiving continuous prophylactic treatment, 25 were receiving intermittent prophylactic treatment, and 13 patients had on-demand treatment. Based on the severity of the pathology, we noticed that 45% of patients with severe hemophilia A and 12.5% of patients with moderate hemophilia A had more than 5 bleedings episodes in the last 3 months. In the severe type B hemophilia , 66.6% of patients had more than 5 bleeding episodes in the last 3 months, while no patient with moderate form had any bleeding. Depending on the type of treatment, the percentage of patients who experienced more than 5 bleedings in the last 3 months before the study was 33.33% for hemophilia A patients with continuous prophylaxis, 42.85% for hemophilia A patients with intermittent prophylaxis, 50% for patients with hemophilia A with on-demand treatment, 25% Hemophilia B with continuous prophylaxis, 75% Hemophilia B with intermittent prophylaxis and 100% Hemophilia B with on-demand treatment. 94.74% patients with A hemophilia and all of the patients with B hemophilia reported joint damage. Complications of severe bleeding requiring surgery, other than articular, were reported in 8.95% of cases. Among the severe bleedings cranio-cerebral or subdural hematomas, peritoneal hemorrhages and severe muscular hematomas were cited.

Conclusions. A significant percentage of Romanian patients with hemophilia had important bleeding complications. The effectiveness of continuous prophylactic therapy versus intermitent or on-demand treatment is obvious, with a lower rate of bleeding both for patients with hemophilia A and B in case of the former. The prevalence of hemophilic arthropathy is influenced by the type of treatment and the method of administration, by the recurrence of bleeding episodes and their severity, the physical activity of the patient, and the blood concentration of the coagulation factors. The early and adequate management of hemophilia can prevent such complications.

12. LOW-INTENSITY CHEMOTHERAPY IN RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA: WHAT IS THE BEST CHOICE?

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2 Hematology Department, Regional Oncology Institute, Iaşi

Introduction: Patients with relapsed or refractory(R/R) acute myeloid leukemia (AML) have limited treatment options and poor prognosis, with many patients unable to tolerate intensive chemotherapy. Non-intensive therapy is the treatment of choice for elderly AML patients or patients with significant comorbidities.

Aim: We aimed to evaluate the safety and efficacy of Venetoclax combinations in comparison with low-dose Ara-Cytosar(LDAC) and Cladribine.

Materials and methods: We analyzed 19 patients with R/R AML treated with Venetoclax combinations and 10 patients treated with LDAC and Cladribine admitted in the Hematology Department of Regional Institute of Oncology Iasi from 2018 to 2022.

Results: The intention-to-treat population included 29 patients (19 in the Venetoclax combinations group and 10 in the LDAC-Cladribine group). The median age was 58 years in both groups (range, 21 to 75). The median overall survival was 20 months in the Venetoclax group and 13 months in the LDAC-Cladribine group (p=0,043). The incidence of complete remission was higher with Venetoclax than with the LDAC-Cladribine regimen (50% vs. 30%). Key adverse events included febrile neutropenia, thrombocytopenia, and infections.

13. VENETOCLAX WITH HYPOMETHYLATING AGENTS (HMA) FOR THE TREATMENT OF PATIENTS WITH ACUTE MYELOID LEUKEMIA---THE EXPERIENCE OF THE EMERGENCY UNIVERSITY HOSPITAL CLINIC OF HEMATOLOGY

Authors: Anca Nicolescu, Diana Cisleanu, Horia Bumbea, Dana Vasile, Irina Voican, Elena Lupoaia Andrus , Ana Maria Neagu, Cristina Mambet, Cristina Enache, Ion Dumitru, Cristina Ciufu, Cristina Marinescu, Andreea Neculcea, Claudiu Popescu,

Ana Maria Vladareanu.

Clinic of Hematology, Emergency University Hospital, Bucharest

Acute myeloid leukemia in elderly is associated with poor outcomes, because of the high risk disease profile, comorbidities and ineligibility for intensive chemotherapy.Seven patients diagnosed with Relapsed/refractory AML or AML-MR were treated with targeted combination of Venetoclax plus HMA.The limited experience of the SUUB Hematology clinic (only 2 years) does not allow to assess the impact of treatment on long term survival. The most favorable therapeutic effect were the decrease of tumor mass and blast clearance observed after the first cycle of treatment.Even with persisting severe pancytopenia in most of the patients, there were no grade 3 or 4 infectious or hemorrhagic adverse events, but dose modification for Venetoclax was almost required..

Therefore in our limited experience, the treatment with Venetoclax and HMA was a feasible and effective therapeutic option for patients with r/r AML and AML -MR, due to efficacy, good tolerability and safety profile.

14. EXTRAMEDULLARY RELAPSE OF ACUTE MYELOGENOUS LEUKEMIA

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Background: Extramedullary relapse (EMR) is a relapse of leukemia in sites other than the bone marrow, which can be estimated in 3-5% of cases of acute myeloid leukemia. Predisposing factors for EMR in LAM are: an abnormal karyotype (eg, t(8; 21), inv(16) and t(11q23)) FAB type M4, male gender, leukocytosis >50,000/L. Patients with EMR show higher overall survival compared to those who develop medullary relapses, but in most cases they report a systemic relapse. The aim of the study: to describe the rare presentation of a mastoid sinus as an extramedullary manifestation of acute myelogenous leukemia (AML) recurrence without bone marrow or central nervous system involvement. Methods: Case report. Results: An 34-year-old male with acute myeloid leukemia (AML) M4 (FAB classification) with the diagnosis confirmed in 10.2020 based on medullary aspirate research (44% blast cells). Spent induction therapy 2 courses:" 3+7", subsequently small doses of cytarabine intensified with Caelyx (liposomal doxorubicin) on the ground of bearing the severe form of COVID-19, but with the getting of complete remission (01.2021). Then followed 2 "3+7" consolidation courses followed by maintenance therapy. In 03.2022, based on infectious complications - acute mastoiditis, CT(from 29/03/2022: total opacification of mastoid cells, involving the mastoid antrum - subtotal opacification, altered intercellular septums – thinned, sclerotic), ENT consultation(bilateral acute media/external otitis with acute left mastoiditis), left mastoidectomy was performed. In the histological material there is found malignant tumor proliferation of medium/large size cells with fine granular chromatin, visible nucleoli arranged in the delicate stroma. Immunohistochemical tumor cells are positive for MPO (+diffuse); CD34 (+diffuse); TdT (+focal); CD117 (+focal); CD68 (+focal) and are negative for CD3; CD20; PAX5; ALK; Desmin. Conclusion histopathological aspect in correlation with immunohistochemical tests more advocates for malignant tumor proliferation composed of cells of the myeloid row. Conclusions: Acute Leukemia can cause various extramedullary manifestations. This case demonstrates the potential for mastoid biopsy to secure the diagnosis of extramedullary relapse in order to initiate prompt treatment and systemic workup. The diagnosis of EMR is possible based on clinical presentation, radiologic studies, and especially biopsy and histopathologic examination.

FRIDAY - OCTOBER 7th, 2022

POSTERS SESSION

1. IRON DEFICIENCY ANEMIA, A PUBLIC HEALTH PROBLEM

Daniela Georgescu 1, Aron Ramona 2

1. Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
2. AIS Clinics&Hospital, Bucharest, Romania

Introduction

Iron deficiency is a major public health problem in infants, young children, women with heavy menstruation, pregnant women, the elderly and cancer patients. Iron deficiency anemia independently increases morbidity and mortality. In France, an epidemiological study (SUVIMAX) showed that approximately 93% of women have an insufficient dietary intake of iron and 23% of women of childbearing age are iron deficient, of which 4% are anemic. Identifying and treating the cause that led to the iron deficiency is mandatory for any patient with iron deficiency anemia, and this is where interdisciplinary collaboration comes into play.

Objectives and methods

Analyzing the data from the specialized literature, we studied 100 adult patients with iron deficiency anemia who addressed the AIS Clinics&Hospital between June and July 2022. Demographic data, Hemoglobin (Hb) value, iron deficiency investigations, comorbidities are presented.

Results

100 patients with iron-deficiency anemia, diagnosed between June and July 2022 in the AIS Clinics&Hospital, were included. The median age was 53 years (with values between 19 and 87 years), and the ratio of men (13%): women (87%) was 1:6.6. The average value of Hb was 9.51 g/dl (N: 12 - 17 g/dl), with values between 7.12 and 11.9 g/dl. The average value of ferritin is 20.45 ng/ml (N: 21.81 - 274.66 ng/ml), with values between 3.02 and 37.89 ng/ml. The average value of sideremia was 60 ug/dl (N: 65 – 175 ug/dl), with values between 12 and 96 ug/dl. The pathologies encountered were: diabetes (22%), chronic kidney disease (5%), dyslipidemia (10%), Helicobacter pylori positive gastritis (1%), pyelonephritis (6%), hypertension (27%), heart disease ischemic (3%), Atrial fibrillation (1%), Varicose veins of lower limbs (2%), Venous thrombosis (2%), Oral anticoagulant treatment (3%), Lipothymia (1%), Pelvic inflammatory disease (13%), Fibromatous uterus (8%), Genital prolapse (1%), Menstrual cycle disorders (7%), Pregnancy (3%), Hypothyroidism (4%), Chronic bronchitis (2%), COVID 19 (2%), steatosis liver disease (1%), liver cirrhosis (1%), HCV hepatitis (2%), gastroesophageal reflux disease (1%), hiatal hernia (1%), hemorrhoids (2%), sigmoid diverticula (1%), polyps colon (1%), operated intestinal occlusion (1%), right lower limb amputation (1%), right hip arthropathy (1%), gonarthrosis (3%), Parkinson's disease (1%), headache (1%), depression (2%), malignant tumors (5%): colon (3%), lung (1%), lip (1%).

Conclusions

Iron deficiency anemia is frequently encountered in medical practice. Although prevalences may vary between communities, iron deficiency anemia affects approximately 15% of the world's population. The challenge for clinicians is to identify and treat the cause that led to anemia.

Thanks:

This work was carried out with the logistical support of EGIS PHARMACEUTICALS

2. ATYPICAL MANIFESTATIONS IN CASTLEMAN DISEASE

Irina Florentina Carpen, Luana Alexandra Marian, Catalin Danaila, Angela Dăscălescu
Department of Hematology , Regional Institute of Oncology Iasi, Romania Keywords:

Castleman Disease, angiofollicular lymph node hyperplasia

Castleman Disease or angiofollicular lymph node hyperplasia is a disease that is part of the group of atypical lymphoproliferative diseases, being at the border between benign and malignant. The angiofollicular lymph node hyperplasia represents a lymphoid proliferation, probably initially reactive, but insufficiently controlled by a deficient immune system, which allows the appearance of cell clones in which chromosomal abnormalities may occur and oncogenes/antioncogenes may be involved, with possible evolution toward malignancy. Objectives: In this paper we aim to explore the clinical characteristics,the evolution and outcome of the treatment of two patients hospitalized in our institution, diagnosed with Castleman Disease (hyalino-vascular multicentric form and plasmocytic multicentric form). Methods: The cases of two young patients with Castleman Disease have been evaluated using histological and immunohistochemical examinations to establish the diagnostic certainty. Results: The two disease forms can be characterized by clinical-biological manifestations and various evolutionary modalities, involving different therapeutic implications. The patient may be asymptomatic, but the onset of the disease may also be manifested by type B symptoms. The most constant sign of tumor manifestations are represented by the appearance of adenopathies. Conclusions: Castleman disease is an atypical lymphoid proliferation, in which paraclinic explorations are not specific and sufficient to establish the diagnostic certainty, which remains histopathological. The disease must be differentiated from lymphomas, the histopathological variant identification being mandatory to administer adequate treatment and to estimate a correct prognosis.

3. DIAGNOSIS CHALLENGES AND PARTICULARITIES OF A T-LGLL ASSOCIATED WITH NEUROENDOCRINE TUMOR

Olarasu, Catalina1, Munteanu, Diana-Andreea1, Dascalescu, Angela1 Hematology Clinic, Regional Institute of Oncology, Iaşi

Introduction:T-LGLL is a chronic and indolent lymphoproliferative disorder of the clonal CD3+ CD8+ cytotoxic T lymphocytes usually associated with autoimmunne disorders and cytopenias. Aproximatively 40% of the patients diagnosed wtih T-LGLL have been found to express STAT3 mutation, a known regulator gene of oncogenesis. The treatment of choice is immunosuppresion as a first-line therapy with methotrexate, cyclophosphamide or cyclosporin A; however, the rate of response is low (under 40%), with a high relapse probability. Objectives: This poster aims to highlight the particularities and therapeutical challenges found in S.D, a 34-year-old female, diagnosed in October 2019 with T-LGLL STAT3+, manifested by repeated infectious episodes and neutropenia. Materials and Methods: First hospitalisation in our service was in February 2022, when she was admitted for severe abdominal symptoms; biologically, she displayed leukopenia with grade IV

neutropenia, cytolysis and cholestasis. Due to her increased digestive tract manifestations, she is suspected of an inflammatory bowel disease, which was confirmed by imagistic, biochemical and investigations, as well as multiple biopsies. The results certifiy the occurrence of the second neoplasm: the well-differentiated neuroendocrine tumor NET-G1. Second neoplasms can be found in around 5% of patients with LGL. The initial treatment consisted of immunosuppresive therapy: MTX 10mg/m2, reduced to 5mg/m2 due to the toxicity and adverse reactions and further switched to Ciclosporin A 1mg/m2/12h. Conclusions: This poster presents a rare case of a second neoplasm developed in a patient with T-LGLL STAT3+ and inflamatory bowel disease. Keywords: T-LGLL, NET-G1, STAT3+

4. OLIGOCLONAL BANDS, A TRUE DIAGNOSIS CHALLENGE – CASE PRESENTATION

Loredana Cirlan 1, Monica Popescu 1, Sanziana Barbu 1, Ruxandra Irimia 1,2, Oana Diana Preda 1, Andreea Jercan 1, Daniel Coriu 1,2, Sorina Badelita 1

1. Center of Hematology and Bone Marrow Transplantation, Fundeni Clinical Institute, Bucharest

2. Carol Davila University of Medicine and Pharmacy

Monoclonal gammopathies represent a group of clonal diseases, which include multiple myeloma and are characterized by plasmocytic cell proliferation.

The diagnosis is sustained through serum proteins electrophoresis which detects a monoclonal peak.

However, in literature there are multiple case reports of oligoclonal bands detected by serum proteins electrophoresis. Their detection can lead to a false diagnosis of monoclonal gammophathy, especially in patients with autoimmune disorders. Oligoclonal bands are seen as faint small bands in the gamma region and are usually non-quantifiable.

We present a case of a 68 year old patient, who has been diagnosed for 40 years with systemic lupus erythematosus which has cutaneous and articullar involvement, treated with systemic steroids and hydroxychloroquine. The patient was reffered to the Hematology clinic of Fundeni Clinical Institute with a suspicion of multiple myeloma as a result of acute kidney injury and hypergammaglobulinemia. The hematological investigations reveal oligoclonal bands on the serum proteins electrophoresis. How do we interpret them?

5. MANAGEMENT OF MGUS WITH ORGANIC IMPACT- CASE REPORT

Ramona-Ingrid Corbeanu[1], Monica Popescu[2], Ruxandra Maria Irimia[2], Sânziana Barbu[2], Loredana Cîrlan[2], Prof. Univ. Dr. Gener Ismail[3], Dr. Mirela Drăghici[2], Prof. Univ. Dr. Daniel Coriu[2], Dr. Bădeliță Sorina[2]

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Abstract: Monoclonal gammopathy of undetermined significance (MGUS) represents a premalignant clonal plasma cell, defined by the presence of a serum monoclonal protein (M protein) at a concentration <3g/dl, a bone marrow with <10 percent monoclonal plasma cells and absence of end-organ damage (hypercalcemia, renal insufficiency, anemia, lytic bone lesions). This benign condition does not require specific treatment. Long-term follow-up is generally recommended at 6-month intervals. In the last four years, a new clinical entity was described in the specialized literature, called ″MGUS with organic impact″, which requires treatment. The treatment is chosen depending on the type of monoclonal protein and the affected organs. We present the case of a patient with MGUS with multiorgan involvement, in whom specific treatment was initiated within a multidisciplinary team.

6. THE IMPORTANCE OF VAF MUTATIONS OF THE TP53 GENE IN THE PROGNOSIS OF MULTIPLE MYELOMA

Mihaela Dragomir[1], Onda-Tabita Calugaru[2], Sorina Badelita[1], Silvia Aposteanu[1],Ana-Maria Mihalache[1], Georgiana Stoica[1], Daniel Coriu[1,2], Cerasela Jardan[1,2]

1 – Fundeni Clinical Institute – Hematology Department

2 – „Carol Davila" University Of Medicine - Bucharest

Introduction: Deletions of chromosome 17p (del17p) (involving the tumor suppressor gene TP53) are associated with poor prognostic in Multiple Myeloma. Even VAF (Variant Allele Frequency) mutation present low clonality, they can be considered red flags in diagnosis and evolution of the patient.

Material and Methods: The study included a group of 35 patients diagnosed at the onset of MM for whom FISH analysis (del 17p; t(4;14); t(14;16) and chromosome 1 abnormalities) and Targeted Sequencing (gene TP53) were performed.

Results: After analyzing FISH and NGS data, the most common cytogenetic abnormality associated with TP53 mutations is del 17p. In 63% of MM, pathogenic and potentially pathogenic mutations in TP53 were identified, but only 42% associated del 17p. Of the total TP53 mutations identified, 40% were located in exon 5. The majority of mutations are VAF (72,73%) and 27,27% are clonal.

Conclusions and discussions: Most of the identified mutations were located in exon 5 of the TP53 gene, which is included in the most extensive functionally conserved domain of the gene (DBD – DNA Binding Domain). Thus, the mutations in this hotspot region have high pathogenic potential. Also, most subclonal mutations, which are frameshift, lead to the insertion of a premature stop codon, producing truncated or null proteins. In conclusion, TP53 gene mutations, regardless of the clonality percentage, represent a red flag that can change the patient's prognosis.

7. ASSESSMENT OF QUALITY OF LIFE IN BCR-ABL1-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS

Mihnea-Alexandru Găman[1,2], Nicoleta Pîrciulescu[2], Toma Lascăr[2], Ioana Gheorghiu[2], Loredana Cîrlan[2], Denisa Bărbulescu[3], Melen Brînză[1,2], Iulia Constantinescu[4], Bogdan Ionescu[2], Aurelia Tatic[1,2], Mihaela Cîrstea[1,2], Ana Manuela Crișan[1,2], Iulia Ursuleac[1,2], Amelia Maria Găman[5,6], Daniel Coriu[1,2], Camelia Cristina Diaconu[1,7], Robyn M. Scherber[8]

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Introduction: Blood cancers are associated with a decreased quality of life (QoL). Moreover, there are few specific, culturally adapted and validated instruments available in Romanian to assess QoL in patients with hematological malignancies.

Objectives: Translation, cultural adaptation and validation to Romanian of the MPN-10 questionnaire. Assessment of QoL in patients with BCR-ABL1-negative chronic myeloproliferative neoplasms (MPNs).

Methods: In order to test its psychometric properties, the MPN-10 questionnaire was translated from English and adapted to Romanian and distributed to a group of patients diagnosed with MPNs. The study was approved by the Ethics Council of Fundeni Clinical Institute. All patients signed an informed consent form agreeing to partake in medical education/research activities..

Results: A total of 100 patients (median age: 64 years; 57% females) filled the MPN-10: 38 cases of polycythemia vera (PV), 34 cases of essential thrombocythemia (ET) and 28 cases of primary/secondary myelofibrosis (MF). Mean QoL of the study group was 7.5 points/10 points. The mean MPN-10 score was 21 points/100 points. Patients suffering from MF (QoL=7.4/10; MPN-10=26) and PV (QoL=7.5/10; MPN-10=22) registered lower QoL and higher MPN-10 scores versus those diagnosed with ET (QoL=7.9/10; MPN-10=16.4). Fatigue and daily inactivity contributed the most to the reduction in QoL. A positive correlation was detected between these two items of the questionnaire ($r=+0.33$, $P<0.001$).

Conclusions: Patients diagnosed with MPNs display a decreased QoL despite specific treatment. Taken into consideration that the psychometric properties of MPN-10 were satisfactory, this instrument can be employed to assess QoL in MPNs.

Keywords: MPN-10; polycythemia vera; essential thrombocythemia; myelofibrosis; myeloproliferative neoplasms.

8. TREATMENT WITH LUSPATERCEPT - EXPERIENCE OF THE COLENTINA CLINICAL HOSPITAL

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Abstract Text

Introduction

Myelodysplastic syndromes (MDS) represent clonal diseases of the hematopoietic stem cell, characterized by heterogeneity and the tendency of evolution towards leukemia now. The treatment is stratified according to the risk group, and the main therapeutic method is the transfusion of blood products. Studies on large groups of patients have demonstrated that transfusion dependency is a negative prognostic factor, being associated with increased morbidity and mortality rates. Treatment with erythropoietin significantly influenced the quality of life in patients with MDS, but there is a category of patients with a low risk of transformation into acute leukemia, transfusion dependent, who do not respond to erythropoietin therapy.

Luspatercept (Reblozyl) is a recombinant fusion protein that binds to certain ligands of the transforming growth factor-β (TGF-β) superfamily. By binding to specific endogenous ligands (eg, GDF-11, activin B), luspatercept inhibits Smad2/3 signaling, which leads to erythroid maturation through the differentiation of late-stage erythroid precursors (normoblasts) in the bone marrow. Smad2/3 signaling is abnormally elevated in disease models characterized by ineffective erythropoiesis, such as MDS and β-thalassemia. Reblozyl is approved now being indicated for the treatment of adult patients with transfusion-dependent anemia due to very low, low and intermediate risk myelodysplastic syndromes (MDS) with ring sideroblasts, who have shown an unsatisfactory response or are ineligible for treatment with erythropoietin as well as for patients with beta thalassemia major or intermedia.

The efficacy and safety of therapy with Luspatercept have also been demonstrated in the case of patients with Thalassemia major or intermedia form, requiring transfusion.

Objectives

The main objective was to evaluate the effectiveness of treatment with Luspatercept in patients with thalassemia and in those with refractory anemia and ring sideroblasts admitted to the Colentina Clinical Hospital, the effectiveness defined by the decrease in transfusion requirements. The secondary objective was to evaluate the safety of treatment with Luspatercept in patients admitted to the Colentina Clinical Hospital, by recording all adverse events.

Methods and Results

We present adult patients diagnosed with Thalassemia major or intermedia, requiring transfusion, as well as patients with refractory anemia and ring sideroblasts (RARS) with transfusion dependency, who require red blood cell transfusions (≥ 2 units/8 weeks) due to MDS and who received previously treated with an erythropoiesis-stimulating agent (ESA), to which they had an inadequate response or were intolerant to ESA treatment.

The statistical data from the source are analyzed: Table in Excell, with the data from enrollment in the study (S0) and respectively from Week S8 of treatment, S12, S24 and S48, for each patient, regardless of whether they are still on treatment or not with Luspatercept.

The data presented are: 1. Demographics (age, sex): at enrollment; 2. Characteristics related to the disease (at enrollment): date of diagnosis, risk group according to IPSS for MDS; 3. Ferritin: S0/ S8/S12/S24 and S48; 4. Hemoglobin: at enrollment/ S8/S12/S24 and S48; 5. The transfusion requirement to reach the target value of Hb = 8g/dl: at enrollment/in S8/S12/S24 and S48.

Conclusion

Patients treated outside of clinical trials with innovative drugs are the subject of observational research, in order to determine the effectiveness and safety of the treatment in current medical practice: the Real - world report concept. The work includes categories of patients without a therapeutic solution and for whom the reduction of the transfusion requirement is associated with the important improvement of the quality of life, thus being the main goal of the treatment.

9. ITP ASSOCIATED WITH MDS/ CMML- EVOLUTION PATTERN - CASE REPORT

Georgescu Georgeta Daniela 1,2, Silvia Ciortan 1

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Abstract Text:

Introduction

Myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML) are clonal diseases of the hematopoietic stem cell characterized by inefficient dysplastic hematopoiesis, resulting in cytopenias and the risk of transformation into acute leukemia. Immune thrombocytopenia (ITP) is an immune-mediated condition, defined by the transient or persistent decrease in the number of platelets in the peripheral blood below 100 x 10 9/L, excluding other causes of thrombocytopenia.

In 10 to 20% of cases there is the association between systemic inflammatory or autoimmune diseases with MDS or CMML: vasculitis, neutrophilic dermatosis and polyarthritis; immune cytopenias have been described in 1 to 16% of cases.

Vincent Jachiet publishes in 2021 in Haematologica (Volume 106(5):1414-1422) the results of a study carried out by the French Network of Dissymune Disorders Associated with Hemopathies (MINHEMON), a study that evaluated the clinical spectrum, therapeutic management and evolution of patients with associated ITP with MDS/CMML compared to patients with ITP without MDS/ CMML and respectively with patients with MDS/ CMML without ITP.

The author concludes that patients with MDS/ CMML associated with ITP have more severe bleeding than those with ITP without MDS, but a lower rate of progression to acute leukemia (AML) than those with MDS without associated ITP.

Objectives and Methods

Analyzing the data from the literature, we present the case of a 58-year-old female patient from an urban environment, diagnosed in 2005, in the Hematology Clinic of the Colentina Clinical Hospital, with ITP, with a dependent response to therapy with Methilprednisolone 4

mg/ every 2 days and who in October 2011 was diagnosed with RAEB II, IPSS score 1.5 points, intermediate 2 risk group. Considering the young patient, fit for bone marrow transplant, HLA typing was performed: incompatibility with her sister. Between 2011 and 2016, patient refused Azacitidine therapy, continuing with Methilprednisolone 8 mg/day peros, maintaining the number of platelets between 79,000 and 110,000/mmc. Cardiovascular complications occur secondary to cortisone treatment, evident during the Holter EKG examination. In June 2016, in the context of the reduction of the dose of Methilprednisolone to 4 mg/ every 2 days, Platelets decrease to 30,000/mmc. Abdominal tomography reveals splenomegaly with hypo- and hyperabsorbing lesions in the spleen. Splenectomy is refused by the patient.

In July 2016, the bone marrow evaluation revealed the same diagnosis: RAEB II, IPSS score 1.5 points, intermediate 2 risk group. With the patient's consent, therapy with AZACITIDINE 75 mg/m² x 7 days was initiated plus Methilprednisolone 4 mg/ every 2 days, under which the number of platelets remained between 26,000/mmc - 45,000/mmc. Subsequent evaluations from July 2016 to June 2022 revealed a stable hematological disease, with a partial hematological response, with persistent thrombocytopenia, but the appearance of corticotherapy complications: Hypertension, Ischemic Heart Disease, Osteopenia, Type 2 Diabetes, insulin-requiring.

In June 2022, the patient returns with a severe hemorrhagic skin-mucous syndrome, the investigations revealed a transformation into acute leukemia - AML M4 FAB hyperleukocytic form, with high risk, with the presence of del(11)(q23) and the positive FLT3 ITD mutation. During the evolution, the patient suffered a cerebellar hemorrhagic stroke, which led to death.

Results

From the ITP point of view, patient had a 17-year evolution, marked by the complications of corticosteroid dependence: Hypertension, Ischemic Heart Disease, Osteopenia, Type 2 Diabetes, insulin-requiring.

From the REAB II point of view, patient had an evolution of approximately 11 years, far exceeding the median survival period, related to the prognostic score: IPSS 1.5 points, intermediate 2 risk group, median survival 1, 2 years. According to data from the literature, a quarter of patients with RAEB II and IPSS 1.5 points, intermediate 2 risk group transform into AL in 1.1 years. The transformation into AML in our patient's case took place after approximately 11 years.

Conclusion

Our patient with ITP associated with MDS had a stable evolution under the treatment with Methylprednisolone plus Azacitidine, but was affected by the complications of corticosteroid dependence. Our patient with RAEB II and ITP presented transformation into AML after approximately 11 years.

The cause of death was cerebral hemorrhage, confirming the data of the study published by Vincent Jachiet in 2021 in Haematologica, according to which patients with MDS/CMML associated with ITP have more severe bleeding and a lower rate of progression to acute leukemia.

10. THE ROLE OF TREATMENT IN MYELOFIBROSIS – CASE REPORT

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Abstract Text:

Introduction

Myelofibrosis (MF) is part of the category of BCR/ABL1 negative chronic myeloproliferative neoplasms.

Objectives and Methods

The cases of two patients with MF, hospitalized in the Hematology Clinic of the Colentina Clinical Hospital are presented. The diagnostic criteria, the classification in the risk group and the indication for treatment, as well as the evolution, were followed.

Results

Case 1: Woman 45 years old; diagnosed with MF in August 2019. At onset: upper digestive hemorrhage in July 2019, Splenomegaly: spleen 17 cm (axis long). Bone marrow biopsy: Primary myelofibrosis, hypercellular prefibrotic stage, G/E~6/1. Present the heterozygous Mutation V617 F in JAK II gene. Total Symptom Score (MPN – FES STS): 71 (increased). Risk score: DIPSS score 3 points. Risk group: Intermediate-2. The treatment criteria were: MF with splenomegaly and symptoms secondary to the disease. From September 2019 until now, she is on treatment with Ruxolitinib: cp 20 mgx2/day, with good tolerance, good control of the disease: the total score of MPN – FES STS symptoms: 32 (down from 71 initially).

Case 2: Woman 65 years old; diagnosed with Polycythemia Vera (PV) since 2007, and in January 2022 the osteomedullary biopsy revealed diagnosis of secondary MF after PV (Bone Marrow Biopsy: MF grade 2). Onset with itching, hypermelalgias since 2004; Progressive splenomegaly under treatment with Hydroxyurea: spleen 22 cm (long axis) in January 2022. Bone marrow biopsy: MF sec. post PV: hypercellular marrow with densification of the reticulin network (myelofibrosis grade 2) on Gomori staining. Present the homozygous Mutation V617 F in JAK II gene. High risk due to symptomatic splenomegaly and progressive hyperleukocytosis under Hydroxyurea treatment. The treatment criteria were MF sec. post PV with progressive splenomegaly under Hydroxyurea treatment and persistence of disease symptoms. From February 2022 until now she is under treatment with Ruxolitinib: cp 20 mgx2/day, with good tolerance, good control of the disease: Spleen axis long 16.3 cm (down from 22 cm initially), improvement of QoL (MPN score decreasing from 70 to 50).

Conclusion

Early initiation and according to the indications of treatment in Myelofibrosis, both in primary and secondary form, is associated with a good control of the disease and a good quality of life.

11. MULTIPLE MYELOMA ASSOCIATED WITH MYELOFIBROSIS - EVOLUTION PATTERN - CASE REPORT

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Abstract Text:

Introduction

Patients who associate Multiple Myeloma and Myelofibrosis present clinical and biological aspects that predispose to a negative prognosis.

Objectives and Methods

We present the clinical and biological data of a patient diagnosed with multiple myeloma and myelofibrosis, to emphasize the negative impact on the evolution.

We analyzed from the patient's medical file: clinical characteristics, laboratory parameters, imaging, therapeutic approach, evolution.

Results

We present the case of a 58-year-old patient, smoker, chronic ethanol user, diagnosed in February 2020 with lambda micromolecular multiple myeloma stage II ISS, with bicitopenia (anemia, thrombocytopenia), with left shift to blast, with kidney injury (creatinine 2.2 mg / dl), without elements of bone disease, associated with elements of myelofibrosis on osteomedullary biopsy: dense fibrous stroma in Gomori staining. JAK2 and BCR / ABL1 mutation were negative. The patient underwent 3 VCD cycles, with complete response (negative immunofixation), but the bone marrow biopsy from March 2020 revealed the appearance of grade 3 hypercellular myelofibrosis (Gomori), without the presence of myelomatous plasma cells. Molecular tests show absent MPL and CAL R mutations. Considering the diagnosis of myelofibrosis, the stem cell harvest is delayed. Due to the COVID 19 pandemic, the patient was biologically monitored and did not continue the specific hematological treatment, with negative PET / CT (December 2020).

In June 2021, in the context of the recurrence of bicitopenia, the investigations reveal a relapse of myeloma objectified by plasma cell infiltrate> 75% and biochemical progression (free lambda 9280 mg / l, K / L ratio <0.01, b2M 17.2 mg / l) framing the patient in stage lll ISS. Chemotherapy is resumed according to the VCD protocol, the first cycle being followed by severe sepsis with respiratory starting point, which required admission to the ICU.

Chemotherapy continued, followed by stem cell harvesting and autograft in June 2022. We mention that following autotransplant, the patient presented with severe sepsis that required broad-spectrum antibiotic therapy and antifungals.

Post-transplant evaluations reveal bicitopenia, renal impairment and 10% myelomatous plasma cells on bone marrow biopsy without myelofibrosis.

Conclusion

The presence of myelofibrosis and recurrent, life-threatening infectious complications gives the young patient with multiple myeloma a poor prognosis.

12. AMYLOIDOSIS, A FEARED ENEMY AMONG PATIENTS WITH MULTIPLE MYELOMA; CASE PRESENTATION AND LITERATURE REVIEW

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Abstract: Primary amyloidosis represents a group of rare diseases characterized by the accumulation of amyloid, an abnormal protein, in organs and tissues, producing organ failure. There are multiple types of amyloidosis, and the light chain type (AL) is the most common one, representing for more than three quarters of amyloidosis cases. In Europe is estimated an incidence of 9 cases/ 1 million peoples/year. However, amyloidosis is still underdiagnosed in Romania. This condition can be present in patients with Multiple Myeloma or alone. Multiple myeloma (MM), like amyloidosis, is part of Monoclonal Gammopathies, characterized by the accumulation of monoclonal plasmocytes in the bone marrow, producing marrow failure. Objectives: To review the diagnostic criteria of amyloidosis and MM, to raise awareness of the importance of early diagnosis of these conditions. Material and method; the case of a patient who presented himself to the clinic after palpation of 2 cm subcutaneous nodules at abdominal level, diagnosed with kappa light chain amyloidosis with soft tissue (subcutaneous nodules) and kidney involvement (subnephrotic proteinuria) and IgG kappa multiple myeloma stage 3 ISS.

Key words: amyloidosis, multiple myeloma, nephrotic syndrome, subcutaneous nodules

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13. CAUSES OF IRON DEFICIENCY ANEMIA IN THE HEMATOLOGY CLINIC. SINGLE CENTER EXPERIENCE

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Background. Iron deficiency anemia (IDA) is the common nutritional deficiency worldwide. The studies concerning various causes of IDA in adult men are rare, although it is assumed that chronic gastrointestinal blood accounts for the majority.

Aim of the study is to evaluate retrospectively adult men with IDA that were hospitalized in our Hematology Clinic.

Methods. One hundred seventy male with IDA were enlisted at this study from January 2005 to december 2021. Anemia was defined as Hg<13g/dL using the WHO criteria. IDA was considered present if serum ferritin was <15ng/ml combined with serum iron concentration <30ug/dL with a transferrin saturation of <10%. Complete physical examination, the history

of the disease and fecal occult blood test (FOBT) of three spontaneously passed stools was done in all patients. All patients had complete blood count, serum and total iron binding capacity, and a serum ferritin level. Most patients underwent esophagogastroduodenoscopy (EGD). Colonoscopy was performed if lesion that caused IDA was not found, and/or THO was positive.The abdominal CT scan were performed according to clinician's recomandation together with other tests related with blood lost.

Results. The median age was 65 (range 30 to 85) years old. 130 of 170 (76.47 %) men with IDA had symptoms such as fatigue, dizzines, or digestive complaints. The history of prior gastrectomy, hemorrhoid, that probably had caused IDA were reported in 28 (16.47%), 36 (21.17%), patients, respectively. FOBT was positive in only 64 (39.41%) subjects. 157 (92.35%) patients underwent EGD. The most common findings from EGD were gastritis (37 patients) and peptic ulcer (28 patients). Fifty one (30%) patients were found to have upper gastrointestinal disorders (13 patients with erosive gastritis, 12 gastric ulcer, 11 duodenal ulcer, 15 gastric cancer. Seventy one (41.76%) patients underwent colonoscopy. That showed 35 clinically important lesions that probably caused IDA; colon cancer in 12 patients, colon polyp in 10 patients and hemorrhoid in 13 patients. Concerning malignant lesions which are responsible for IDA, the malignant lesions were found more frequent in patients older than 50 years accounting for 22.5 % and patients younger than 50 years 16.8 % .

Conclusions: This study demonstrated that gastrointestinal blood loss is the main cause of IDA in adult men, and that there is a high rate of malignancy in men older than 50 years.

14. MANAGEMENT OF AUTOIMMUNE HEMOLYTIC ANEMIA. SINGLE CENTER EXPERIENCE

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Background: Autoimmune hemolytic anemia (AIHA) is characterized by the production of autoantibodies to red blood cell surface antigens with destruction of red blood cells by complement and reticuloendothelial system; usually idiophatic, it is also associated with infection, lymphoproliferative disorders, autoimmune diseases, and some drugs.

Aims: To evaluate in this study the clinical, biological and therapeutic aspects of AIHA.

Methods: We presented this retrospective study about 110 cases of AIHA observed in the our hematology clinic, over a period of 10 years (2001-2021). We have tried to describe the clinical aspects of AIHA and evaluate the management of AIHA.

Results: There were 45 men and 67 women with a mean age of 48 years [21-78]. Regarding the medical history, 12 patients were with hipertension of whom 3 were receiving Methyldopa, 14 patients were diabetic, 10 had thyroid dysfunction and 20 had a history of autoimmune disease. The clinical aspects of discovery were an anemic syndrome in 82 of patients, mainly due to paleness and asthenia found in 75 and 62 patient respectively. Physical examination revealed icterus in 84 causes, splenomegaly in 49 causes, hepatomegaly in 16 cases, lymph node in 15 cases and fever in 30 cases. The blood tests reveald that anemia was normocytic in 45 cases and macrocytic in 60 cases. There were biological signs of hemolysis hyperbilirubinemia in 68 patients, high LDH rate in 77 patients.

Direct Coombs test was positive for IgG in 77 cases, C_3 in 14 cases, IgG+C_3 in 19 cases. AIHA was idiophatic in 58 cases and secondary to lymphoproliferative desorders in 4 cases, autoimmune disorders in 25 cases, 3 cases were secondary to Methyldopa. The therapeutic consisted of transfusion in 65 cases and all patients underwent a corticosteroid treatment in addition to folic acid theraphy in 76 cases and etiological treatment in the non idiopathic cases.

The patients that were resistant or relapse therapy were treated by splenectomy, immunosupresive drugs (azathioprine, cyclophosphamide) and anti CD20 monoclonala antibody

Immunosuppressive therapy was prescribed in 24 patients, anti-CD20 monoclonal antibody were prescribed in 8 patients and splenectomy was permormed in 24 patients and intravenous immunoglobulins in 14 patients.

Conclusions: Glucocorticoids and/or intravenous immunoglobulins are the mainstay of the treatment in the majority of patients with warm AIHA. When these treatments fail, patients often require cytotoxic drugs or splenectomy.

15. BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM - AN ORPHAN HEMATOLOGIC MALIGNANCY

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare type of hematologic malignancy with an aggressive course, that most frequently manifests as cutaneous lesions with or without bone marrow involvement and leukemic dissemination. Early recognition of BPDCN has been challenging because its clinical features can be heterogeneous and can overlap both lymphoma and leukemia manifestations. There can be a significant delay between the onset of symptoms and diagnosis. The exact incidence is unknown because it is very often misdiagnosed and underreported, but it is thought to occur an estimated 1.000 to 1.400 cases annually in the US and Europe combined. The average age at diagnosis is 60 to 70 years. There is a male predominance with a male to female ratio of approximately 2,5:1. Currently, there is no standard of care for BDPDCN and various approaches have been used including acute myeloid leukemia, acute lymphoblastic leukemia and lymphoma-based regimens with or without stem cell transplantation. Patients diagnosed with BPDCN have a poor prognosis with a median overall survival from diagnosis of approximately 1 year despite the use of combination chemotherapy.

In this manuscript, we present a 7 case series of patients diagnosed and treated in our clinic in a 5 year period (from September 2017 -September 2022). The group is composed of 5 men and 2 women with an age range of 63 to 75 years old at diagnostic. Cutaneous involvement was the initial presentation in all patients, with deep purple or red-brown macules, plaques or tumors. Cytopenias were also present in all cases indicating bone marrow involvement. Diagnosis was based on a comprehensive analysis of histopathologic, morphologic, immunophenotypic and clinical criteria. The therapeutic approach consists of regimens used for acute lymphoblastic leukemia in the elderly (VCR+Doxorubicin+Dexamethasone), CEOP, COP, low dose chemotherapy, high dose corticosteroids and palliative chemotherapy. The efficacy of conventional chemotherapy was limited, with a median survival less than 12 months. One patient was recently diagnosed and

still being treated with acute lymphoblastic leukemia-type regimen used for the elderly, with regression of cutaneous lesions, normalisation of hematologic parameters and improvement of symptoms.

16. POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE – EXPERIENCE OF HEMATOLOGY DEPARTMENT OF FUNDENI CLINICAL INSTITUTE

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Introduction: Posttransplant lymphoproliferative disease is a heterogeneous group of disorders, arising after solid organ transplant or hematopoietic stem cell transplantation. There are described four types of lymphoproliferation:

1. Early type – consisting in a nondistructive lymphoplasmacytic proliferation
2. Polymorphic PTLD – histopathological with distructive lymphoplasmacytic proliferation, but not enough criteria for malignancy
3. Monomorphic PTLD – histopathological criteria for malignancy
4. Sporadic cases of Hodgkin Lymphoma

More than 70% of PTLD have their origin in B lymphocyte; the most frequent malignant B cell proliferations are: Burkitt lymphoma, DLBCL, plasmablastic and immunoblastic lymphoma, multiple myeloma, primary CNS lymphoma. T cell lymphoproliferation and Hodgkin Lymphoma are uncommom findings.

Objectives; This is a clinical, epidemiological and biological characterization of the patients who went through a transplant (solid organ or HSC) in our hospital and developed earlier or later a form or another of PTLD.

Material and methods: We present the experience of Hematology Department of Fundeni Clinical Institute with the diagnosis, treatment and follow up of 14 cases od PTLD that were addressed to our unit over a 12 years period (2010-2022). We looked over clinical, biological, histopathological and therapeutic data, alongside the complications following treatment.

Results: Our review analysed 14 cases of PTLD (10 men and 4 women), average age was 52 yo. They underwent solid organ transplant in 13 cases (7 renal and 6 hepatic) and one patient had bone marrow transplant. The PTLD types (according to WHO 2016 classification) were: DLBCL (5 cases), multiple myeloma (2 cases), Hodgkin lymphoma (1 case), hairy cell leukemia (1 case), mycosis fungoides (1 case), lymphocytic NHL (1 case) and 3 cases of nondistructive lymphoproliferation. Time between these two events (transplant and diagnosis of PTLD) was about 8 years; 4 patients deceased due to sepsis and/or progressive disease.

Conclusion: PTLD ia a rare, heterogeneous disease that requires a multidisciplinary team for the best aproach of the patient.

TRANSFUSIONAL MEDICINE

1. A NEW PLATELET STORAGE METHOD APPROVED FOR THE AMERICAN ARMY - IN PERSPECTIVE ALSO FOR ROMANIA, A NATO MEMBER COUNTRY?

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Introduction

Platelets play a critical role in normal hemostasis and control of bleeding. Platelet concentrates are used to prevent bleeding in patients with thrombocytopenia, to treat patients with dysfunctional platelets, or to treat active bleeding (in massive transfusions or surgical bleeding). Platelet components are prepared by whole blood collection or collected by apheresis, platelets can be stored in plasma or platelet

additives that can undergo further modifications, such as reduction of pathogens.

Material

Worldwide, platelet components are generally stored at 20 - 24 ºC for 5-7 days, depending on the storage container and additional measures to control the bacterial risk. Storage at 20 - 24ºC, requires continuous agitation to facilitate oxygen utilization and maintain optimal morphology, physiology, function and pH during storage. For storage at 20 - 24ºC, the shelf life is currently limited to 5 days,

unless extended (up to 7 days) using an FDA-approved bacterial safety test device.

Most platelet transfusions are given prophylactically to reduce the risk of spontaneous bleeding in patients who are thrombocytopenic following chemotherapy or hematopoietic stem cell transplantation. While the role of platelets stored at 20-24ºC has been extensively studied in this clinical setting, only limited data are available to support the transfusion of cold-stored platelets in other patient populations for other clinical indications, such as perioperative or traumatic bleeding. The FDA

recently granted approval to the South Texas Blood & Tissue Center to manufacture and distribute cold- stored platelets with a 14-day shelf life for the treatment of patients with active bleeding when conventional platelets are unavailable or impractical.

With this new process, developed by researchers at the Trauma Hemostasis & Oxygenation Research Network and the US Army, platelets are refrigerated within 2 hours of collection. This process extends their viability to 14 days for use in patients with active bleeding; however, the platelets made in the new process are only intended to treat bleeding and are not indicated to prevent bleeding in patients with

low platelet counts. This new process increases the availability of platelets for the treatment of actively bleeding patients when conventional platelets are not available, and also helps maintain platelet concentrate availability to rural critical access hospitals so they can treat bleeding patients when conventional platelets are not available.

Cold platelets undergo cytoskeletal rearrangements that allow platelet priming and provide a hemostatic advantage over room temperature platelets in the bleeding patient. Cold-stored platelets are activated during storage, providing the advantage of improved coagulation and hemostatic effects.

Ultrastructurally, refrigeration results in cytoskeletal rearrangements that cause actin filaments to grow and microtubule bands to lose.

In vitro analysis shows improved clot formation in cold-stored platelets. At approximately 24 hours, the effects of refrigeration become irreversible and platelets will exhibit a permanent disc-to-sphere

configuration and rapid clearance by the liver after transfusion. Compared with cold-stored platelets, room-temperature platelets offer the advantage of providing increased platelet counts with predictable recovery and improved corrected count growth, and are the preferred method of platelet storage used for prophylaxis in nonbleeding patients with thrombocytopenia or hyporegenerative thrombocytopathies.

Cold-stored platelets have increased aggregation and reduced risk of bacterial contamination compared to room-temperature platelets. Bacterial risk in platelets at room temperature reduced the shelf life to 5 days. STBTC, a subsidiary of BioBridge Global, is the first US civilian blood center to receive supplemental approval to produce cold-stored platelets up to day 14 of storage. The Mayo Clinic has produced and transfused 3-day cold-stored platelets, and the Army has received FDA approval to produce 14-day cold- stored platelets for the treatment of actively bleeding patients as of 2019.

Conclusion

Cold platelets mitigate the risk of bacterial contamination, enabling not only a product that offers improved hemostatic potential, but also an improved microbial safety profile and potentially an extended shelf life of up to 14 - 21 days for transfusion services, for improve the safety and availability of platelets for transfusion. Cold platelets bring a new perspective to the future, having the potential to alleviate much of the burden of the problems related to the limited supply of platelet concentrate.

2. ASSESSMENT OF FVIII LEVEL IN REGULAR BLOOD DONORS FROM BUCHAREST BLOOD BANCK

L. Rusen
INTS

Introduction

Plasma is a blood component obtained either from a unit of whole blood by primary processing or by apheresis with an automatic separator from the venous blood of a donor. After obtaining it freezes quickly. Fresh frozen plasma (FFP) can be transfused to patients or the surplus can be used to obtain medicines (concentrates of coagulation factors, immunoglobulins, albumin, etc.) through industrial fractionation.

Material and method

The Bucharest Transfusion Center (CTSMB) implemented a new automatic blood processing method in the last year, the first processed bags being hematologically and bacteriologically controlled to validate the method. The Guide for the Preparation, Use and Quality Assurance of Blood Components recommends dosing of FVIII. On this occasion, in the second stage, in 703 whole blood donors (of which 480 men and 223 women), the level of FVIII C was determined on the automatic Sysmex CS 2500. The PPC obtained from these donors was tested at one month and at 3 months after obtaining to see what level of FVIIIC is maintained in the bag during processing, freezing, storage and then thawing.

Results and discussion

Analysis of the FVIII level in the 703 donors shows that those with blood group O have lower average FVIII values than the other blood groups. It was also found that donors older than 50

years have higher FVIII values. Testing the level of FVIII in the PPC bag shows that the percentage of recovery of FVIII through the process of freezing, preservation, thawing was on average 80% after the first month of storage and 85% after 3 months of storage.
Conclusions:

- The specialized literature suggests that there is a loss of FVIII during storage, transport and thawing of plasma before administration to the patient or industrial processing;
- FVIII level testing at each blood bank for 10 units every 3 months after the first month of storage must be continued to verify the technological process of processing, freezing and storage.
- Both PPC intended for transfusion and that intended for fractionation must meet quality standards.

3. BACTERIOLOGICAL CONTROL OF BLOOD AND BLOOD COMPONENTS. THE BLOOD CULTURE CONTAMINATION RATE

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Blood culture is the gold standard method for detecting blood infections. Blood cultures can become contaminated with microorganisms from the skin or the environment, which multiply in the culture bottle, giving the false impression that these organisms are present in the blood .

The quality control of blood units and blood components is carried out within the LCCC within INTS, with strict compliance with the CoE methodology and norms from the Guide for the preparation, use and quality assurance of blood products, as well as with national legislation (Ord. MS 1237 /10.07.2007, completed by 13361/19.09.2011 and 814/14.08.2012.

Bacteriological control of blood and blood components is a control that aims to permanently monitor the risk of bacterial contamination of blood components.

False positive results in blood cultures can occur due to contamination during pre-analytical procedures such as sample collection and sometimes during sample processing. (inoculation of vials with aerobic and anaerobic media) .

Material and method

Type of study - Observational study.

Study duration - 6 months

Sample size - 220 samples

A total of 220 blood products were collected (positive samples sent for confirmation within LCCC + samples inseminated in LCCC)

Positive samples - 6 products

The blood culture contamination rate in LCCC is 2,72 %, which is within the limit according to the Standard Guide. The reference value of the blood contamination rate . proposed by the Standard Laboratory Institute (CLSI) is less than 3.

Conclusion

Monitoring the contamination of blood cultures is an important indicator of ensuring the quality and performance of the laboratory.

The contamination occurred mainly due to improper skin disinfection and environmental contamination.

4. BBTC – STRATEGY FOR PROMOTING BLOOD DONATION AND ACTIONS TO INFORM THE POPULATION WITH THE PURPOSE OF INCREASING THE NUMBER OF DONORS

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In Europe, the majority of the national and regional transfusion centres have reported a decrease in the collection of blood and blood components during the pandemic. In the context of various challenges and unexpected changes, all transfusion centres have made significant efforts to rethink blood collection.

The behaviour of donors has changed greatly within this time period, so the greatest challenge remains recruiting them and, especially, maintaining their loyalty.

The actions of transfusion centres have required new approaches, and they are now focused on sustained promotion of blood donation and on active information of the community, but also on the individual's motivation to become a donor and to come back to donate.

The Bucharest Blood Transfusion Centre does not benefit from people specialized in promotion, but lately, through collaboration with partner institutions, various organizations and associations, it has managed to diversify and adapt its promotion campaigns, to adapt them to various organizational styles, to run specific projects to inform the youth and to implement programs adapted to specific target demographics.

The ultimate goal is to increase the level of awareness, and this will help us deal with future challenges!

5. BLOOD COMPONENTS FOR NON-TRANSFUSION USE

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In recent years, the use of blood components for non-transfusions has expanded, including in Romania, in various specialties (dermatology, dentistry, orthopedics, ophthalmology, etc.).

Numerous publications describe the evolution of these procedures, the results obtained, and the manufacturers reacted quickly by creating special kits and equipment, for example, for the preparation of platelet-rich plasma, a generic term for various variants of preparations prepared in the medical office. Allogenic or autologous platelet concentrate, platelet gel, eye drops prepared from human serum or platelet concentrates are preparations of this category, which are prepared in medical offices or blood transfusion centers in various countries.

The evolution of research and implementation in medical practice of the use of these blood preparations occurred despite the fact that, although they came from human blood, there were no provisions regarding this category of products in the European directives that regulate, since 2002, the field of substances of human origin. As the phenomenon develops, various EU Member States have discussed the need to create a European legislative framework on harvesting, preparation, storage, transport, administration conditions. Some States have developed recommendations, guidelines for the use of these components obtained from human blood, but not used for transfusion purposes.

In Romania, platelet-rich plasma is already used in routine, in the individual cabinet.

The paper summaries the various types of blood components intended for uses other than intravenous administration.

The extension of the field of activity of some blood transfusion centers in Romania, in the future, by introducing the preparation of such products, following the example of other countries, can represent an opportunity for development, with benefits for Romanian patients, in collaboration with specialists with experience in their use.

6. BLOOD DONOR – FROM INTENTION TO DONATE TO LOYAL DONOR PROFILE

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TSNI

The Covid-19 pandemic affected the society and has had a negative impact on blood donation, leading to a significant reduction of blood supplies not only at national level but worldwide. The lockdown and restrictions in terms of physical presence, combined with fear of unknown when it came to Covid-19 transmissibility pathway, determined a significant reluctance of donors to participate at donation, regardless of their stage in the process. The actual online social survey explored the motivators and detractors which influence blood donation decision, on the pathway from intentional stage to recurrence stage, at socio demographic and emotional level.

The questions were focused on what the respondents think, feel, speak and do, aiming to identify the perceptions which influence the participation or nonparticipation to blood donation. The survey approaches the full spectrum of donors, from those interested to participate to optimal recurrent donors. The goal of the survey is to identify intangible resources and support the blood donation advertising, contributing to enhanced predictability and efficiency of the process.

The research tools engaged for the survey implementation were quantitative consisting in psychometric scale and qualitative consisting in open questions.

7. CHALLENGES IN THE MANAGEMENT OF ACUTE PANCREATITIS WITH CONCURRENT AUTOIMMUNE HEMOLYSIS

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Introduction: In autoimmune hemolytic anemias, autoantibodies are produced that bind to and destroy the patient's red blood cells (RBC). Cold agglutinins are antibodies that bind to RBC antigens at temperatures below 37ºC. They can cause RBC agglutination and extravascular hemolysis, with secondary anemia without hemoglobinuria.

Case report: A 67-year-old male patient is admitted to the general surgery department with a diagnosis of acute pancreatitis, vesicular lithiasis, T2DM, hypertension. When performing a complete blood count – there were errors in validating the Hb and MCV values, which were

resolved after warming the blood sample to 37ºC. Also, in the transfusion department, the blood type cannot be determined, as agglutination occurred in both the Beth-Vincent and Simonin tests. It was necessary to use additional techniques (heating the sample to 37ºC and RBC washing) to validate the blood type – OI positive. The clinical status required emergency surgery, the patient presenting a serum lipase value: 18812 U/L and a total bilirubin value: 20.8 mg/dL. Laparoscopic cholecystectomy with intraoperative cholangiography and transcystic tube placement is performed.

In post-op, the patient presented a sudden drop in Hb from 8.8 g/dL to 4 g/dL within a couple of hours without overt blood loss. Secondary to this sudden reduction, the clinical status worsened, raising the suspicion of acute coronary syndrome, the patient requiring emergency PRBCs administration. Detection of anti-erythrocyte antibodies was positive and the DCT was also performed: intensely positive +4 (polyvalent and monovalent / IgG +4, IgG+C3d +4). The presence of cold agglutinins was observed, in high titer of 1/2048 – 1/4096. Peripheral blood smear showed signs of extravascular hemolysis and very frequent erythrocyte agglutination. Using additional techniques a few compatible PRBC units were identified, which were administered cautiously resulting in Hb correction.

Conclusion: Patients with cold agglutinins may develop acute hemolytic reactions during surgery or after cold exposure due to complement activation. In autoimmune hemolytic diseases and especially in cold agglutinin disease, there are difficulties in validating both the blood count and the pre-transfusion tests. Thus, interdisciplinary collaboration is indispensable.

8. CLINICAL CHALLENGES IN THE PRE-TRANSFUSION TESTING ACTIVITY WITHIN THE UTS-SCUB

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The motivation for choosing this topic debated in the work is represented by the complexity of the specific activities of the Emergency Hospital carried out within the UTS. This hospital represents the point of contact for the most critical cases in Bucharest, the province and not infrequently even some cases from outside the borders (the last case the accident in Bulgaria - publicized).

In the last 2 years and with the outbreak of the SARS CoV-2 pandemic, the activity of the Vascular Surgery clinic has intensified by dealing with extremely complex cases, becoming a big consumer of blood products. The number of polytransfused, hemodynamically destabilized patients (with very low Hb values) presented in the UPU (polytraumas, road accidents, domestic accidents, burns, digestive hemorrhages, tumors etc.) has also increased.

Simultaneously with the closure of the collection point for blood donors and blood components in UTS-SCUB during the pandemic, the decrease in the number of blood donors and the increase in the number of patients who required transfusion treatment in the period Jan 2019-Dec 2021, as well as compliance with quality standards according to law 328/2018 on pre-transfusion tests, the workload and degree of complexity of the activity of the medical staff in UTS-SCUB increased.

Thus, between January 2019 and December 2021, the following types of tests were carried out: 96.417 group determinations, 15.518 DAI, 17.608 phenotype determinations, 32.486

compatibility tests, - 2,500 detection of anti-D antibodies.

In certain cases, besides the fact that they constituted emergencies from the point of view of transfusion, they also assumed a special degree of difficulty in elucidating the blood group determination or in choosing a compatible blood product. There have been cases of major emergency in which the emergency procedure was applied by administering MERDl O neg due to discordant blood group, the presence of non-specific antibodies and autoantibodies.

9. COMPLICATIONS OF TRANSFUSION IN PATIENTS WITH MAJOR THALASSEMIA - NATIONAL INSTITUTE OF BLOOD TRANSFUSION EXPERIENCE

D. Voicu, F. Vladareanu, L. Nitu, C. Mitru

NIBT

Introduction: Blood transfusions along with iron chelation treatment still remain the basic therapeutic option in β Thalassemia major. Although it has brought enormous benefits, the chronic transfusion regimen, through prolonged exposure to blood components, subjects polytransfused patients to associated risks, the most important being iron overload, transmission of infections, transfusion reactions, alloimmunization against some erythrocyte antigens.

Material and method: The 100 patients with Thalassemia major with evidence of INTS between 12 and 55 years of age, chronic transfusion regimen at intervals of 2/5 weeks were evaluated, all patients are transfused with erythrocyte components, leukodepleted, isogroup, isoRh, in RhKell phenotype, compatible according to the pre-transfusion protocols. All patients are on iron chelation treatment, either oral or injectable.

Results: For the population of patients with β Thalassemia major, the population that has the highest transfusion exposure among chronic diseases, hemosiderosis remains an important and extremely widespread complication. Although the introduction of the oral chelator in 2008 improved treatment compliance and there are patients who do not have a pathological iron load, there is still a significant percentage of patients with severe post-transfusion hemosiderosis with a history of organ dysfunction: heart failure, gonadal dysfunction, diabetes , cirrhosis.

The patients in our group show evidence of previous exposure to transfusion-transmitted infections: HCV(48%), HBV(1%), HTLV(21%), all of them being adults, transfused before the introduction of the extended virological testing protocol of blood donors. Transfusion reactions occurred were allergic ones, rashes, itching (10%) or non-hemolytic ones, chills-fever (9%) of mild or medium intensity. No anaphylactic reactions or acute hemolysis were recorded. Alloimmunization is present in 6% of the patients in our group, their specificity being anti-C, Anti-K, Anti-Cw.

Conclusions: Posttransfusion hemosiderosis and immunological and non-immunological complications still remain an important challenge in the management of polytransfused patients with thalassemia major.

10. CONTINGENCY AND EMERGENCY PLAN FOR THE SUPPLY OF BLOOD AND BLOOD COMPONENTS

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Introduction

Emergency planning and preparation are key elements of a transfusion system. It is essential to ensure that when the transfusion system is faced with emergency situations, a safe and adequate blood supply can be maintained and made available for all essential transfusions, ensuring that when faced with interruptions, the ability of the transfusion system to continued delivery of blood, blood components

and related services is maintained. Emergency preparedness is the assurance that a transfusion system manages the impact of an unexpected event, and can provide the blood, blood components, and associated services needed by the healthcare community during the ongoing emergency/disruption.

Material

In order to create a CONTINGENCY AND EMERGENCY PLAN FOR THE BLOOD SUPPLY, the Prahova, Constanta, Buzau transfusion centers started creating a PLAN targeting the following elements: system organization, functions, interactions and roles in ensuring the continuity of the blood supply; legislation, guidelines / standards in force applicable to the activities carried out, taking into account those

applicable to planning for emergency situations, existing emergency plans relevant to the transfusion system; approach to patient blood management and clinical management of blood and blood components in emergency situations; arrangements in place for interregional collaboration/backup services relevant to the transfusion system.

In an attempt to prepare a CONTINGENCY AND EMERGENCY PLAN FOR THE BLOOD SUPPLY, the Prahova, Constanta, Buzau transfusion centers began an evaluation of the way of working and of the available equipment including: collection and processing strategies, testing methods within blood supply chain, donor, blood component testing (screening for blood-borne infections; immunohaematological

testing, ABO and RhD grouping, phenotyping, irregular antibody screening; additional tests; blood component quality control tests), assessment of equipment available for storage of blood and blood components, methods of distribution of blood and blood components in hospitals, the data processing system used for the traceability of the collection, processing, release, distribution and release of blood

components, the labeling system. A possibility of creating emergency protocols for blood supply chain activities was taken into account, emergency protocols for transfusion chain activities being related to short and long-term unavailability, partial or complete interruption of activities (donation, collection, testing, processing, storage, distribution) or premises, including collection/processing sites and testing

laboratories.

In creating this BLOOD SUPPLY CONTINGENCY AND EMERGENCY PLAN, the key equipment and materials used for blood supply chain activities and their list of suppliers have been assessed, assessing supplier agreements, considering measures to facilitate the mitigation of the effects of supplier-dependent shortages which could include measures to reserve sufficient safety stocks of single-use materials for

donation/processing/testing, reserve equipment/spare parts and service contracts; critical backup materials compatible with routine collection/processing/testing procedures; temporary replacement with appropriate equipment from other suppliers/brands compatible with routine donation/processing/testing procedures.

Emergency protocols between the three centers will provide for measures to alleviate the reduced capacity for donation, processing or testing; strategies for temporarily increasing donations (general or specific blood groups/component/characteristics), processing or testing capacity; priorities of components to be processed in case of reduced processing capacity; collection and processing sites, including partial or full reserve of blood supply, materials and equipment and/or personnel; testing

laboratories for back-up testing, including transport of samples and transfer of test results to their own data processing system, materials and equipment and/or personnel; agreements to share/exchange blood components. The protocols taken into account will include defined arrangements for transport; reserve storage of blood, blood components or tests or increased storage needs; preparation for acceptance of external blood components, preparation for storage site/capacity and transfer of test

results for external blood components; preparation for accepting the results of external tests in its own data processing system; coordination of new donation sites, processing of new blood components, transport alternatives, testing procedures, as appropriate; data processing system failure including, where applicable, manual paper backup systems and tagging strategies.

Conclusion

For unforeseen situations that may arise at any time, at least the following national risk scenarios should be assessed: disruption of the supply chain or critical activities associated with the blood supply including infectious risks/epidemics/pandemics, extreme weather events, mass casualties/terrorist attacks, damage to business premises or facilities, power outages, computer system failure, etc., and a NATIONAL BLOOD SUPPLY CONTINGENCY AND EMERGENCY PLAN should be made.

11. COVERING THE NEED FOR BLOOD BETWEEN CHALLENGE AND ACHIEVEMENT

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Plan to promote blood donation, different approach in the context of the Covid 19 pandemic and in the current global economic and social context

I. FINDING / TRAINING GROUP LEADERS

1 Definition of key elements

2 Elaboration of the message

3 Broadcasting the message to the public

II. CONVINCING DECISION-MAKERS OR POLITICIANS (LOBBY) TO CHANGE POLICIES

CAREFULLY PREPARING FOR MEETINGS – Lobby

III. USE OF THE MASS MEDIA

Communication is the key element of any promotion campaign.

IV. CREATION OF PARTNERSHIPS

A successful promotional campaign also means creating alliances between various organizations.

V. MOBILIZING THE COMMUNITY TO ACHIEVE CHANGE

The essence of any social change is represented by people. A good campaign manager listens before he acts.

Other group leaders are being identified, prepared and will be promoted. - Deadlines are set for the actions undertaken.

CTS plan for the permanent promotion of blood donation to protect blood donors and health workers also in the context of the COVID-19 pandemic

A permanent collaboration between all the CTS in the country and a special collaboration between the CTS from neighboring counties is necessary.

Today, blood transfusion is a crucial element of medical care. To ensure the sustainability of the blood supply, it is essential to have a supply system that is resilient and capable of withstanding widespread crises.

A clear, proactive and consistent communication strategy is essential. Donor mobilization is essential every day to meet patient needs that remain constant throughout the year. Indeed, blood donations must be regular and constant, because the shelf life of blood products is limited.

As a transfusion center, we cannot do everything. We need the will of the authorities, with a concerted effort from all departments. There needs to be a national blood donation strategy with a real communication strategy.

The national blood transfusion strategy should be reviewed based on the current scenario (pandemic, war) to avoid future blood shortages by collaborating with transfusion specialists, transfusion centers and doctors in transfusion centers and hospital clinicians who use transfusion therapy .

12. DIFFICULTIES AND PARTICULAR ASPECTS OF THE PRE-TRANSPHYSICAL STAGE IN NEWBORNS AND INFANTS

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Constanta Blood Transfusion Center

Newborns, especially those with low birth weight, are among the categories of patients who receive frequent transfusions. Since, due to physiological particularities, in this category of patients the transfusional risks are higher than in other categories, there are many specific

aspects to be considered when prescribing transfusional treatment to newborns and infants. Age particularities generate differences in transfusional practice compared to protocols and procedures applied to children and adults. Among the specific physiological aspects that require particular protocols for prescribing, selecting, administering blood components to newborns and infants, we mention the prenatal transfer of maternal anti-erythrocyte antibodies into the circulation of the fetus, immature immunologically, which determines a unique model and precautions for ensuring immunomatological compatibility, different from those required in other age groups.

The paper presents the particular aspects of the procedures applicable in hospitals, in the pre-transfusion stage, in the case of the prescription of transfusional treatment to newborn and infant patients, as a result of the physiological particularity mentioned.

The national guidelines on the administration of transfusions to newborns and infants shall include recommendations on the pre-transfusion test protocol, including requirements on the type and volume of blood samples, the minimum set of tests required for the selection of compatible units, alternative solutions for situations where blood samples cannot be secured according to standard procedures (blood samples from the mother, 2 samples from the patient for blood type validation, etc.). At the level of each hospital with departments of neo-natology, pediatrics, the development, validation and implementation of protocols and procedures for the administration of transfusional treatment to newborns and infants represents a mandatory minimum requirement, condition for ensuring the safety of patients and the consistency of medical assistance to this particular category of patients.

The collaboration of the commission of Neo-natology with the Transfusion commission of the Ministry of Health could facilitate the development of the mentioned guides. Collaboration between specialist neo-natologists, pediatricians, the UTS coordinator and the blood transfusion center specialist is a prerequisite for ensuring timely optimal blood components for this category of patients.

13. DIFICULTIES IN THE INTERPRETATION OF ELISA TECHNIQUES IN THE DIAGNOSIS OF PARENTERALLY TRANSMITTED VIRAL INFECTIONS IN HUMAN BLOOD AND BLOOD COMPONENTS DONORS

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PREMISES: Viruses such as hepatitis B virus (HBV), hepatitis C virus (HCV),human immunodeficietcy (HIV), Human T- lymphotropic virus (HTLV) can be transmetted through blood and human blood components obtained from blood donors. The diagnosis of infections with these viruses at the level of yhe blood transfusion network in Romania is made trough the use of immunoenzymatic techniques (ELISA), as screening tests.

In countries with low and moderate incidence and prevalence, a significant proportion of blood donors whose donations are „REACTIVE” in screening tests are not actually infected.

Objectives:

- ELISA testing of blood and blood components obtained from blood donors

- Correlation of the reliability of the results obtained at the level of Craiova Regional Blood Transfusion Center of the samples interpreted as „REACTIVE" with the results of the testing carried out by the Central Laboratory of the „Ştefan Nicolau" National Institute of Blood Transfusion Bucharest where these samples were sent for confirmation.

Material and methods

a)_ Material:

- 17.000 donations from 2021 -2022 tested at Craiova Regional Blood Transfusion Center; 165 „REACTIVE" samples to HBsAg, anti- HCV and anti- HIV sent for confirmation to the Central Laboratory of National Blood Transfusion Institute.

b)_ Methods:

- ELISA testing of blood and blood components obtained from blood donors at Craiova Regional Blood Transfusion Center for viruses : HBV, HCV, HIV 1+2;
- at the level of the Central Laboratory of National Blood Transfusion Institute were used:

  - for HBsAg: an ELISA serological screening test, an alternative serological screening test, specific inhibition test;

  - for anti- HCV: an ELISA serological screening test, an alternative ELISA serological screening test from another manufacturer, immunoblot;

  - for anti- HIV 1+2: an ELISA serological screening test, CLIA test for determination anti- HIV 1+2 antibodies, a test for determination HIV 1 p24 antigen;

If the first sample was interpreted as „REACTIVE", the recomandation of Central Laboratory was to retest on the second new sample 4-8 weeks after the first. The diagnosis was made after testing the second sample by the Central Laboratory .

RESULTS and DISCUSSION

I. For HBV: the presence of the virus was investigated by detecting HBsAg at Craiova Regional Blood Transfusion Center; 44 sera were interpreted as „REACTIVE" for HBsAg.

At Central Laboratory the results were the following:

- 4 positive sera;
- 22 negative sera (50%) - not confirmed for the presence of HBsAg;
- 18 sera were „REACTIVE" (40.91%) in ELISA serological screening test, but using a specific inhibition test or when combining a specific inhibition test with an alternative serological screening test, the result was „NEGATIVE".

II. For HCV: the presence of the virus was investigated by detecting anti- HCV antibodies.

At Craiova Regional Blood Transfusion Center 61 sera were interpreted as „REACTIVE"

At Central Laboratory the results were the following:

- 9 positive sera;
- 22 negative sera (unconfirmed)- 36.06%;
- 30 „REACTIVE"sera (49,18%) using an ELISA test for serological sreening; when using the immunoblot for HCV the results were: NEGATIVE - 28 units and 2 „INCERT", showing anti- S3 antibodies on the immunoblot. For these 2 units the

opinion formulated was: possible HCV infection in the past or non- specific anti- S3 reactivity in a serological screening test.

III. For HIV 1+2: the presence of the virus was investigated by detecting anti- HIV 1+2 antibodies at Craiova Regional Blood Transfusion Center where 60 sera were interpreted as „REACTIVE".

At Central Laboratory where, in addition with anti- HIV 1+2 antibodies, the p24 HIV 1 anigen was performed and the results were the following:

- 20 negative sera (33.33%);
- 40 „REACTIVE"sera (66.66%) using an ELISA serological screening test. For the samples „REACTIVE" at the first test, the recomandation was to retest a new sample, collected over an interval of 4-6 weeks from the first.
- For all sera the p24 HIV 1 anigen was „NEGATIVE".

Comparing the result obtained in a serological screening test in the second sample with the one obtained in the first, the conclusion was that is non- evolving reactivity compared to the previous sample, so a persistent non-specific reactivity in a serological screening test. The serological diagnosis for these samples was „NEGATIVE".

Conclusions

1)_ The concordance rate of reactivity diagnosed at Craiova Regional Blood Transfusion Center with Central Laboratory was 61,20%:

- 53,33% non- specific reactivity;

- 7,87% positive sera for the investigated viral infections

2)- The rate of non- concordance of reactivity between the two laboratories was 38,78%;

3)- The causes of non- specific reactivity of the sera could be:

- the type of ELISA test used for testing with a certain constellation of antigens/antibodies;

- the sensitivity and specificity of the ELISA test used;

- possible contamiation of the wells during plate washing;

- the value of „ gray" or „uncertainty"area;

- the presence in the donors serum of other substances or antibodies/antigens (e,g Anti-Herpes Simplex IgG, Influenza Virus antibodies);

4)- Equipping the laboratories at the County Blood Transfusion Centers with a second test (alternative serological screening test) or with NAT.

14. EPIDEMIOLOGICAL ASPECTS OF SARS CoV 2 INFECTION IN BLOOD DONORS FROM WESTERN ROMANIA

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Aim: To evaluate the burden of SARS CoV 2 infection in blood donors declared eligible at the Regional Blood Establishment Timișoara, after the first and the third pandemic wave and to search for correlations between SARS CoV2 antibody seroprevalence and age, gender, area of residence or blood group.

Material and method: In order to estimate the SARS CoV2 seroprevalence, in July and August, we have screened 2115 donors in 2020 and 2395 blood donors in 2021. All the serum samples were tested for total anti - SARS CoV 2 antibodies (IgA, IgM, IgG) using an electrochemiluminescence assay, based on a recombinant nucleocapsid protein (N) (Elecsys, Roche Diagnostic GmbH, Germany).

Results: The majority of blood donors included in this study, aged between 18-65 years, were males and residents of urban areas. The overall seroprevalence of SARS CoV 2 antibodies was 1,51% in 2020 (32/2115) and increased to 41,04% in 2021 (983/2395). No statistical differences, between seroprevalescence and age groups, gender, area of residence, or the ABO, Rh blood group, were observed.

Conclusions: The present study demonstrated a significant increase of the SARS CoV 2 seroprevalence, after the third pandemic wave, meaning an increase in the spread of the virus. We are equally exposed to the risk of infection with SARS CoV 2, regardless of age, gender, area of residence or blood group. The only way, in order to reduce transmission of Covid 19, is to respect the prevention measures.

Key words: blood donor, SARS CoV 2, seroprevalence.

15. FACTORS THAT CAN INFLUENCE THE QUALITY OF PLATELET BLOOD COMPONENTS

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Premises: Haematological and bacteriological quality control of labile blood products, along with other donation qualification tests, are the main tools that ensure the safety and quality of whool blood and blood components.

Objectives: Verification of the quality of platelet- type blood components obtained at the Craiova Regional Blood Transfusion Center in 2022, units that must meet haematological parametres specified by national and international standards.

Material and methodes

a)- MATERIAL: a number of 35 platelet concentrates were qualitatively evaluated: 23 standard platelet concentrates and 12 platelet units obtained by apheresis.

b)- METHODS: to obtain standard platelet concentrates, the classic methodology imposed by good practice in the blood transfusion network used, and for Platelet Units obtained by apheresis: the Trima Accel- Terumo BCT automatic equipment.

Results and discussions

I)- In the case of standard platelet concentrates:

- total number of qualitatively evaluated units: 23/2022;

- the standard quality hematological parameters that these components must meet: volume: 50- 60 ml, platelet count: > $60x10^9$/unit, leukocytes< $0.2x10^9$/unit, pH >6.4.

At the standard platelet concentrates units under study:

a)- Volume: 34.12- 90.73 ml, which means higher volume at 17 units (therefore non-compliant), and 6 unitas compliant;

b)- The number of platelets/unit: 47.55- 127.75 $x10^9$; 4 units were non- compliant(45.55- 58.67 $x10^9$/unit), 17 compliant units and 2 at the limit of acceptability(59.99- 59.42 $x10^9$/unit);

c)- The number of residual leukocytes: all units were compliant;

d)- pH value: could not be determined pH value because we didn′t have the appropriate equipment for this determination.

II)- In the case of platelet units obtained by apheresis:

- total number of qualitatively evaluated units: 12 in July and August 2022;

- the standard quality hematological parameters that these components must meet: volume: > 40 ml/$60x10^9$/unit, total platelet count: > $200x10^9$/unit, residual leukocytes < 1 $x10^9$/unfiltered unit or < 1 $x10^6$/filtered unit, pH: >6.8- 7.4.

At the platelet units obtained by apheresis under study:

a)- Volume: corresponding to the requirement in the nomenclature for these blood components, between 189.03- 226.84 ml;

b)- Total platelet count/unit: 179.39- 387.08 $x10^9$/unit;9 units were compliant, 2 at limit acceptability (196.75 $x10^9$/unit; 198.15 $x10^9$/unit) and 1 non- compliant (179.39 $x10^9$/unit)

c)- The number of residual leukocytes: all units were compliant; in all units the number of residual leukocytes was < 1 $x10^6$/filtered unit, compliant results;

d)- pH value: could not be determined pH value.

Conclusions

1)- Quality of platelet units obtained by Apheresis:

If we consider the haematological parameters provided by national standatds, compliant units and the limit of acceptability as criteria, the conclusion is: 91.66% of the units were compliant and only 8.33% (1 unit) was non- compliant, so the platelet units obtained by apheresis at the Craiova Regional Blood Transfusion Center correspond qualitatively.

2)- Quality of standard platelet concentrates:

a)- Volume: 73.91% of the units were non- compliant, with a higher volume compare with that stipulated by national legislation, which highlights an incorrect processing pertformed to obtain these components;

b)- The number of total platelets/unit: 82.60% of these blood components met the quality requirement;

c)- The number of residual leukocytes/filtered unit: all units (23) were compliant;

3)- The causes that could determine these non- compliant aspects of platelet concentrates could be: an incorrect processing for obtain these units or an incorrect processing of point of the quality assessment of these units which could mean:

- an inadequate centrifugation parameters;
- an incorrect elimination of the plasma in the case of Standard Platelet Concentrates;

- incorrect storage of these units until processing;
- not properly shaking the units before analysis;
- keeping the samples for qualitative determinations in the test tube without a stopper for a long period of time.

16. IMMUNOHEMATOLOGICAL DISCORDANCES AND ABNORMALITIES IN THE ABO SYSTEM

A. Zagrean
Bucharest Blood Transfusion Center

Objectiv

To make known the most common discordances encountered in the laboratory routine in the ABO system.

To present some ways of resolving these discords.

Materials/Methods

For this purpose, the usual immunohematology techniques and equipment from the Immunohematology Laboratory : ORTHO-Vision, DIAMED- IH1000, DIAGAST - Qwalys 3 machines as well as manual techniques were used.

Results

In our routine work, we encounter countless grouping difficulties due to discordants:

agglutination intensity lower than normal, weak variants, discordance between Beth Vincent and Simonin, double erythrocyte population, rolling phenomenon, polyagglutinability. I tried to identify these problems and to present the way to solve them both by classical methods (macromethod) and with automatic equipment (micromethods)

Conclusions

Discords not elucidated in time can lead to transfusion accidents, therefore quick solutions must be found to avoid the wrong administration of blood putting patients at risk.

Choosing quality reagents and mastering the necessary knowledge are binding criteria.

17. IMMUNOHEMATOLOGICAL DISCORDANCES AND ABNORMALITIES IN THE Rh SYSTEM

A. Zagrean
Bucharest Blood Transfusion Center

OBJECTIV

To make known the most common discordances encountered in the laboratory routine in the Rh system.

To present some ways of resolving these discords.

MATERIALS/METHODS

For this purpose, the usual immunohematology techniques and equipment from the Immunohematology Laboratory - ORTHO-Vision, DIAMED- IH1000, DIAGAST - Qwalys 3 machines as well as manual techniques were used.

RESULTS

In our routine work, we encounter numerous difficulties in determining Rh due to: lower than normal agglutination intensity, weak variants (partial D, DVI), double erythrocyte population. They can also appear due to drug treatments or alteration of antigens due to certain diseases of the patients. Discordant results can also appear in multiparous Rh negative pregnant women

I tried to identify these problems and to present the way to solve them both by classical methods on the board (macromethod) and with automatic equipment (micromethods)

CONCLUSIONS

The RhD category is very important in order to establish the transfusion strategy.Using appropriate reagent and methods it is possible to detect the variants D week.

Discords not elucidated in time can lead to transfusion accidents, therefore quick solutions must be found to avoid the wrong administration of blood putting patients at risk. Correct monitoring of pregnant women immunized with Anti D antibodies eliminates the risk of repeated pregnancy loss.

The choice of quality reagents and the mastery of the necessary knowledge are binding criteria in resolving discordant issues.

18. MANAGEMENT OF POTENTIAL DONORS WITH A HISTORY OF VIRAL HEPATITIS
CRTS EXPERIENCE CONSTANT

A.. M.. Dobrota

Blood Transfusion Center Constanta

Introduction: The rigorous and well-founded selection of potential blood donors is one of the critical processes that contribute to transfusional safety. Declaring a viral hepatitis B, C virus in a pathological history contra-indicates blood donation. A number of potential donors, on their first attempt to donate blood, declare a history of “mild” hepatitis, “dirty hands”, etc., convinced that they had an episode of viral hepatitis A, in which situation, 3 months after clinical and biological healing (who 1193/2007), they would be eligible as blood donors in the absence of other identified contraindications. The lack of medical documents attesting the diagnosis of the declared / assumed viral hepatitis by the potential donor does not allow his admission as a blood donor, even in the absence of other reasons for exclusion from donation, which led, for a long time, to the to exclude these people from blood donation.

Objective: To establish a decision-making algorithm and a procedure to reduce the risk of excluding from blood donation potential donors who would in fact be eligible if they excluded hepatitis B and/or C from their history, when there was an episode of viral hepatitis, undocumented at the time of presentation. The benefit of this approach is to increase the

number of donors and, implicitly, to increase the collection and the capacity to respond to hospital requests.

Method: A project has been developed on the management of potential donors with a history of viral hepatitis presumed to be type A, without medical documents. The adjacent procedure has been validated in the routine work of the center and subsequently applied in all the cases described above, provided that the potential donor has expressed his intention to become a loyal blood donor after the procedure has been presented. Potential replacement donors, who expressed their intention to donate only as a "substitute donor", were not included, being suspended/excluded.

Materials: Potential donors with a profile corresponding to the one established in the project were registered in the database and entered the evaluation procedure in order to establish eligibility as a blood donor. All those who have not been identified other causes of suspension/exclusion, other than the history of possible viral hepatitis type A, have been granted the consent for sampling and testing according to the procedure, for anti-HIV AG/AC, AG/AC anti-HCV, AC anti-TP, AC anti-HTLV, AG HBs, Needle. Anti-HBc, anti-HVA needle. The tests were carried out in the CRTS CTA laboratory and the INTS laboratory.

Results: Between 1.01 and 30.06.2022, non-donation control samples were collected from 116 potential donors. Of these, 89 proved eligible, confirmed a history of viral hepatitis a, denied a possible history of viral hepatitis B and/or C. 24 people had a positive anti-HBc AC test and a history of viral hepatitis a disproved. Another 3 potential donors investigated were excluded due to confirmed positive results for Anti-TP CA (2) and CA respectively. Anti-HCV (1).

Conclusions: The project implemented a few years ago proved beneficial, as it allowed the recruitment of potential donors who would have been excluded by applying the previous procedure. They appreciated the CTA CRTS measures, did not feel discriminated against, some of those who proved to be eligible becoming blood donors, with regular and/or repeated donations.

19. MANAGEMENT OF THE STOCK OF BLOOD COMPONENTS IN THE TRANSFUSION UNIT

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Constanta Blood Transfusion Center

Blood components continue to be a critical element of therapeutic protocols in various medical and surgical emergencies, despite advances in medical practice. Their human origin and limited validity are unavoidable constraints in ensuring that blood components are at the level of requirements.

Difficulties in maintaining a stock of blood components are found, at least seasonally, in any country, both in blood transfusion centers and in hospitals. The lack of predictability regarding the range and amount of blood components needed in the various hospitals supplied, as well as the donors who present themselves daily to donate blood, generates difficulties in maintaining an adequate level of stock in blood transfusion centers.

Blood transfusion units estimate their blood component stock level according to the profile of the hospital, existing specialties, cases treated, taking into account the history of transfusions at the hospital level. The challenge is to identify the optimal level for each category and type of blood component, so that it can provide any patient with access to transfusional treatment when indicated, but minimizing the risk of expiration.

A certain degree of flexibility is necessary, in maintaining the optimal stock level, for rapid adaptation in unforeseen cases of increase/reduction of demand.

In the absence of programs dedicated to stock management, used both in blood transfusion centers and transfusion units, incidents by failure to provide the minimum need can be avoided only through an adequate organization of transfusions at the hospital level, communication of the UTS-section and THE UTS-transfer center respectively, Introduction of a pre-order/reservation system for scheduled interventions and patients with chronic transfusional needs, and last but not least, ensuring a 24/7 distribution and delivery service in transfusion centers and UTS.

20. NEW PERSPECTIVES IN REGULATING THE FIELD OF SUBSTANCES OF HUMAN ORIGIN AT THE LEVEL OF THE EUROPEAN UNION

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In 2003, the European Parliament and the Council adopted Directive 2002/98/EC on the setting of quality and safety standards for harvesting, control, processing, Storage and distribution of human blood and blood components and amending Directive 2001/83/EC. Subsequently, 4 other directives, with technical content, The geeral objective of the development and adoption of a common legislative acdru for the Member States was to ensure a high level of protection of the health of the population of the European Union and to ensure their access to quality and effective, safe substances of human origin. 20 years after the adoption of the first directive, following the evaluation process of the provisions in force, it was concluded that the legal framework for regulating the field of substances of human origin should be reviewed, as they have been overtaken by the development of new methods, procedures, therapeutic practices and technologies; gaps have also been found.

As a result, a new regulatory proposal in the form of a new Regulation was launched for evaluation in July 2022, repealing Directive 2002/98/EC. The new form of Regulation – Regulation – is considered instrumental at best, as it does not require delay and is directly applicable.

Romania, as a Member State of the European Union, has the possibility, through the representatives of the competent authority in the field of the Romanian Republic and the specialists in the transfusion, to actively engage in the evaluation process of the proposal, by formulating opinions, proposals

21. OUT OF STORAGE TIME" IDENTIFICATION AND MONITORING

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Introduction

The project to reorganize the Romanian transfusion system started in October 2020, currently underway, started with a research part of the transfusion activity in Romania. One of the aspects identified by the project team as gaps in the Romanian system, was the lack of "out of storage time" monitoring, i.e. the time and conditions in which the blood components are outside the regulated storage equipment. The project team noticed that there are no constant monitoring of how the

components sit outside of storage equipment in transfusion centers, during transport, and in blood transfusion units in hospitals.

Material

To clarify these aspects, we addressed the issue of regulations related to monitoring the time that blood components normally and usually sit outside of storage equipment.

Most regulations on blood components outside of storage equipment concern transfusion units in hospitals, and relate to delivery and transfusion on the hospital ward: the 30-minute rule and the 4-hour rule, which regulate the time elapsed in the delivery stage , from the time the blood component has been removed from the storage equipment in the transfusion unit, until the start of the actual transfusion, which is currently regulated to be no more than 30 minutes and the time related to the

transfusion itself, which must be completed within a maximum of 4 hours. In recent years there have been opinions - the USA, Canada - that are in favor of increasing the limit from 30 minutes to 60 minutes launched on the basis of bacteriological and biochemical studies carried out on blood components.

Time monitoring in the transfusion center: we have identified that the times when the blood components stay outside the storage equipment are: during processing when entering the computer system, when validating and releasing from quarantine, when labeling.

During processing, "Out of storage time" is not very long, being only related to the weighing and introduction of the components into the system. The quarantine release process is the longest because it includes checking the group and Rh of the sample from the bag, checking the test results, labeling with the final label. This process should take place in a maximum of 30 minutes, an interval that must be

validated and monitored as time and ambient conditions. Concretely, the ambient temperature in which the testing for the /Rh group, the verification of the analysis results and the labeling of the components is carried out must be controlled, and the temperature of the premises should be between 20 and 24 °.

There are only a few references to these processes - ISBT site, so by extension, the regulations applicable to delivery must be respected, the 30-minute rule for each blood component. Together, CTS Ploiești, CTS Buzău, CTS Constanta systematically monitored

the "out of storage" time in the 3 transfusion centers, simultaneously validating the conditions for keeping blood components outside the

storage equipment.

Conclusion

By introducing a strict monitoring of the time during which the release from quarantine takes place, we concluded that in order to shorten the "out of storage" time, the number of blood units subject to testing and release from quarantine should be reduced, this procedure being released from quarantine

as many a small number of bags simultaneously. In this way, the "out of storage" time for checking the group and Rh and checking tests, labeling will be reduced to 50-60% of the maximum regulated time.

22. PROFESSIONAL TRAINING IN THE FIELD OF BLOOD TRANSFUSION - DEVELOPMENT DIRECTIONS AND PERSPECTIVES

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Bucharest Blood Transfusion center

Transfusion medicine training for blood establishments and hospitals staff ensures the basis of a safe and efficient national transfusion system. The introduction of specific training programs in university and post-university medical education, as well as in nursing schools in Romania, must be a priority for decision-makers. The educational process must be addressed to all categories of personnel involved in transfusion activity. Training programs must provide staff with a theoretical basis and technical skills and also cover all activities. An important limiting factor is represented by the lack of specialist doctors or doctors with attested skills in blood transfusion. In the present paper, the development directions of the medical education in transfusion medicine are identified, taking into account the national and international legislation in the field, as well as the models from other countries.

23. QUALIFICATION OF CRITICAL EQUIPMENT IN THE TRANSFUSION CENTER

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Prahova Blood Transfusion Center

Introduction

In accordance with MHO 329/2018, Art.1.2.9. The CTS policy includes equipment qualification activities, according to art. 4.1.1 "All equipment must be qualified." According to GMP, qualification is "the act of demonstrating that any equipment works correctly and actually leads to the expected results". One of the critical pieces of blood processing equipment is the floor centrifuge. In order to guarantee that quality blood components will be obtained, it is mandatory that these equipments are qualified.

Material

The qualification of the equipment is done when purchasing the equipment, after a major overhaul or after an important repair with the replacement of some essential parts. If the qualification was not performed when the equipment was purchased and installed, a retroactive qualification will be made,when the equipment is already put into operation and work is being done on it. The design qualification is the qualification stage in which the first checks are made to determine if the purchased equipment meets the requirements. If, following a direct comparison between the requested characteristics and the characteristics of the purchased one, it is found that the equipment corresponds, the Design

Qualification has passed. The installation qualification will be done strictly following the steps in the equipment manual, from the installation chapter. Installation, electrical connection must be performed by qualified persons of the supplier. It is essential to correctly connect the device to an effective earthing installation, in accordance with the provisions of the law in force. It is important to carry out checks before starting work to identify any damage incurred during transport, movement and connection. Connect the device to the electrical network, as described in the technical book. If the

equipment starts and does not give errors, it is considered that the installation qualification has also been done.

Operational qualification is carried out by the supplier's team of technicians who start the specific operations, instructing the designated medical staff. Check if the equipment is working as required. The staff is trained on the use of the equipment. The technicians do some usual operation tests, and train the medical personnel regarding the operation in optimal conditions, provide instruction in case of

alarm signals, in case of malfunctions, and after finishing the operation tests, a Minutes of training that concludes Equipment Operational Qualification. The performance qualification follows the operational one, to evaluate the performance of the floor centrifuge: precise rotation speed, timer action and temperature must meet the requirements. The checking team has a traceable tachometer (certified),

traceable stopwatch (certified), traceable thermometer, delivered with a validity period for which it is certified. The centrifuge to be checked, identified by a unique number. At least two floats should be balanced with weights—one containing glycerin or 2 well-tied control CER bags—into which the probe from the traceable thermometer can be inserted. Check the rotation speed: Record the rotation speed

indicated by the centrifuge on the display, and through the built-in tachometer, on the centrifuge check registration sheet. Record the reading from the certified tachometer on the Record Sheet.

The difference between the two rotation readings is calculated and recorded. Assess the acceptability of the difference using the criteria specified in this procedure. Check the centrifugation timer at a setting frequently used in procedures and simultaneously start the timer. Record both stopwatch and display timer times as accurately as possible on the centrifugation check record sheet. The difference between

the two times is calculated. Refrigeration temperature check: it is done with the balanced check bags, one of which contains glycerine, or 2 tied control bags, in the centrifuge baskets and the centrifuge setting is made at the temperature required in the procedure with the traceable thermometer probe in the glycerine, run the centrifuge for five minutes at the speed required in the procedure or at the highest speed normally used, record the temperature of the centrifuge refrigeration setting and the certified thermometer on the Verification Record Sheet. It is drawn up at the end: The

equipment qualification report

Conclusion

Equipment qualification, "the action by which it is proven, in accordance with GMP principles, that any procedure, process, equipment, actually leads to the expected results" is a complex stage, difficult to achieve, which requires going through, together with the supplier, important steps to be sure that the equipment leads us to obtain quality components.

24. RELEASE OF BLOOD COMPONENTS AND CRITICAL ITEMS FROM QUARANTINE

A.M. Dobrota

Constanta Blood Transfusion Center

Quality control, as part of good practice, shall include specifications, sampling and testing, and the organization, documentation and procedures for release from quarantine, ensuring that materials are not released for use, and blood and blood components are not released for distribution until the necessary and relevant tests have been performed and the quality has been assessed as satisfactory.

Until the evaluation of the prepared blood components, respectively of the purchased critical items, they are kept in quarantine, i.e. physically and administratively isolated, in specially designated spaces, which comply with the storage conditions for each category of blood component, critical Article. Following the evaluation, carried out according to specific procedures, which include acceptance criteria, the decision of the person who is disposed of for this activity may lead to the acceptance, maintenance or disposal of the blood components or materials/reagents received;

The release of blood components and critical items from quarantine is a critical step in the chain of activities specific to a blood transfusion center, with an impact on the quality of all processes, from pre-donation testing to the administration of blood components. This stage is also found in the activity of transfusion units in hospitals, for the release from quarantine of materials and reagents used in UTS, respectively at the level of the department.

Records shall be kept manually and/or by other means of registration demonstrating that all the necessary quality control procedures have been carried out. Any deviation is fully documented and investigated; release from quarantine is an activity under the responsibility of the responsible person, the decision to release blood and final blood components being equivalent to assuming responsibility for compliance with the specifications and correct labeling. To ensure traceability, records shall be kept, manually and/or by other means of recording, with the results of the evaluation, demonstrating that the critical articles, respectively the final blood components evaluated, have complied with the pre-established specifications.

The rigor of organizing, carrying out and documenting the process of release from quarantine contributes to the achievement of the level of quality and safety expected and predetermined in the policy and strategy of quality assurance adopted in the respective institution. Beyond the adoption of policy, strategy, implementation of procedures, an essential impact on the added value of this activity, to ensure the safety and quality of all the specific activities carried out in the institution, has the level of training of the responsible medical staff,

understanding the process, in-depth knowledge of the importance of acceptance criteria, the potential risks arising from the lack of rigor and accuracy in carrying out the checks.

25. STANDARDIZATION OF THE PROCESS OF ESTABLISHING THE ELIGIBILITY OF POTENTIAL BLOOD DONORS BETWEEN PRINCIPLES, REGULATIONS AND REALITY

A.M. Dobrota
Constanta Blood Transfusion Center

Rigorous selection of potential blood donors and blood components is one of the critical processes for ensuring an adequate level of safety of donated blood. The European Directives adopted in 2002 and 2004 contain, inter alia, explicit requirements regarding the obligations of competent authorities and blood establishments in organizing, implementing and conducting the selection process for potential blood donors.

According to the European regulations, transposed into national legislation, establishing the eligibility of potential blood donors and blood components requires the controlled and documented completion of several stages: Identification of the potential donor, informing him about aspects regarding the donation, his obligations, etc., filling out a questionnaire, medical interview, medical examination, pre-donation testing.

The organization of the blood donation activity is the responsibility of the Ministry of Health, directly and through the designated institutions. Blood transfusion centers have the obligation to develop procedures, with reference to the European and national rules in force, in which to describe succinctly, clearly, accurately, the steps to be taken by the responsible staff at each stage of the process. Thus, it ensures the premises of a consistent and sustainable activity, without variability depending on the medical team, location or other factors that could influence compliance with the procedures.

However, despite the existence of European and national rules, procedures, The evaluation of the practices reported by the representatives of the blood transfusion centers during the evaluation carried out by the team of experts within the project for the reorganization of the national transfusion system in Romania showed the existence of a considerable degree of heterogeneity in the application of requirements and criteria regarding the eligibility of potential donors.

Experience shows that in routine work there are numerous and diverse situations, not covered by regulations and procedures, in which the person responsible for the selection process is responsible for assessing the risks that the particular aspect identified could generate to the donor and/or patients who would receive the blood components resulting from the donation, if the person is considered eligible. In such situations, a correct decision is conditioned by the level of qualification, competence, experience of the person responsible for the selection process, real-time information on modern, scientifically based approaches in this field.

The risk of different interpretations in similar situations at national level can be reduced by coordinated measures of information and regular training of doctors and nurses responsible for carrying out these activities, development of good practice recommendations, use of the Council of Europe guide, collaboration between specialists, under the coordination of a group of designated specialists, so as to ensure coherence, consistency and limitation of the

variability of decisions on unregulated situations, but which impure the evaluation of rashes and case-by-case analysis.

26. THE COMPATIBILITY OF KIR LIGANDS IN HAPLO-TRANSPLANTATION – THE EXPERIENCE OF THE NATIONAL HLA LABORATORY FROM INTS

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In the case of patients who do not have a perfectly HLA-compatible sibling for Allo-transplant, the alternative of an unrelated donor, preferred over many years, tends to be replaced in many cases by the haplo-compatible family donor

The selection of the donor for haplo transplantation is based on well-standardized criteria that involve testing the HLA-A, B, C, DRB1, DQB1 alleles to identify the common haplotype and the absence of specific donor antibodies. Recent studies also discuss HLA incompatibilities in interaction with alloreactive Natural Killer (NK) cells and their impact on the evolution of a transplant.

NK cells recognize target cells through activating and/or inhibitory regulatory receptors - killer immunoglobulin-like receptors (KIRs). Their specific ligands are represented by HLA class I molecules and the pre-transplant evaluation of the KIR-ligand interaction can be an indicator of the predictability of the post-transplant evolution.

A number of 145 patients (F=62/B=83) and 268 family donors, first degree relatives, were investigated to establish compatibility for a haplo-transplantation. All patients and donors were tested for HLA by biological methods low and high resolution molecular. The ``KIR ligand calculator" (https://www.ebi.ac.uk/ipd/imgt/hla/matching/) was used to identify KIR-ligand HLA incompatibilities.

Iy was evaluated the rate of of identification of a donor with at least 1 KIR-ligand HLA-B/C/B+C incompatibility, in relation to the number of donors proposed for testing. This was, for incompatibilities in GvH direction, of 39% in patients with 1 donor / 47% in patients with 2 donors and 46% in patients with 3 donors and for incompatibilities in HvG direction, of 47% in patients with 1 donor / 45% in patients with 2 donors and 56% in patients with 3 donors.

The authors look to establish retrospectively, on a limited group of patients transplanted from a haplo-identical donor, the existence of a correlation between the unidirectional KIR-ligand incompatibilities in the post Haplo-transplant evolution, respectively the occurrence of GvH / chronic GvH, relapse rate and overall survival.

27. THE EFFECTIVENESS OF THE MOBILE BLOOD COLLECTION DRIVES ORGANIZED BY CTSMB AND CONCRETE ACTIONS FOR INCREASING PERFORMANCE

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The mobile collection drives organized by the Bucharest Centre for Blood Transfusions have had a sinusoidal evolution in the past 5 years, recording a progressive growth until 2019 and, subsequently, a drastic drop at the start of the Covid-19 pandemic, followed by suspension in March 2020. After their resumption in 2021, they have been registering a growing trend, albeit a slow one, with pauses, without presently reaching the performance levels from 2019.

The evaluation of mobile blood collection drives organized by the centre between 2018 and 2022 has confirmed the efficiency of this type of collection, but has also revealed the vulnerabilities of the way in which it is organized, with it not being a viable option over the course of the pandemic.

For the Bucharest Centre for Blood Transfusions, the suspension of mobile collection drive meant a decrease by 25% in blood and blood component collection in May – June 2020 compared to the same period in 2019.

Consequently, post-pandemic, special attention was given to reinvigorating the mobile collection drives, but actions taken to that end had to be modified and adapted, taking into consideration both the lessons learned during the pandemic, as well as new problems that have arisen on top of existing ones.

28. THE FREQUENCY OF NON-SPECIFIC HIV REACTIVITY IN THE LABORATORY OF BLOOD-TRANSMISSIBLE DISEASES OF THE BLOOD TRANSFUSION CENTER BRAŞOV

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Introduction.

HIV is one of the 6 diseases tested within the Blood Transfusion Center Brașov in order to determine HIV reactivity.

Aim:

This work aims at determining the frequency of non-specific HIV reactivity in the Blood Transfusion Center Brasov donors during the years 2020-2022 (August).

Materials and methods:

Identifying the donors with HIV reactivity above 0.8 using the Genscreen Ultra/ Biorad kit.

Case study:

The reactivities will be presented in extenso in the paper.

Conclusions:

In the Blood Transmissible Diseases department, donor blood samples are mandatory tested for HIV disease.

29. THE IMPORTANCE OF ROUTINE RH/KELL PHENOTYPING IN TRANSFUSION SAFETY

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Introduction: Along with determination of blood group (OAB) and Rh (D), the determination of Rh/Kell phenotype and the examination of irregular antibodies are essential for transfusion safety. Therefore, they will be performed for each patient requiring a transfusion. Irregular antibody testing should be repeated at the appropriate time for each polytransfused patient.

Materials and methods: Determining the OAB/Rh blood group, the Rh/Kell phenotype, highlighting the presence of irregular antibodies, their identification and carrying out compatibility tests in blood recipients, by the hemagglutination reaction in column (micromethod) on the ID-Diamed line. In the immunohematology laboratory of the Blood Transfusion Center Brașov, blood recipients from several hospitals in Brașov county were evaluated in 2021.

Case study: The clinical cases are presented in extenso in the work.

Conclusions: The systematic performance of complete immunohematological tests, both for the donor and for the recipient, significantly contributes to the reduction of transfusion risk and to the achievement of an effective blood transfusion, as a therapeutic and replacement support, as immunohematological security is an important level of transfusion security.

30. THE QUALITY OF BLOOD COMPONENTS PREPARED USING THE REVEOS AUTOMATED PROCESSING SYSTEM - THE RESULTS OF THE STUDY CARRIED OUT IN BUCHAREST BLOOD ESTABLISHMENT

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Introduction: The automatic blood processing method - Reveos, allows obtaining standardized blood components (BC) in a single step. In this paper we present the results of the BC quality control obtained with this technology, in the Bucharest Blood Transfusion Center (BBTC).

Method: In the period January - June 2022, two Terumo BCT automatic blood processing equipment, REVEOS model, TOMES software system, 3C LR model collection bags were validated for obtaining three BC. The quality control results of BC obtained from 75 units of whole blood processed automatically were analyzed and compared with a similar number of BC resulting from manual processing. Statistical analyzes were performed with Excel software (Microsoft).

Results: Using the automatic method, all BC are leukodepleted; erythrocyte units have a higher Ht (58% ± 3.1 vs 57% ± 3) and a lower volume (266mL ± 17.7 vs 294mL ± 24.5), which means a higher plasma recovery; in the platelet units, the number of platelets is significantly higher (76 ± 30.2 vs 61.9 ± 18), there is no erythrocyte contamination and aggregates; the volume of the plasma unit is significantly higher (216 ± 22.8 mL vs 179 ± 26

mL), and 100/101 (99.01%) of the plasma units tested after 3 months of preservation had a recovery of factor VIII > 70% . The system allows obtaining the pool of leukodepleted platelets and data management in the computer system.

Conclusions: The automatic processing technology ensures the obtaining of high quality, standardized BC and contributes to transfusion safety.

31. THE RELEVANCE OF OF STUDYING THE TRANSMISSION OF FAMILY HAPLOTYPES TO ESTABLISH THE HLA COMPATIBILITY IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Allo-Transplant of hematopoietic stem cells (Allo-HSCT) is one of the curative options for many patients suffering from high-risk hematological diseases. Identifying a compatible stem cell donor (DCS) represents one of the main challenges and limitations for performing Allo-HSCT. The Major Histocompatibility Complex (HCM) is one of the most polymorphic genetic systems, currently over 22,000 class I HLA alleles and over 9,500 class II HLA alleles have been identified. The fastest and easiest option for identifying a DCS is to search in the family. Testing the extended family, at least siblings and parents/children will allow the validation of an identical or haplo-compatible DCS. In the process of selecting a compatible DCS, knowledge of CMH properties such as codominance, segregation and block transmission, recombination and linkage disequilibrium are useful tools for establishing patient-donor compatibility. The authors present 3 cases of selecting a family donor in which compatibility could be defined by studying the transmission of haplotypes after testing the entire family.

32. TRALI –TYPE SEVERE ADVERSE REACTION-case reports

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The investigation of post transfusion adverse reactions due to leuko platelet causes is an important part of the tests carried out in the histocompatibility laboratories.

One of the severe adverse reactions is TRALI (transfusion –related acute lung injury) and involves a lung injury associated with transfusion, which can usually appear within 4 hours of the transfusion. The symptoms are severe such as a acute respiratory distress with hypoxemia and fulminant pulmonary edema.

The present work supports specialist doctors in order to perform HLA tests that can investigate and determine the causes that can lead to TRALI.

An important point in this regard is the fastest and most complete collection of clinical data provided by the Transfusion Centers to the HLA testing laboratories.

The data are related to the confirmation of severe adverse reactions and the blood product involved, the amount administered, the blood group and Rh of the product that was administered and are accompanied by the form for sending biological samples to the testing laboratories.The forms will be discussed by the authors.

The TRALI investigation protocol of the National HLA Laboratory includes the classic HLA testing schemes using SSP and SSO molecular biology techniques and the determination of anti HLA antibodies using LUMINEX tehnology. All testing will be explained in detail.

The National HLA Laboratory presents its experience in testing for the investigation of TRALI presenting 4 patients who presented suspicion of TRALI after administration of labile blood products. The results are discussed by the authors.

In conclusion, TRALI is a clinical diagnosis that must be very carefully monitored and investigated to elucidate the causes of the occurrence of this severe reaction.

33. TRANSFUSION MEDICINE IN THE FUTURE - CULTURED RED BLOOD

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Prahova Blood Transfusion Center

Introduction

Anemia is an extremely common disorder affecting more than 2 billion people worldwide with the highest incidence among the elderly, a common symptom of cancer therapies, major surgery and trauma, requiring the delivery of more than 16 million units of red blood cells each year in the United States alone. The need for RBC transfusions is projected to increase as our population continues to age.

Currently, red blood cell products are obtained from voluntary donors, which involves biological risks and requires expensive screening, and donors for rare blood types are few and far between, creating frequent supply bottlenecks.

Moreover, it is likely that blood donations will become insufficient to meet future requirements.

Demographic calculations based on recent changes in the median age of the US population predict that the number of people who are likely to require transfusions, primarily older individuals, will outnumber those who are likely to donate, younger people, making the blood supply inadequate by 2050. In addition, disruption of normal blood collection due to natural disasters and socio-political emergencies

could lead to unpredictable, long-lasting and severe blood component shortages at any time.

Material

A strategy to solve these problems, using synthetic hemoglobin substitutes, is associated with numerous side effects, including hypertension and increased risk of myocardial infarction, currently avoiding clinical use. Another potential strategy, the production of blood cells in vitro.

In view of these serious concerns, alternative sources of erythrocytes are sought, being essential for the future. Normal erythropoiesis is characterized by the progressive expansion

of progenitor cells to morphologically identifiable precursors, which eventually enucleate to form mature red blood cells. In

vivo, erythropoiesis originates from a small number of hematopoietic stem cells that generate increasing numbers of lineage-committed progenitors called erythroid burst-forming units and erythroid colony- forming units that later generate erythroid precursors called proerythroblasts, basophilic erythroblasts, polychromatophilic erythroblasts and orthochromatic erythroblasts, which accumulate hemoglobin and

condense their nucleus. Enucleation results in the generation of reticulocytes that lose all internal organelles to become mature erythrocytes.

Erythropoiesis has been modeled in vitro using two or more liquid culture steps. The first step being associated with the expansion of multipotential and lineage-specific erythroid progenitors. In vitro, dexamethasone synergizes with erythropoietin and stem cell factor to induce immature erythroblasts to undergo self-renewing cell divisions. When dexamethasone and SCF are removed from the cultures,

these erythroblasts complete terminal maturation. This complex process of erythropoiesis, consisting of progressive phases of: expansion of progenitors, amplification and maturation of precursors, and remodeling of reticulocytes into terminal erythrocytes, has been modeled with variable success in vitro.

The ability to differentiate erythroid cells in vitro is based on several fundamental studies, including the generation of erythroid colonies in semisolid media and the cloning of erythropoietin, stem cell factor, and other cytokines.

Since its introduction, the 2-step erythrocyte culture system has undergone significant improvements that have resulted in the synthesis of increasing numbers of mature erythrocytes. The ultimate goal of these in vitro erythroid cultures is to generate enucleated erythrocytes with deformability and oxygen delivery potential similar to erythrocytes generated in vivo. Currently, several ex-vivo generated cell therapy products are in clinical trials, including stem cells for transplantation, dendritic cells as a cancer vaccine, activated lymphocytes, mesenchymal stem cells to prevent graft-versus-host disease, and chondrocytes to accelerate bone repair.

These cellular products require ex-vivo generation of cell numbers between 107 and 1010, which is feasible with current technologies. However, a single unit of CER contains two orders of magnitude more cells (about 2.5 × 1012 erythrocytes). Although it is estimated that current in vitro erythroid culture protocols could generate between 3–50 units of erythrocytes from a cord blood donation, only one transfusion of 1010 erythrocytes derived from in vitro culture has been published recently.

Conclusion:

The production of sufficient blood cells for clinical needs will ultimately require advances in erythroblast expansion and bioreactor technology. The costs associated with ex vivo erythroid cell expansion and differentiation make it unlikely that these erythrocytes will be produced in clinically useful numbers in the near future, and obtaining erythrocytes from blood donors will remain the trend for a long time to come.

34. TRANSFUSION SAFETY IS A PERMANENT GOAL

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Introduction and objectives

Transfusion safety responds to the following principles:

• Do not bring an absent antigen to the recipient through transfused red blood cells (to prevent the recipient from being immunized by transfusion).

• Do not bring through an transfused red blood cell an antigen corresponding to an antibody present in the recipient's serum or plasma (to avoid a transfusion reaction related to an antigen-antibody conflict).

Material and methods

In this paper we describe new clinical cases encountered in our activity lately.

Through usual techniques: DAI, Gr. Sang, phenotype, compatibility tests and additional techniques: TCD, extended phenotype, allo and self-absorption techniques we tried to solve difficult clinical cases.

The main purpose of performing compatibility is to ensure, as far as possible, safe blood transfusion. Compatibility procedures should ensure that the safest possible blood is available to the patient as soon as possible.

The objectives of a compatibility test are:

Detection of as many clinically significant antibodies as possible - highlights both private anti-antigen antibodies or unidentified or masked antigens by a known antibody (eg, anti-Jka is masked by an anti-C), and responsible immune antibodies of posttransfusion reactions

Detection of clinically insignificant antibodies as few as possible,

Increasing transfusion safety

Completion of the procedure in a timely manner.

We described in the paper several clinical cases from our transfusion practice that we solved using usual laboratory techniques or in some cases additional techniques were needed.

Results, conclusions

• In the conditions of the increase of the blood demand, as well as of the number of transfusions, of the patients, the number of polytransfused patients also increased.

• As a result, it becomes increasingly difficult to select the appropriate blood component for a patient to avoid immunization and thus make a future transfusion almost "impossible."

• Blood transfusion services - both Blood Transfusion Centers and Hospital Transfusion Units

will always need highly qualified specialists to solve increasingly difficult clinical cases.

35. TREATMENT OF TRANSFUZIONAL ADMINISTERED IN DAY HOSPITALIZATION

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Constanta Blood Transfusion Center

Patients with acute and/or chronic conditions benefit from daily transfusions. The organization of healthcare at national level is under the responsibility of each state. Depending on the decisions and measures adopted, various models of organization of

transfusional activity, intended for the administration of transfusion treatment, can be met at international level: Transfusion in conditions of continuous hospitalization, day hospitalization, outpatient, at home.

Recognizing unanimously that transfusions are not risk-free, each competent authority shall establish regulations ensuring a safety framework for patients receiving transfusions, with the obligation to monitor them both during and after administration, so that manifestations caused by adverse reactions, incidents and, where appropriate, appropriate therapeutic measures can be identified quickly. As a result, the responsibility of supervision rests with doctors and nurses trained to recognize, treat adverse reactions to transfusions.

In Romania, traditionally, transfusions are administered under continuous hospitalization conditions; the legislation in force establishes the attributions and responsibilities regarding the monitoring of the transfused patient. There are no explicit formulations regarding the administration of transfusional treatment under the conditions of day hospitalization. In recent years, in some hospitals, this way of providing transfusion treatment in day hospitalization was introduced for patients with oncological and hematological diseases, most of them requiring repeated transfusions, according to the therapeutic plan established by the attending physician. This approach can be supported as an option from the point of view of eligible patients (they prefer not to stay in the hospital), but requires a prior analysis of the initiation of these services from the legislative perspective, of the risks for the patient, of the limitation of the real possibility of monitoring the patient in the next 48 hours post-transfusion. Measures to reduce the risks posed by leaving the hospital shortly after the transfusion, with the identification and introduction of remote surveillance modalities by the attending physician, are more than necessary for the safety of the transfused patient. The local hemo-vigilance coordinator shall establish ways of monitoring compliance with the pre-established measures at the level of the health unit, periodically evaluating the reports in the hemovigilance system.

The centralization and analysis of data on the administration of the transfusional treatment in day-to-day hospitalization, at national level (legal framework, organization, documentation, compliance with pre-transfusions and therapeutic testing procedures, etc.) can provide the competent authority with a database, arguments for or against the elaboration of regulations for the introduction of transfusion administration in day-to-day hospitalization conditions in the legislation, with the establishment of minimum requirements for carrying out this form of health care in safe conditions for patients with periodic transfusions needs.

36. VALIDATION OF THE PROCEDURE FOR PREPARATION OF STANDARD PLATELET CONCENTRATES. CRTS EXPERIENCE CONSTANT

A.M. Dobrota

Blood Transfusion Center Constanta

The peculiarities of total blood as raw material for obtaining blood components, among which we emphasize the physiological variability of composition in erythrocytes, platelets, between donors, between sexes, as well as between cells of the same type, from the same donation, implicitly generates differences in the composition of units of blood components of the same category and type, prepared in a blood transfusion center.

As a result, unlike the production of drug factories, each unit of blood component obtained constitutes a batch. However, beyond the accepted physiological variability, a minimum content of target blood elements must be ensured in each unit of a particular type of blood component established, together with other characteristics, in the set of specifications laid down by national rules and local procedures. The conformity of the prepared blood components in terms of content is dependent on the suitability of the total blood centrifugation programs or intermediate products, as appropriate. The quality check of the obtained components is carried out within the quality control, both during the preparation process and on the final components. The results of the quality control tests carried out on different sets of components in accordance with the procedures and pre-established sampling plan must determine whether they can consistently meet all quality and process parameters. The accepted level of compliance shall be determined in accordance with the quality policy of the institution.

The procedures for obtaining various categories and types of blood components can be validated only after confirmation of the consistency and sustainability of the results obtained.

The paper presents the Constanta BTC experience on validating the procedures for the preparation of standard platelet concentrates, from total blood collected in 2 different collection systems.

The validation phase was prolonged by local factors, such as low collection, low number of eligible donors to target the donation to obtain standard platelet concentrates, limited availability of the technical representative of the company that provides maintenance of the centrifuges used.

Increased demands for platelet concentrates required the release of compliant units from quarantine for administration.

37. VIROLOGY COMPLEMENTARY BLOOD TESTING USING MOLECULAR BIOLOGY NAAT METHOD OVER 12 MONTHS OBTAINED BY THE MINISTRY OF DEFENSE CENTRAL BLOOD BANK "COLONEL PROFESOR DOCTOR NICOLAE NESTORESCU"

I. Butte, A.E. Zamfirescu, M.C. Ranetti,

Ministry of defense Central Blood Bank "Colonel Profesor Doctor Nicolae Nestorescu"

Routine NAAT testing of donors introduced in CTS MapN yielded inharmonious results compared with classic virology testing method ELISA. Out of 8800 donors tested, DNA-VHB has been detected in 11 donors for wich Ag HBs was negative. Further investiogations showed a common element: the presente of AC – antiHBc in all samples tested, some of them exhibiting other markes of HBV infection. Non-specific reactivity obtained for HIV (through ELISA) on a certain kit were infirmed on other kits after NAAT testing. Our conclusion is that the introduction of routine NAAT testing brings clear benefirts for the safety of transfusions.

SUNDAY - OCTOBER 9th, 2022

POSTER SESSION

1. THE RELEVANCE OF OF STUDYING THE TRANSMISSION OF FAMILY HAPLOTYPES TO ESTABLISH THE HLA COMPATIBILITY IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Allo-Transplant of hematopoietic stem cells (Allo-HSCT) is one of the curative options for many patients suffering from high-risk hematological diseases. Identifying a compatible stem cell donor (DCS) represents one of the main challenges and limitations for performing Allo-HSCT. The Major Histocompatibility Complex (HCM) is one of the most polymorphic genetic systems, currently over 22,000 class I HLA alleles and over 9,500 class II HLA alleles have been identified. The fastest and easiest option for identifying a DCS is to search in the family. Testing the extended family, at least siblings and parents/children will allow the validation of an identical or haplo-compatible DCS. In the process of selecting a compatible DCS, knowledge of CMH properties such as codominance, segregation and block transmission, recombination and linkage disequilibrium are useful tools for establishing patient-donor compatibility. The authors present 3 cases of selecting a family donor in which compatibility could be defined by studying the transmission of haplotypes after testing the entire family.

2. THE COMPATIBILITY OF KIR LIGANDS IN HAPLO-TRANSPLANTATION – THE EXPERIENCE OF THE NATIONAL HLA LABORATORY FROM INTS

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In the case of patients who do not have a perfectly HLA-compatible sibling for Allo-transplant, the alternative of an unrelated donor, preferred over many years, tends to be replaced in many cases by the haplo-compatible family donor
The selection of the donor for haplo transplantation is based on well-standardized criteria that involve testing the HLA-A, B, C, DRB1, DQB1 alleles to identify the common haplotype and the absence of specific donor antibodies. Recent studies also discuss HLA incompatibilities in interaction with alloreactive Natural Killer (NK) cells and their impact on the evolution of a transplant.
NK cells recognize target cells through activating and/or inhibitory regulatory receptors - killer immunoglobulin-like receptors (KIRs). Their specific ligands are represented by HLA class I molecules and the pre-transplant evaluation of the KIR-ligand interaction can be an indicator of the predictability of the post-transplant evolution.
A number of 145 patients (F=62/B=83) and 268 family donors, first degree relatives, were investigated to establish compatibility for a haplo-transplantation. All patients and donors were tested for HLA by biological methods low and high resolution molecular. The ``KIR ligand calculator'' (https://www.ebi.ac.uk/ipd/imgt/hla/matching/) was used to identify KIR-ligand HLA incompatibilities.
Iy was evaluated the rate of of identification of a donor with at least 1 KIR-ligand HLA-B/C/B+C incompatibility, in relation to the number of donors proposed for testing. This was, for incompatibilities in GvH direction, of 39% in patients with 1 donor / 47% in patients with 2 donors and 46% in patients with 3 donors and for incompatibilities in HvG direction, of 47% in patients with 1 donor / 45% in patients with 2 donors and 56% in patients with 3 donors.

The authors look to establish retrospectively, on a limited group of patients transplanted from a haplo-identical donor, the existence of a correlation between the unidirectional KIR-ligand incompatibilities in the post Haplo-transplant evolution, respectively the occurrence of GvH / chronic GvH, relapse rate and overall survival.