

■ Stem Cell Transplantation

P-001 Abstract Reference: 79

EFFICACY OF HIGH DOSE CHEMOTHERAPY AND AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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Background: Primary central nervous system lymphoma (PCNSL) is a rare type of lymphoma with poor responses to chemotherapy, which is mainly based on less penetrance of chemotherapeutic agents through blood brain barrier. Consolidation approaches including high dose chemotherapy and autologous hematopoietic stem cell transplantation (AH SCT) have been developed to overcome this obstacle. The aim of this study is to evaluate the efficacy of AH SCT in PCNSL patients in terms of progression free and overall survival.

Methods: A total of 11 patients [median age: 43(28-62) years; male/female: 6/5] who had undergone AH SCT for a diagnosis of PCNSL were evaluated retrospectively.

Results: First-line chemotherapy regimen was BONN protocol [A: methotrexate 5 g/m² (day 1), vincristine 2 mg (day 1), ifosfamide 800 mg/m²/day (days 2-5), dexamethasone 10 mg/m²/day (days 2-5); B: methotrexate 5 g/m² (day 1), vincristine 2 mg (day 1), cyclophosphamide 200 mg/m²/day (days 2-5), dexamethasone 10 mg/m²/day (days 2-5); C: Ara-C 3 g/m²/day (days 1,2), vincristine 2 mg (day 1), dexamethasone 10 mg/m²/day (days 2-5)] in 9 patients (81.8%), Rituximab-BONN in one patient (9.1%) and high dose methotrexate in one patient (9.1%). Complete response was achieved in 4 patients (36.4%), partial response in 6 patients (54.5%), and refractory disease was observed in one patient (9.1%). Intrathecal prophylaxis was administered to all patients during the induction therapy. Hematopoietic stem cell mobilization was performed after BONN C protocol with granulocyte colony stimulating factor (G-CSF) at a dose of 10 mgr/kg/day in 10 patients (90.9%) and G-CSF-Plerixafor in one patient (9.1%). Median time from diagnosis to AH SCT was 123(94-668) days. Pre-transplant disease status was complete response in 5 patients (45.4%), partial response in 5 patients (45.4%) and refractory disease in one patient (9.1%). Pre-transplant Sorror comorbidity index score was 0(0-3). Conditioning regimen consisted of thiotepa [300 mg/m²/day (2 days), cyclophosphamide 2 gr/m²/day (2 days) and busulfan 3,2 mg/kg/day (3 days)]. Median infused CD34⁺ cell count was 5(3,35-6,95)x10⁶/kg. Grade 2(1-4) mucositis was observed in 7 patients (63.6%). All patients experienced grade 4 hematological toxicity and peri-engraftment infection. Median neutrophil and platelet engraftment days were 11(10-17) and 11(8-17) days respectively. Complete response was demonstrated in 9 patients (81.8%) at median 75(60-90) days after AH SCT. Relapse was observed in 5 patients (45.4%) at median 4(2-30) months after AH SCT. Median progression free survival and overall survival were found to be 33.9% and 48.5% respectively at 12(1-104) months of follow-up (Figure 1, Figure 2).

Conclusions: Autologous HSCT is considered as a feasible treatment modality in patients with PCNSL with complete response rates reaching up to 90%. Thiotepa based conditioning should be preferred considering high CNS penetrance of the drug. Furthermore, addition of rituximab to induction regimens may help to improve response rates. Our results seem to be concordant with the previous reports which confirm the efficacy of AH SCT in PCNSL treatment.

Keywords: Primary Central Nervous System Lymphoma, Hematopoietic Stem Cell Transplantation

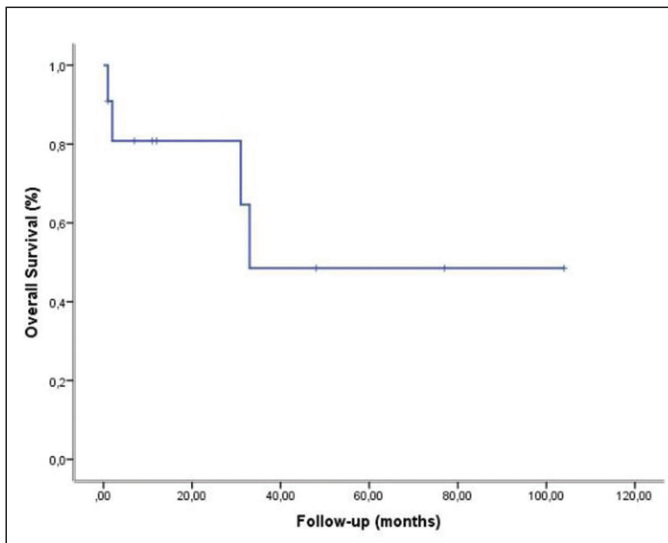


Figure 1. Overall survival was 48.5% at 12(1-104) months of follow-up

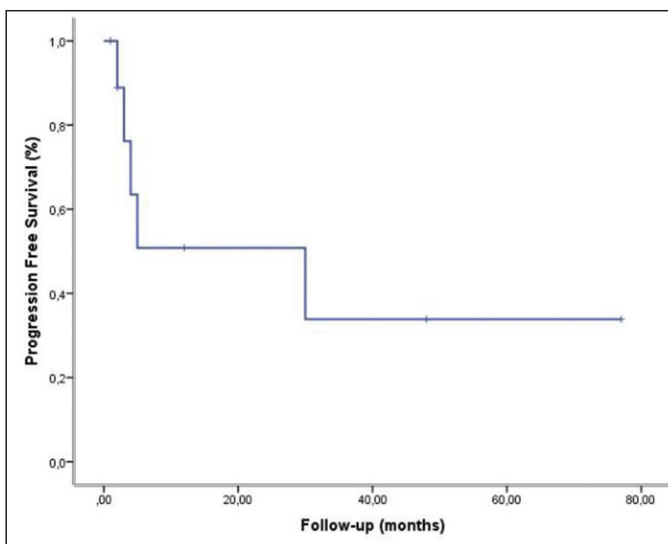


Figure 2. Progression free survival was 33.9% at 12(1-104) months of follow-up

■ Non-Hodgkin's Lymphoma

P-002 Abstract Reference: 154

IS AGE AN IMPORTANT FACTOR FOR AUTOLOGOUS PERIPHERAL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ELDERLY PATIENTS WITH NON-HODGKIN LYMPHOMA?

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Introduction: High-dose chemotherapy followed by autologous hematopoietic cell transplantation (auto HSCT) may provide survival benefit in patients with non-hodgkin lymphoma (NHL). Retrospective analyses suggest that the benefit of HDT extends to elderly patients with NHL, which is an important finding considering that the median age at diagnosis is 67 years (range: 65-74) for NHL in United States, using 2010-2014 US SEER data. We

aimed to define the efficacy and toxicity of auto HSCT in patients >60 years with NHL compared with younger patients.

Patients and Methods: From January 2005 through August 2017, data from 102 chemosensitive aggressive NHL patients below the age of 60 were compared to 26 lymphoma patients above 60 years of age who were eligible for auto HSCT according to geriatric assessment (GA). All these data were obtained from the Ankara University Faculty of Medicine, Department of Hematology and Bone Marrow Transplant Unit. Patients were excluded if they had an indolent lymphoma, chemo refractory disease, or underwent a second autologous or allogeneic HSCT. We compared the toxicity profile and outcome between the research group: patient aged 60 years and above and the control group: patient <60 years.

Results: Median age of research group was 47.5 (range, 18-74) years, and 2 patients were 70 years and older. The majority of patients (n=55, 43%) underwent an autologous HCT due to relapsed DLBCL. Median follow up of surviving patients was 20.5 (range, 1-60 mos) months at the time of data collection, 82 patients (64.6%) were alive. Patients' characteristics were similar between the two age cohorts. All of the patients were stage III or IV at diagnosis; ten out of 26 elderly patients had active disease at the time of auto HSCT. The median follow-up was 20.5 months (range, 1-60 mos). Prior to transplantation majority (85%) of the elderly patients received BEAM protocol as conditioning treatment. Bone marrow stem cell was used in only 1 patient. None of the patient had mobilization failure, the median peripheral CD34 level was $5.24 \times 10^6/\text{kg}$. Forty-eight percent of the elderly patients experienced grade 3-4 mucositis and 77% of the patients had microbiology-documented infection. Sixty-two percent of the elderly patients had diarrhea with median duration of 8 days (range, 5-20 days). Renal toxicity was occurred in 7 (27%) patients while hepatic toxicity in 1 (10%) patient in the elderly cohort. There was no difference in the toxicity profile between patients ≥ 60 years and those aged <60 years. Median time to neutrophil recovery was 10 days (range, 8-18 days) and platelet recovery 11 days (range, 10-32 days) in elderly cohort. Interestingly, neutrophil and platelet engraftments had not occurred in six out of 102 patients in the younger group. Overall response was obtained from all elderly patients (23% CR). At the time of data collection, 4 patients (15%) of patients' ≥ 60 years have deceased. Relapse (n=3) was the main course of death. The probability of 4-year progression free survival (PFS) and estimated overall survival (OS) in elderly patients were 44.4% and 39.4%, respectively.

Conclusion: Based on this single center study, auto-HSCT is safe and efficacious in the treatment of elderly lymphoma patients. We emphasize the need for further research in order to determine the risk-benefit threshold for HSCT based on age coupled with comorbidity and fragility.

Keywords: autologous hematopoietic cell transplantation, non-hodgkin lymphoma, elderly

■ Acute Myeloid Leukemia

P-004 Abstract Reference: 137

SINGLE CENTER EXPERIENCE: COMPARISON OF REDUCED INTENSIVE CHEMOTHERAPY AND LOW-DOSE CYTARABINE TREATMENT AS REMISSION INDUCTION IN OLDER AGE AML CASES

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Aim: The aim of this study was comparison of treatment with reduced dose of cytosine arabinose (100 mg / m², continuous intravenous infusion) and daunorubicin (45 mg / m² 2-3 days) treatment protocol versus low dose cytarabine treatment as the remission induction treatment of aged 65 years and older AML patients.

Methods: The data of the over the age of 65 years of cases diagnosed as AML between 2010 and 2018 at Hematology Clinic of Atatürk Training and Research Hospital were retrospectively analyzed. Statistical analyzes were

performed using chi-square test using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). A value of less than 0.05 was considered significant.

Results: The data of 67 cases with AML were evaluated. Eight cases were excluded because they were diagnosed with acute promyelocytic leukemia. In Table 1, clinical and laboratory findings at the time of diagnosis were compared according to the treatment choice. Mean survival of 59 patients was 19 ($\pm 3,9$) months. The mean survival of the patients who received Ara-C + daunorubicin treatment and low-dose cytarabine treatment was 26.4 (± 6.2) and 14.8 (± 4.1) months, respectively (**p = 0.044**) (Figure 1). After the first induction treatment, 16 (27.1%) cases were obtained in all series recovery in peripheral blood, and 12 (75 %) of these patients were treated with Ara-C + daunorubicin (**p = 0.001**). Total survival of 21 (35.6%) cases with neutrophil recovery at the first month and 38 (64.4%) cases without neutrophil recovery at the first month were 36.1 (± 7.7) and 5.8 (± 0.9) months, respectively (**p = 0.001**). The OS was 27.7 \pm (5.4) months in patients with platelet recovery at the first months of induction treatment, while the OS 2.1 \pm (0.2) months in the patients who had no platelet recovery at the first months of induction treatment (**p = 0.001**) (Figure 2). The OS of the patients with erythrocyte recovery at the first months of induction treatment was 29.6 \pm (5.7) months, while the OS of the patients without erythrocyte recovery was 2.4 \pm (0.3) months (**p = 0.001**) (Figure 2). Table 2 was showed that the comparison of treatment response and treatment-related complications at the first months of induction treatment. There was 25 cases with neutrophil recovery during follow-up. 14 patients with neutrophil recovery at the first months of induction treatment, total survival rates of 11 cases without neutrophil recovery were 54.05 (± 11.7) and 20.8 (± 6.6) months, respectively (**p = 0.042**) (figure 2). There were 9 (64.3%) patients treated by low dose Ara-C + daunorubicin induction chemotherapy among the 14 patients with neutrophil recovery at the first months of induction treatment (p=0.648). Among 41(69.5%) patients treated with low-dose ARA-C, the number of patients with ANC $\geq 0.5 \times 10^3$ cells/ μL at the end of the first month was 7 (17.1%). The mean duration of neutrophil recovery was 21 days. The survival rates of cases with neutrophil recovery events and those without neutrophil recovery were 25.9 \pm 14.6 months and 5.8 \pm 0.9 months, respectively (p = 0.001).

Discussion: The choice of treatment for advanced age AML patients is decided by considering the performance status and comorbid diseases of the patient. We found that the absolute neutrophil count at $\geq 0.5 \times 10^3$ cells/ μL (recovery of neutrophil) at the first months of induction treatment as low-dose Ara-C in patients with advanced age AML was associated with an increase in overall survival.

Keywords: acute myeloid leukemia

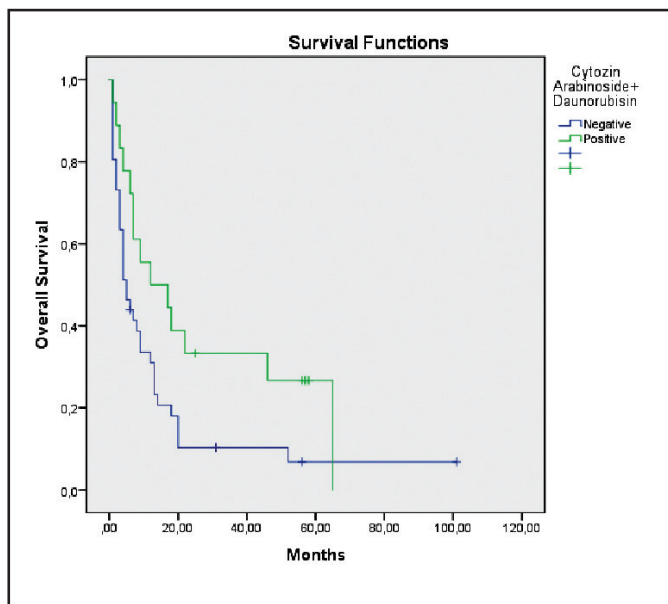


Figure 1. Comparison of the total survival of patients receiving low-dose cytarabine versus patients receiving Ara-C + daunorubicin

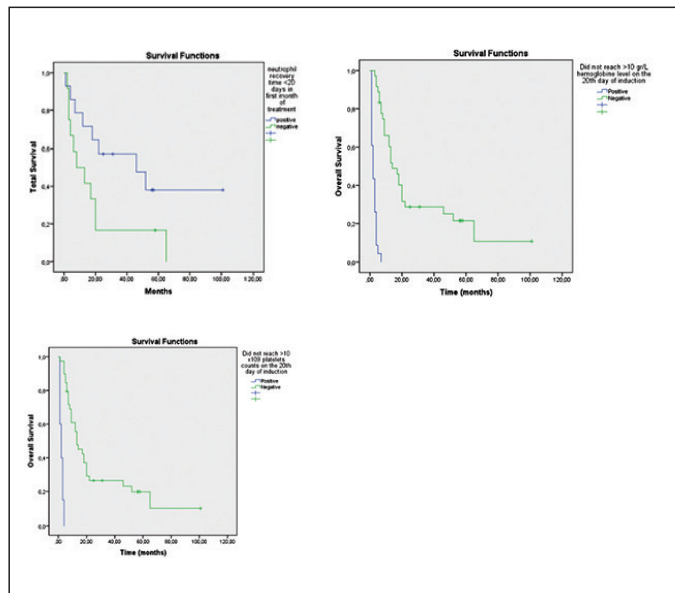


Figure 2. Overall survival curves according to neutrophil, platelet and erythrocyte recovery at the first months of induction treatment

Table 1. Comparisons of clinical and laboratory findings at the time of diagnosis according to the treatment choice.

	Total n:59 patients	Low dose cytarabine n:41 (69.5%)	Reduced intensive chemotherapy (5+2) n:18 (30.5%)	P Value
Gender (f/m)	21(35.6%)/38 (64.4%)	12 (29.3%)/29 (70.7%)	9 (15.3%)/ 9 (15.3%)	0.109
Age (median)	73 (min 65 max 88)	75 (min 65 max 88)	70 (min 65 max 86)	
Age 65-75 years 75-88 years	34 (57.6%) 25 (42.4%)	20 (48.8%) 21 (51.2%)	14 (77.8%) 4 (22.2%)	0.048
Hemoglobine level(g/dL)	9.4 ±2.04	8.9 (±2.08)	10.3 (±1,6)	
Leucocyte count (x10cells/μL)	5600 (min 730 max 291000)	5750 (min 730 max 291000)	4900 (min 730 max 113000)	
Neutrophil count (x10 cells/μL)	2895 (±12691)	200 (min 0 max 92800)	280 (min 0 max 8700)	
Platelet count (x1000 cells/μL)	78.508 (±84.771)	40000 (min 7000 max 202000)	102500 (min 5000 max 451000)	
Sedimentation(mm/h)	57.4(±38.07)	57,3(±40.5)	57.6 (±32.8)	0.852
CRP (mg/L)	59.1(±60.6)	59.8 (±56.4)	65.3 (±63.7)	0.210
<==== td====>	41 (69.5%)	30(73.2%)	11 (26.8%)	0.374
Fit (ECOG 0) Unfit (Ecog 1-2-3)	13 (22%) 46 (78%)	5 (12.2%) 36 (87.8%)	8 (44.4%) 10 (55.6%)	0.014

Table 2. Comparison of treatment response and treatment-related complications at the first months of induction treatment

	Total 59 patients	Low dose cytarabine 41 (69.5%)	Reduced intensive chemotherapy (5+2) 18(30.5%)	P Value
Did not reach ANC of 0.5 × 1000 cells/μL after the first months of induction treatment	33(54.2%)	30 (90.6%)	3 (9.4%)	0.001
Did not reach >10 g/dL hemoglobine level after the first months of induction treatment	36 (61 %)	28 (77.8 %)	8 (22.2 %)	0.076
Did not reach >100x1000 cells/μL platelets counts after the first months of induction treatment	32 (54.2 %)	28 (87.5%)	4 (12.5%)	0.001
Cases of recovery in all series of blood cells after the first months of induction treatment	16 (27.1%)	4 (25 %)	12 (75 %)	0.001
Grade 3-4 infection in first month of chemotherapy	11 (18.6%)	5 (45.5%)	6 (54.5%)	0.074
Presence of FEN	24 (40.7%)	13 (31.7%)	11 (61.1%)	0.046
Time of hospitalization at the first chemotherapy	15 day (min 1 max 51 day)	8 day (min 1 max 45 day)	27 day (min 1 max 51 day)	0.003
Hospitalization time for more than 1 month at the first chemotherapy period	11 (18.6%)	4 (36.4%)	7 (63.6%)	0.025

■ **Non-Hodgkin's Lymphoma**

P-005

Abstract Reference: 131

THE EFFECT OF SARCOPENIA ON PROGNOSIS IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Backgrounds: Sarcopenia is known to be associated with poor clinical outcome in patients with diffuse large B-cell lymphoma (DLBCL).

Methods: We retrospectively reviewed 139 DLBCL patients who treated with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) and rituximab plus cyclophosphamide, vincristine, and prednisone R-CVP therapy. Sarcopenia was classified by the region where the pretreatment skeletal muscle index (SMI) was measured.

Results: Both the sarcopenia-L3 and sarcopenia-pectoralis muscle (PM) groups had increased incidences of severe treatment-related toxicities and treatment discontinuation compared with the non-sarcopenia-L3 and non-sarcopenia-PM groups, respectively. We compared the patients' sarcopenia status before and after treatment according to CT measurements. The sarcopenia and non-sarcopenia- groups had 5-year overall survival (OS) rates of 50 % and 63 % (p =0.028) in after treatment, respectively. We found that the sarcopenia and non-sarcopenia- groups had 5-year overall survival (OS) rates of 63 % and 59 % (p =0.9) in pre- treatment, respectively. When the sarcopenia and non-sarcopenia groups were compared, there were no differences in baseline characteristics, treatment toxicity.

Conclusions: L3- and PM-SMIs are equally useful to define sarcopenia. In this study, sarcopenia was associated with poor survival in patients' sarcopenia status after treatment of patients with DLBCL. More prognostic information can be obtained when examined the status of sarcopenia.

Keywords: Sarcopenia, diffuse large B-cell Lymphoma (DLBCL).

■ Acute Lymphoblastic Leukemia

P-006 Abstract Reference: 106

A NEW MARKER IN CHILDHOOD CANCER: ZONULIN

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Introduction: Zonulin is an important protein synthesized by intestine and liver cells associated with intestinal permeability. It was identified to play an important role in maintaining tight junctions in the intestinal walls. Additionally, zonulin is reported to be associated with a variety of pathologic situations like autoimmunity and malignancies.

Material and Method: A prospective case-control study was performed with pediatric cancer patients monitored by the Pediatric Hematology and Oncology ward in Hatay State Hospital. The study included a total of 20 patients and 35 healthy controls. Demographic data, clinical findings and laboratory parameters were recorded. A total of 32 blood samples were taken from patients. Samples were centrifuged at 4000 rpm and then separated serum was stored at -40 degrees. Serum zonulin level was measured with the enzyme-linked immunosorbent assay (ELISA) method.

Results: In the study 12 female and 8 male pediatric patients were analyzed. Mean age was 7.3±4.4 years. Seven patients had acute lymphoblastic leukemia, 5 patients had Hodgkin’s lymphoma, 3 patients had rhabdomyosarcoma, 3 patients had neuroblastoma, 1 patient had Wilm’s tumor and 1 patient had hepatoblastoma. Serum zonulin levels were identified to be statistically significantly high in the patient group compared to the healthy control group (p=0.013).

Conclusion: The high level of serum zonulin identified in cancer cases may be associated with both the cause of malignancy, side effects of chemotherapy and disrupted gastrointestinal structure linked to causes like mucositis. This study is important as the first study in the literature to assess serum zonulin levels in pediatric cancer cases.

Keywords: Zonulin, Childhood Cancer

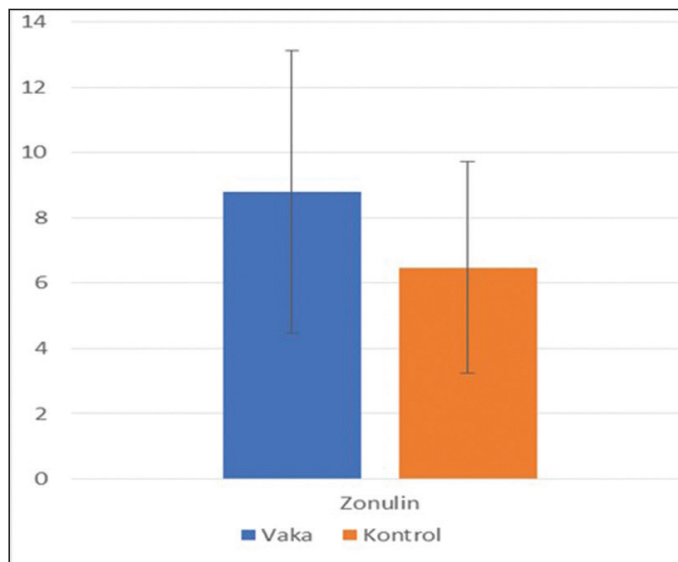


Figure 1. Zonulin

Table 1. Serum zonulin levels

	Case group	Control group	P
Zonulin (ng/ml)	8.80±4.33	6.48±2.52	0.013

■ Acute Myeloid Leukemia

P-007 Abstract Reference: 55

ALTERED EXPRESSION OF TGF-BETA SIGNALING PATHWAY COMPONENTS CONTRIBUTES TO ACUTE MYELOID LEUKEMIA

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Background: TGFβ signaling pathway is a crucial element with tumor suppressive effects, which its malfunction may lead to tumor formation. AML is a heterogeneous disorder caused by defective differentiation and enhanced proliferation in white blood cells and their precursors in the blood and bone marrow. In this study we measured gene expression levels of TGFβ, TGFβRII, smad3 and smad7 in peripheral blood and bone marrow samples of acute myeloid leukemia patients.

Methods & materials: Peripheral blood & bone marrow samples of 93 newly diagnosed AML patients & 13 healthy subjects as control group were examined. The gene expression of TGFβ, TGFβRII, smad3 and smad7 were examined by Real time PCR (polymerase chain reaction). We used SPSS statistical software release 16.0 for analysis between different groups.

Results: Expression levels of TGFβRII & smad3 were significantly increased in AML group versus control group. Also a significant decrease was observed in smad7 expression in AML patients compared with control group. There was no significant change in TGFβ expression between the two groups.

Conclusion: According to upregulation of TGFβRII and smad3 and down-regulation of smad7, it seems TGFβ signaling pathway is over-activated in AML patients, which suggests in despite of conventional role of TGF-β in normal cell cycle, it could be controversial role in the leukomogenesis of these patients.

Keywords: Acute myeloid leukemia, TGFβ, signaling pathway

■ Multiple Myeloma

P-008 Abstract Reference: 107

SLEEP QUALITY OF GERIATRIC PATIENTS WITH MULTIPLE MYELOMA: AN UNDERESTIMATED QUALITY OF LIFE PROBLEM

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Introduction and aim: Multiple myeloma accounts for 1 to 2 percent of all cancers and 19% of all newly diagnosed haematological malignancies, and it is estimated that its incidence will rise considerably due to an increasingly aging population in the Western world¹. Adults with cancer may have disturbed sleep regardless of age. In a study of 2646 patients with cancer, 39% reported insomnia². A couple of previous studies have shown that myeloma patients reported day-time fatigue and sleep problems^{3,4}. However, There is no study evaluating the sleep quality of geriatric patients with myeloma in the literature.

Methods: A total of 35 geriatric aged patients with multiple myeloma who were admitted to the hematology outpatient clinic between December 2018 and February 2019 were included in the study. while sleep quality of the patients were evaluated by Pittsburgh Sleep Quality Index (PSQI), geriatric

assessments were made by using G8 scale. In addition to these scores, serum hemoglobin (Hb), creatinine (Cr), β_2 microglobulin (β_2 MG), calcium, albumin levels were recorded.

Results: Median age of the patients was 73,3 \pm 5,7 years (range 65-91). Global PSQI score of 26 of patients (74.3%) were ≥ 5 indicating that they had poor sleep quality. An impaired G8 score was found in 18 (51.4%) of all patients (Table-1). There were no statistically significant relationship between serum Hb, Cr, β_2 MG, calcium, albumin levels and PSQI or G8 score (Table-2). On the other hand, there was a statistically significant association between PSQI and G8 groups ($p < 0.05$). There was a linear, opposite, moderately strong (42.1%) and statistically significant correlation between total PSQI and G8 scores (Pearson correlation coefficient: -0.421, $p < 0.05$).

Discussion: Poor sleep quality and impaired G8 scores are a frequent problem in geriatric multiple myeloma patients. Neither sleep quality nor G8 scores were related with serum Hb, Cr, β_2 MG, calcium, albumin levels or disease activity. A routine evaluation of sleep quality and geriatric assessments in clinical practise might be helpful to identify this underestimated quality of life problem.

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Keywords: Multiple myeloma, sleep quality

Table 1. Descriptive statistics of the patients

		N	%
Gender	male	21	60
	female	14	40
	total	35	100
PSQI score	<5 (good sleep quality)	9	25.7
	≥ 5 (poor sleep quality)	26	74.3
	total	35	100
G8 score	≥ 14 (normal)	17	48.6
	<14 (impaired)	18	51.4
	total	35	100

Table 2. Comparisons regarding PSQI scores

	PSQI	N	mean	std dev	median	min	max	25p	75p	p value
hemoglobin	<5 (good sleep quality)	9	11.22	1.45	11.40	9.00	13.40	10.05	12.35	0.83
	≥ 5 (poor sleep quality)	26	11.18	2.08	10.85	6.80	15.70	9.58	12.85	
creatinine	<5 (good sleep quality)	9	0.96	0.37	0.86	0.60	1.80	0.70	1.13	0.97
	≥ 5 (poor sleep quality)	26	1.38	1.95	0.88	0.30	10.60	0.60	1.57	
beta2 microglobulin	<5 (good sleep quality)	7	4142.86	2863.48	3000.00	1600.00	8600.00	2000.00	7800.00	0.47
	≥ 5 (poor sleep quality)	22	4836.36	4165.22	4100.00	1800.00	22200.00	2675.00	5350.00	
albumin	<5 (good sleep quality)	9	3.65	0.60	3.80	2.40	4.30	3.35	4.19	0.77
	≥ 5 (poor sleep quality)	26	3.71	0.53	3.75	2.60	4.60	3.48	4.13	
calcium	<5 (good sleep quality)	9	8.93	0.48	9.00	7.90	9.60	8.70	9.20	0.38
	≥ 5 (poor sleep quality)	26	9.22	1.36	9.30	7.70	14.90	8.38	9.50	

Table 3. Association between PSQI and G8 scores

		PSQI			p value
		<5	≥ 5	total	
≥ 14 (normal)	N	7	10	17	
	%within G8	41.2	58.8	100	
	%within PSQI	77.8	38.5	48.6	
	% of total	20.0	28.6	48.6	
G8 <14 (impaired)	N	2	16	18	
	%within G8	11.1	88.9	100	
	%within PSQI	22.2	61.5	51.4	0.038
	% of total	5.7	45.7	51.4	
Total	N	9	26	35	
	%within G8	25.7	74.3	100	
	%within PSQI	100	100	100	
	% of total	25.7	74.3	100	

■ Myeloproliferative Disorders

P-009

Abstract Reference: 58

DIAGNOSIS ISSUES IN CHRONIC MYELOPROLIFERATIVE NEOPLASMS

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The aim of the study was to analyze the issues of clinical, hematologic and molecular-genetic diagnosis in chronic myeloproliferative neoplasms (CMPN).

Materials and methods: The study enrolled 247 patients (pts) with different phases of idiopathic myelofibrosis (IM), chronic myeloid leukemia (CML) and polycythemia vera (PV), who had been treated and followed up at the Institute of Oncology during 1995 – 2018 years. FISH interphase method was applied for diagnosis of CML. The abnormal mixt signal in nucleuses indicated the presence of t(9;22)(q34;q11) translocation. The quantitative RT PCR was used with the aim to determine the expression of the BCR-ABL gene p210 and p190 transcripts at CML diagnosis and during the chemotherapy monitoring. Five transcription products (b2a2, b3a2, b2a3, b3a3 si e1a2) were analyzed by the usage of the quantitative PCR test. The quantitative detection of JAK2 V617F mutation served as a major criterion for diagnosis of IM and PV.

Results: CML was diagnosed in 125 (50.6%) pts, PV – in 92 (37.3%) and IM – in 30 (12.1%) pts. Prefibrotic stage of IM was determined in 12 (40.0%) cases, fibrotic stage – in 18 (60.0%). The diagnosis of CML was established in chronic phase in 113 (90,4 \pm 2,32%) pts, in the accelerated and acute phases – in 12 (9,6 \pm 2,02%). Erythremic phase IIA of PV was revealed in 87 (94,6 %) pts, phase IIB – in 5 (5,4 %). The age category of 50 – 59 years (46,6%) prevailed in the IM pts structure. The age subgroups of 40–49 (27.4%) and 50–59 (19.0%) years were common in CML, that indicated the predominant involvement of the workable population. The predominance of the age categories of 50–59 years (38.0%) and 60–69 years (22.7%) was registered in PV. Plethoric syndrom occurred in all 92 pts with PV and in 9 (33%) pts with Vaughan type of IM, being more significant in PV. Splenomegaly was detected in all pts with IM and CML and in 67 (72.8%) pts with PV. Hepatomegaly was found in 25 (83.3%) cases of IM, 42 (33.3%) of CML and in 46 (50.0%) of PV. The following blood count limits occurred in pts with IM: hemoglobin (Hgb) – 59–178 g/l, erythrocyte count (EC) – 2.3–5.7 $\times 10^{12}/l$, leukocyte count (LC) – 3.6–54.0 $\times 10^9/l$, platelet count (PC) – 18.0–1302.0 $\times 10^9/l$. The bone marrow (BM) biopsy revealed panmyelosis or myelo-megakaryocytic myelosis, massive

proliferation of megakaryocytes and collagen fibrosis. In CML cases the LC range was $12.2-315.0 \times 10^9/l$ and PC range $- 115.0-640.0 \times 10^9/l$. In the BM aspirates, granulocytic series accounted 47.0-86.4%, blast cells $- 1-69\%$, being increased in the accelerated and acute phases. The PV patients experienced the following blood count limits: Hgb $- 174-230$ g/l, EC $- 5.3-6.5 \times 10^{12}/l$, PC $- 180-1620.0 \times 10^9/l$. The iliac crest biopsy with the BM histological examination in PV demonstrated hyperplasia due to the proliferation of erythrocytes, megakaryocytes and granulocytopenia elements at all steps of maturation. In CML the rate of Ph-positive cells ranged between 20 - 100%, exceeding 80% in the majority of pts (70.6%). The quantitative RT PCR of the peripheral blood cells revealed the large variations of the BCR-ABL p210 and p190 transcripts: 21.84-100% IS.

Conclusions: The association of splenomegaly and hepatomegaly was registered more frequently in IM. The elevation of platelet count was higher in IM and PV. The accuracy of diagnosis of CMPN may be provided by the combination of the histologic, cytologic, cytogenetic or molecular examinations.

Keywords: chronic myeloproliferative neoplasms, myeloid splenomegaly, cytodagnosis, real-time PCR, JAK2 kinase

■ Stem Cell Transplantation

P-010 Abstract Reference: 101

COMPARISON OF AUTOLOGOUS CONDITIONING REGIMENS AMONG LYMPHOMA PATIENTS

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Introduction: Salvage chemotherapy followed by an autologous stem cell transplant (ASCT) is still the standard of care for relapsed or refractory lymphoma. ASCT should be offered to patients who have chemosensitive disease. Myeloablative conditioning regimens are used in this setting. Most commonly we use ; Carmustine (BCNU) or lomustine (CCNU) combination with etoposide, cytosine arabinoside and melphalan.

Methods: 41 relapsed or refractory lymphoma patients who were treated in Yuksek Ihtisas University Korum Hospital Hematology and Bone Marrow Transplant Unit between 2014-2019 are included in this study. 12 patients were Hodgkin Lymphoma and 29 were Non Hodgkin Lymphoma Median age was 47 (range 18-72). Male ratio was 56,1% (n=23) and female patients was 44% (n= 18)of the patients .TEAM conditioning regimen is used for 14 patients LEAM is used for 12 patients and 12 patients for BEAM . The median CD34 amount is 5×10^6 for BEAM group , $4,9 \times 10^6$ for LEAM group and $3,7 \times 10^6$ for TEAM group.

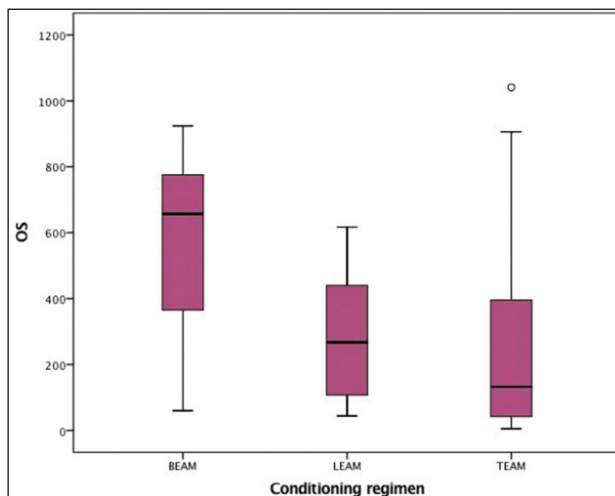
Results: Median neutrophil engraftments were 11,5, 14 and 12,5 days in BEAM , LEAM and TEAM groups respectively. Median platelet engraftments were 13, 12,5 and 12 days in BEAM , LEAM and TEAM groups respectively. PFS were 460, 267 and 83 days for BEAM,LEAM and TEAM. Four patients died because of transplant related mortality all were in TEAM group.

Conclusion:

1. BEAM ,LEAM and TEAM regimens have similar engraftment days.
2. PFS and OS were longer in BEAM group. (BEAM patients have longer follow up)
3. Hospitalization days were equal in three groups.

As a conclusion LEAM and TEAM regimens can be preferred as autologous conditioning regimens beside BEAM.

Keywords: Beam Team Leam Lymphoma Autologous



1. OS

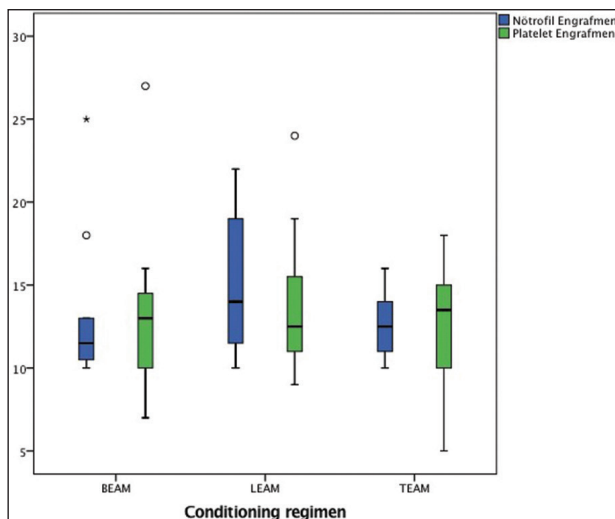


Figure 2. Plt Neu Engraftment

	Total	BEAM	LEAM	TEAM	BEAM/LEAM	BEAM/TEAM	LEAM/TEAM
		median (min-max)					
CD34+	4,8 (2,3-11,2)	5 (2,34-8,44)	4,93 (2,3-11,2)	3,76 (2,46-8,01)	0,665	0,190	0,520
Neutrofil Engraftment	12 (7-25)	11,5 (10-25)	14 (10-22)	12,5 (10-16)	0,153	0,502	0,258
Platelet Engraftment	13 (5-27)	13 (7-27)	12,5 (9-24)	12 (5-18)	0,663	0,642	0,339
Hospitalization time	27 (16-53)	26,5 (23-46)	29 (21-47)	27 (16-53)	0,954	0,796	0,897
PFS	244 (5-1041)	460 (60-924)	267,5 (44-614)	83 (5-1041)	0,133	0,027	0,100
OS	298 (5-1041)	657 (60-924)	267,5 (44-617)	132,5 (5-1041)	0,011	0,018	0,411

■ Non-Hodgkin's Lymphoma

P-011 Abstract Reference: 78

PROGNOSTIC SIGNIFICANCE OF FERRITIN LEVELS IN LOW GRADE NON HODGKIN LYMPHOMA PATIENTS

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Introduction: Low-grade Nonhodgkin lymphoma (LG-NHL) represent more than 50% of malignant lymphomas and characterized by indolent clinical course, which consist of marginal zone lymphoma (MZL), follicular lymphoma (FL), chronic lymphocytic leukemia/small lymphocytic lymphoma,

lymphoplasmacytic lymphoma/waldenstrom macroglobulinemia (WM) as the most common subtypes. These lymphomas usually have a slow clinical course and are limited to the reticuloendothelial system. Some patients may be followed up with the wait-and-see principle until they become symptomatic, while some patients require treatment. Factors which may have prognostic significance after being diagnosed in these patients have long been the subject of research.

Materials and methods: This study was conducted on patients diagnosed with LG-NHL in the Hematology Departments of two centres (Diskapi Yildirim Beyazit Training and Research Hospital and Gulhane Training and Research Hospital) between 2010 and 2018. MZL, FL, hairy cell leukemia (HCL)/ lymphoplasmacytic lymphoma and SLL patients were included. A total of 93 patients were retrospectively analyzed. Demographic information, specific diagnosis, date of diagnosis, treatment regimen, treatment response and follow-up periods were recorded for all patients. At the time of diagnosis, complete blood count (CBC) parameters, albumin, LDH levels, ferritin and B12 vitamin levels were examined. Using these data, response rates, overall survival (OS) and time to treatment duration were calculated. The effect of the parameters on OS and the need for treatment was analyzed.

Results: A total of 93 LG-NHL patients were included in this study, of which 40 were MZL, 28 were FL and 25 were others. The mean age of the patients was 62.96 years and 48 were female. Treatment was required by 69 patients during the follow-up period and was not required by 24. The median time to treatment was 29.8 [17.9-41.8] months in patients who needed treatment. In the comparison of patients with and without treatment, there were significant differences in respect of the number of comorbidities, platelet count, neutrophil count, disease subgroups and ferritin level. Logistic regression analysis was performed and ferritin levels were found to be independent risk factors for the need for treatment (p=0.002). When the survival rates of the patients were examined, it was determined that the median OS of all the patients was 92.9 [34.2-151.6] months. The OS was not significantly different between the subgroups (p=0.990). Only ferritin level was found to be an independent parameter affecting OS in all patients.

Discussion: Several studies have focused on identifying prognostic factors to help clinicians to define the course of the disease and to determine treatment decisions. Some studies have shown that an elevated serum ferritin level is a poor prognostic marker for hematological malignancies. Ferritin levels show iron storage and are elevated in some clinical situations such as inflammation, infection, organ dysfunction, and malignancy without iron overload. In the current study, prognostic markers in LG-NHL patients were investigated and it was demonstrated that higher level of ferritin at the time of diagnosis is a determining factor for treatment requirement and poor prognosis. Given that it is easily available and low-cost at the time of diagnosis, ferritin can be used as a prognostic marker for patients with indolent lymphoma.

Keywords: ferritin, indolen lymphoma, prognosis

Table 1. The clinical and demographic characteristics of patients

	MZL (n=40)	FL (n=28)	Other (n=25)	All (N=93)
Age (median, year)	64.13 (35-81)	63.39 (41-82)	60.60 (41-86)	62.96 (41-86)
Gender (female/male)	25 (62.5%) / 15 (37.5%)	16 (57.1%) / 12 (42.9%)	7 (28.0%) / 18 (72.0%)	48 (51.6%) / 45 (48.4%)
Comorbidity [Median (Min-Max)]	0.5 [0.0-4.0]	0.0 [0.0-4.0]	1.0 [0.0-3.0]	0.0 [0.0-4.0]
IPI/FLIPI score [Median (Min-Max)]	2.0 [1.0-5.0]	3.0 [0.0-4.0]		2.0 [0.0-5.0]
Hb (gr/dL) [mean±SD]	11.73±2.81	12.65±2.59	11.73±3.25	12.01±2.87
Plt (x105/L) [mean±SD]	194000±13200	238000±91000	141000±77000	193000±112000
Wbc (x106/L) [mean±SD]	10280±9360	8050±5890	9860±14160	9500±10300
LDH (U/L) [mean±SD]	294.4±149.6	305.2±320.7	211.4±107.8	276.5±212.4

Table 2. The comparison of patients with and without treatment

(N=93)	Patients with treatment (n=69)	Patients without treatment (n=24)	p
Age (year, mean±SD)	62.26±11.90	64.96±10.48	0.327
Comorbidity [n, Median (Min-Max)]	1.0 [0.0-4.0]	0.0 [0.0-3.0]	0.043
Hb (gr/dL) [mean±SD]	11.79±3.03	12.65±2.31	0.209
Plt (x103/L) [mean±SD]	179217.39±99414.89	234083.33±139107.69	0.039
Wbc (x103/L) [mean±SD]	6000.0 [1900.0-37800.0]	8100.0 [1670.0-65500.0]	0.077
Neutrophil (x103/L) [mean±SD]	2700.0 [500.0-21600.0]	3950.0 [770.0-29600.0]	0.045
Lymphocyte (x103/L) [mean±SD]	1700.0 [200.0-28900.0]	2400.0 [200.0-53700.0]	0.179
LDH (U/L) [mean±SD]	225.5 [111.0-1869.0]	217.50 [158.0-574.0]	0.715
Albumin (mg/dl) [mean±SD]	4.1 [2.4-4.9]	4.3 [2.4-4.8]	0.061
Ferritin (ng/mL) [mean±SD]	91.5 [4.0-1500.0]	44.0 [10.0-290.0]	0.002
Vitamin B12 (ng/mL) [mean±SD]	250.0 [78.0-2000.0]	245.0 [104.0-756.0]	0.575
Disease subtypes (MZL / FL / Other)	25 (%36.2) / 21 (%30.4) / 23 (%32.2)	15 (%62.5) / 7 (%29.2) / 2 (%8.3)	0.030

Table 1. Logistic regression model according to treatment status in all patients

Variable	p	OR
Number of comorbidity	0.337	1.348
Platelets	0.101	1.000
Neutrophil	0.412	1.001
Ferritin	0.032	1.011
Disease subtypes (MZL / FL / Other)	0.084 / 0.391 / 0.028	1.787 / 13.190

■ Non-Hodgkin's Lymphoma

P-012

Abstract Reference: 135

AST/ALT (DE RITIS) RATIO AS A PROGNOSTIC FACTOR IN DIFFUSE LARGE B-CELL LYMPHOMA

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Objective: This study aims to evaluate the prognostic significance of the aspartate aminotransferase (AST) / alanine aminotransferase (ALT) (De Ritis) ratio in diffuse large b-cell lymphoma (DLBCL).

Method: We evaluated the clinical and histopathological data of 225 patients who had diagnosed DLBCL, between December 2003-November 2016 at our hospital. The potential prognostic value of the De Ritis ratio with regard to BC was evaluated using ROC curve analysis. The effect of the De Ritis ratio on the overall survival (OS) was analyzed using the Kaplan-Meier method and multivariate Cox regression models.

Results: The mean age of the patients was 60,3 ± 16,4 (18-95) years, and 57,7 % of them were males. The cut-off value of the De Ritis ratio for OS was calculated as 1.300 in the ROC analysis. In KaplanMeier analyses, the group with a higher De Ritis ratio presented a more unfavorable prognosis for OS (p=0,0001)(Figure 1). Based on the Cox regression models adjusted for

clinical and pathological parameters, for OS, the De Ritis ratio ($p=0.018$), age ($p=0.049$) were determined as independent prognostic factors.

Conclusions: A higher De Ritis ratio can be considered as an independent prognostic factor in DLBCL patients who treated with lymphoma therapy (R-CHOP, R-CVP). Our results need to be confirmed and corroborated by comprehensive prospective randomized studies with an appropriate design.

Keywords: De Ritis, overall survival, Diffuse Large B-Cell Lymphoma

■ Myeloproliferative Disorders

P-013 Abstract Reference: 139

RUXOLITINIB TREATMENT OUTCOMES-SINGLE CENTER EXPERIENCE

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Primary myelofibrosis (PMF) is the least frequent chronic myeloproliferative disorders that characterized by clonal proliferation of myeloid cells. It is more often seen in middle aged and older adults. Most common symptoms are fatigue and other symptoms that are correlated with splenomegaly. Anemia is the most frequent laboratory finding. Patients with polycythemia vera and essential thrombocytosis - two of other myeloproliferative disorders- can develop myelofibrosis (MF) as if it is a PMF. DIPSS-plus score is the best known prognostic tool in this issue.

Allogenic hematopoietic cell transplantation (HCT) is the standart treatment in transplant eligible patient in high risk group. In addition to symptom-related treatments (-like splenectomy, splenic radiation, interferons), hydroxyurea and ruxolitinib are frequently used in transplant ineligible patients. These two agents are good in reducing symptoms but none of them has been proven to improve survival and reduce leukemic transformation.

Although ruxolitinib is a JAK-2 inhibitor, it is not necessary for a patient with MF to have JAK-2 mutation for using this agent. Its mainly goals are to suppress the symptoms and to reduce spleen size. According to COMFORT-1 (Ruxolitinib vs Plasebo) and COMFORT-2 (Ruxolitinib vs Best available treatment) study, ruxolitinib was more effective in reducing spleen volume by ≥ 35 percent.

Here we report our single center experience about ruxolitinib treatment and outcomes in both primary and postessential thrombocytosis (ET) /post-polycythemia vera (PV)/postKMML- MF.

Methods: Regardless of prior treatments, 21 patients with MF who are treated with ruxolitinib in hematology department of Mersin University Research Hospital between 2012-2019, are included in study. Primary endpoint of this study is to determine the decrement in spleen size and secondary endpoint is to determine adverse effects on hemogram.

Results: All patients well tolerated and none of them had to interrupt the treatment because of side effects. Median age was 62,5. 11 of 21 patients were PMF, 3 were postET-MF,5 were postPV-MF.1 was postKMML-MF. JAK-2 mutation status was explored in 12 patients, and 8 of them were positive. DIPSS plus score was calculated in 14 patients and 11 of them were intermediate II in score. Mean hb value was 10.0 gr/dl before the treatment, after 12.7 months-median follow up period, mean hb value decreased to 9,8 gr/dl. Mean spleen was 21.1 cm and 16 cm in size before and after treatment in 10 patients, respectively. Mean leucocyte value was 9053/mm³ and 8790/mm³, before and after the treatment respectively. Mean thrombocyte value was 220300/ mm³ and 185250/ mm³ before and after the treatment, respectively.

Conclusion: Ruxolitinib is the rising star in MF treatment area. Especially spleen size is one of the main items for determining outcomes of this agent. Our results were similar with literature in median age, aduers affects on hemogram and decrease in spleen size. Our patient population is very small in number and median follow up time is a little short. And some of the patients have irregular follow-up condition who have inadequate imaging

and laboratory tests. It would be more informative with large patient population and more disciplined follow up style

Keywords: Myelofibrosis, Ruxolitinib

■ Other

P-014 Abstract Reference: 61

EVALUATION OF CLINICAL MANIFESTATION IN FEBRILE NEUTROPENIC PATIENTS

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Introduction: Neutropenia is one of the most life-threatening and significant complication of intensive chemotherapy treatments. Febrile neutropenia is the major cause of mortality and morbidity in these patients (1).

The aim of this study, was to evaluate the epidemiology and the surveillance factors in febrile neutropenic patients retrospectively.

Methods: This study was undertaken in the Medipol Mega University Hospital Department of Clinical Hematology from December 2014 to December 2017 (3 years).This was a longitudinal retrospective study, which was conducted among 195 patients 400 febrile episodes.

Blood culture was studied by Bact-Alert automated blood culture system.. Antibiotic susceptibility tests were performed according to CLSI (Clinical and LaboratoryStandards Institute) criteria by Kirby Bauer Discus Fusion Method. Resistant pathogens were identified by VITEK-2 ® (Biomérieux, France) automated systems.

Results: A total of 195 patients, 400 febrile neutropenic attacks were assessed. The demographic characteristics of the patients are demonstrated in Table1.

In our study, all the patients categorized as high risk. During FNEs of these patients, 178 of the them(45%) had piperacillin-tazobactam, 145 (36%) had meropenem, 195 (49%) had teicoplanin and 17 (4%) had cefepime.Table 2 shows the distribution of antibiotics applied in the first episodes and 72th hour following the fever-free follow-up in new episodes(secondaryinfections).

In the study, 127 (32%) blood cultures positivity was detected in 400 FNEs. In some cultures more than one growth of microorganisms were detected. 33(8%) urine cultures positivity was detected in 372 FNEs. Table 4 shows the positivity of blood and urinary culture and its distribution.

Sensitivity was studied in 83 of 127 blood culture positivity in FNEs. ESBL was the most common detected resistance mechanisms.Table 5 shows the distribution of the antibiogram results of blood and urinary culture.

Conclusion: For the management and determining empirical antibiotic policies of each centers, it is important to identify their pathogenic microorganisms, to determine their antimicrobial susceptibility and to know resistance profiles for improving survival rates in FEN process.

A shift was detected from gram-positive bacteria to gram-negative in the etiology over the years. The most frequently isolated agents in our hospital were Gram-negative microorganisms.

Infections foci, culture positivity rates, isolated microorganisms consistent with the rates reported in the literature.

Keywords: Febrile neutropenia, Bloodstream infection

Table 1. Demographic characteristics of the febrile neutropenic episodes

	n=400(%)
Age/median (range)	50(18-83)
Female/male	73 / 122 (37%/63%)
Chemotherapy/stem cell transplantation(HSCT)	220/180 (55%/45%)
Autologous/Allogenic HSCT	65/115 (16%/29%)
Hypotension(sys.BP<100mmHg)	38 (9%)
Absolute neutrophil count (<100/>100 mm3)	270/130 (68%/32%)
Mucositis (grade3-4)	59 (15%)
Catheter CVC/HD/PORT	285/85/13 (41%/18%/2%)
GCSF treatment	276 (69%)
Duration of fever (median)	3
Duration of antibiotics therapy (median)	10
Mortality	26 (7%)

Table 2. Categories of infections

	n=400 (%)
Microbiological documented infection	93 (23%)
Clinical documented infection	99 (25%)
Microbiological + clinical documented infection	33 (8%)
Responding to empirical antibiotic treatments without documentation	171 (43%)
Non-infectious fever	2 (0.5%)

Table 3. Positivity of blood and urinary culture and sensitivity of the culture

	Blood culture n=400 (%)	Urinary culture n= 372(%)
Culture Positivity	127 (32%)	33 (8%)
E.coli	50(39%)	17 (51%)
Klebsiella	35 (27%)	10 (30%)
Pseudomonas aeruginosa	8 (6%)	2(6%)
Acinetobacter baumannii	1	1
MSSA	14 (11%)	
MRKNS	21 (17%)	
Sensitivity :		
Sensitive gram -	24 (29%)	8 (27%)
Sensitive/resistant pseudo	6 (7%)/1	
CRE	19 (23)	7(25%)
ESBL	33 (40%)	12 (41%)
VRE		2 (7%)

■ Acute Myeloid Leukemia

P-015 Abstract Reference: 22

IMPACT OF TIME FROM INDUCTION CHEMOTHERAPY TO COMPLETE REMISSION ON OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA PATIENTS

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Background and Aim: The majority of patients with acute myeloid leukemia (AML) receive intensive induction chemotherapy for obtaining a complete remission (CR). Despite consolidation chemotherapy and advances in allogeneic hematopoietic stem cell transplantation (alloHSCT), most of these patients finally relapse and die from AML. The aim of this study is to determine the impact of duration of remission achievement on survival of

patients with newly diagnosed AML who achieve CR after one course of chemotherapy.

Materials and Methods: We retrospectively analyzed patients with AML who received first induction chemotherapy between 2001 and 2018 years. Definition of CR was the presence of less than 5% blasts in the bone marrow, the absence of extramedullary leukemia, and normal values for absolute neutrophil count (>1000/mm³) and platelet count (>100,000/mm³), independence from red cell transfusion. The median time to remission was 29 day (16-48) for all patients. Therefore, in the first 29 days remission was defined as early remission (ER) and entering remission ≥30 days was defined as delayed remission (DR).

Results: Of the 113 patients, 58 (51.3%) patients had ER (<30 days) after induction chemotherapy, 55 (48.7%) patients had DR (≥30) after induction chemotherapy. Median follow-up time was 27 months (range 4-186) for all patients. The 5-year OS for patients who had early remission after induction chemotherapy and patients who had delayed remission after induction chemotherapy were 83% (95% CI: 0.79-0.87) and 35% (95% CI: 0.31-0.39), respectively (p<0.001). The 5-year DFS for patients who had early remission after induction chemotherapy and patients who had delayed remission after induction chemotherapy were 83% (95% CI: 0.78-0.88) and 40% (95% CI: 0.32-0.40), respectively (p<0.001). The OS and DFS were statistically significant higher in patients who had early remission after induction chemotherapy than patients who had delayed remission after induction chemotherapy.

Conclusion: In conclusion, time to entering CR is a predictor factor of overall survival and disease-free survival times for patients with newly diagnosed AML who achieve CR after 1 course of chemotherapy. Patients achieving CR only after a lengthy time, eg. more than 29 days, should be considered to have high relapse rate and should undergo alloHSCT.

Keywords: Acute myeloid leukemia, complete remission, early remission, delayed remission.

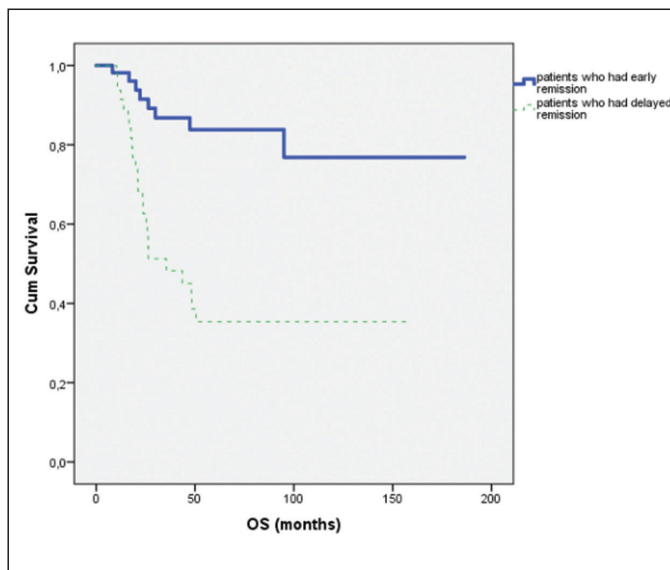


Figure 1. Overall survival for patients who had early CR and patients who had delayed CR after induction chemotherapy (p<0.001).

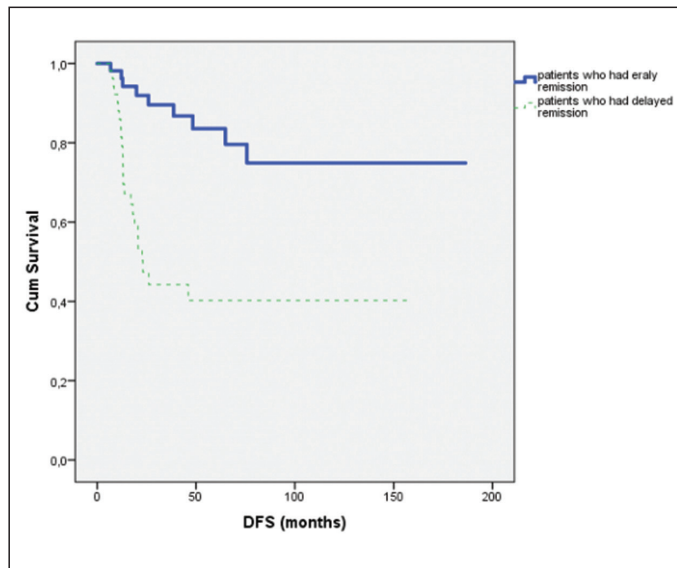


Figure 2. Diseases free survival for patients who had early CR and patients who had delayed CR after induction chemotherapy (p<0.001).

Table 1.

Parameters	Patients who had early remission	Patients who had delayed remission	p
N	58 (51.3%)	55 (48.7%)	
The median age (range), years	46 (20-65)	34/21 (61.8%/38.2%)	0.26
Conditioning regimen			0.78
RIC	30 (51.7%)	27 (49.1%)	
MAC	28 (48.3%)	28 (50.9%)	
ECOG Performance Status			0.08
0	15 (25.9%)	10 (18.2%)	
1	29 (50%)	21 (38.2%)	
2	14 (24.1%)	24 (43.6%)	
Cytogenetic risk group			0.86
Intermediate	40 (69%)	40 (72.7%)	
Adverse	7 (12%)	5 (9.1%)	
Missing	11 (19%)	10 (18.2%)	
GVHD			0.39
Acute GVHD	8 (13.8%)	9 (14.5%)	
Chronic GVHD	18 (31%)	11 (20%)	
Relapse rate (%)	9 (15.5%)	24 (43.6%)	0.001
Mortality (%)	8 (13.8%)	24 (43.6%)	<0.001
Non-relapse mortality (%)	4 (6.9%)	5 (9.1%)	0.66

■ Acute Lymphoblastic Leukemia

P-016 Abstract Reference: 41

RISK OF ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS OF A CASE-CONTROL STUDY IN HAMADAN DURING 2015-2017

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Objective: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Different environmental factors might be effective in the occurrence of this malignancy during childhood. The aim of this study was to find environmental risk factors in childhood ALL in Hamadan-Iran.

Methods: This case-control study was done on 57 children younger than 15 years suffering by ALL during 2015-2017. Patients were matched with 63 controls in respect to age, sex and residential area. Diagnosis of risk factors for ALL was sought based on the comparison of studied variable between cases and controls individuals.

Results: We found a statistically significant increased risk for ALL association with type of delivery (OR: 0.43, 95% CI: 0.20 - 0.92, P<0/02), child care (OR: 4.58, 95% CI: 0.95 - 22.20, P<0/04), father education level (OR: 2.67, 95% CI: 1.10 - 6.45, P<0/02), and father job (OR: 0.2 95% CI: 0.08 - 0.51, P<0/001). We also observed increased odds for ALL regarding boy gender, high mother education level and freelance job, and medium or high family income. No association with ALL incidences was observed for the age, sex, malignancy in first and second-degree relatives, and Use of hair dye during pregnancy by mothers (P> 0.05).

Conclusion: This study showed that father education level and job, delivery type and child care can play a role in incidence of childhood ALL.

Keywords: Acute Lymphoblastic Leukemia, Children, Parents, Risk Factors

Table 1. Comparison of case and controls characteristics and relative risk (odds ratio) of ALL incidence

Characteristics	Cases n = 57	Controls n = 63	Odds ratio (95% CI)	P-value
Sex; n (%) Boys Girls	33 (57.8%) 24 (42.2%)	38 (60.3) 25 (39.7)	1.25 (0.61 - 2.57)	0.54
Type of birth; n (%) Caesarian Normal	41 (71.9) 16 (28.1)	33 (52.4) 30 (47.6)	0.43 (0.20 - 0.92)	0.02
Father's smoking; n (%) Yes No	12 (21) 45 (79)	22 (35) 41(65)	0.50 (0.22 - 1.13)	0.09
Family income; n (%) Low Medium or high	20 (35.1) 37 (64.9)	9 (14.2) 54 (58.8)	3.24 (1.33 - 7.91)	0.08
Malignancy in first-degree relatives; n (%) Yes No	1 (1.7) 56 (98.3)	6 (9.5) 57 (90.5)	0.17 (0.02-1.46)	0.07
Malignancy in second-degree relatives; n (%) Yes No	20 (35.1) 37 (64.9)	23 (36.5) 40 (63.5)	0.94 (0.44 - 1.98)	0.87
Child care; n (%) Home Kindergarten	55 (96.4) 2 (3.6)	54 (85.8) 9 (14.2)	4.58(0.95 - 22.20)	0.04
Father's education level; n (%) ≤ High school ≥ High school	48 (84.2) 9 (15.8)	42 (66.6) 21 (33.4)	2.67 (1.10 - 6.45)	0.02
Mother's education level; n (%) ≤ High school ≥ High school	46 (80.7) 11 (19.3)	46 (73.1) 17 (26.9)	1.55 (0.65 - 3.66)	0.32
Father's job; n (%) Employee Freelance	7 (12.2) 50 (87.8)	26 (41.2) 37 (58.8)	0.20 (0.08 - 0.51)	0.001
Mother's job; n (%) Employee Freelance	4 (7.1) 53 (92.9)	7 (11.1) 56 (88.9)	0.60 (0.17 - 2.18)	0.43
Use of hair dye during pregnancy by mother; n (%) Yes No	8 (14.1) 49 (58.9)	10 (15.8) 53 (84.2)	0.87(0.32 - 2.37)	0.77

■ Non-Hodgkin's Lymphoma

P-017 Abstract Reference: 156

HAPLOIDENTICAL STEM CELL TRANSPLANTATION MAY BE A GOOD ALTERNATIVE AS SALVAGE TREATMENT FOR HEAVILY PRETREATED PATIENTS WITH LEUKEMIA

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Introduction: In the absence of HLA-matched related donor, allogeneic stem cell transplantation from haploidentical donors are potential alternatives for patients with hematological malignancies with an indication to allo-geneic stem cell transplantation. Herein, we retrospectively assessed the outcome of haplo-SCT for patients with refractory hematological malignancies.

Patients and Methods: This analysis included 27 consecutive patients who underwent haplo-SCT for various hematological malignancies at our center between October 2010 and May 2018. We used our institutional database to evaluate details and characteristics of patients and transplant outcomes.

Results: Demographic features of the patients and donors have been summarized in Table 1. All of the patients had advanced disease with a high risk of relapse. The majority of patients underwent haplo-SCT from their parents. Out of 24 patients, early transplant-related mortality was seen in this cohort of 5 patients. Four patients treated with second haplo-SCT and recovered hematopoiesis after second transplant. The remaining 19 patients were followed in a median of 4 months. Donor type ABO group switch was observed in a median of 45 days (30-60 days) after transplant. The median time for engraftment was 19 days (range, 15-60) for all patients. After the first transplant, 9 patients developed acute GVHD (37.5%) with 7 patients having grade II-III acute GVHD. Five (18.5%) had chronic GVHD, none of them with extensive manifestation. The preparative regimen was relatively well tolerated with limited regimen-related toxicity. CMV reactivation occurred in 11 patients (40.7%) during the follow-up of the study. Eight patients (29.6%) relapsed after a median of 132 days post transplant (range, 45-588 days). CR was achieved in 17 (63%) patients after haplo-SCT. Mean estimated 5-year OS and PFS are 66.7%±0.9% and 92.3%±0.7% , respectively. **Conclusion:** Given the growing data on the similarity of outcomes after HLA-matched and haploidentical SCT, further studies are required to determine whether factors may be more important for donor selection than HLA-matching.

Keywords: acute leukemia, haploidentical stem cell transplantation

Table-1: Patient, donor and transplantation characteristics

Variable	n (%)
Median Age, yr (range)	34 (19-66)
Gender (M/F)	11 (40.7%) / 16 (59.3%)
Graft stem cell source	
Bone marrow	7 (25.9%)
Mobilized peripheral blood	17 (63%)
Both	3 (11.1%)
Conditioning regimen	
Myeloablative	19 (70.4%)
Reduced-intensity	8 (29.6%)
GvHD prophylaxis	
PostCy	17 (63%)
CSA+Mtx	10 (37%)
MMF+Tacro	17 (63%)
Median cell dose infused	
TNC, x10 ⁹ /kg	10.26 (1.5-21.1)
CD34+ cells, x10 ⁶ /kg	5.62 (0.97-11.5)
CD3+ cells, x10 ⁷ /kg	15.1 (1.1-11.6)
Engraftment kinetics, day (mean±SD)	
Neutrophil (0.5x10 ⁹ /L)	14.2±9.9
Platelet (20x10 ⁹ /L)	17.8±2.4
Reticulocyte (30x10 ⁹ /L)	18.2±1.7

■ Other

P-018 Abstract Reference: 38

LIFE STYLES, MOTHER AND CHILD HEALTH STATUS AND RISK FACTORS FOR CHILDHOOD LEUKEMIA IN THE GAZA STRIP: CASE-CONTROL STUDY

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Background: Childhood leukemia is one of the most common types of cancer developed in children until 12 years old in Palestine without unknown causes and form 30% of pediatrics cancer, leukemia is one of the top ten-cancer type's killers and has good prognosis if early discovered. The aim of this study is to identify the main life styles and health status risk factors for childhood leukemia among children in Gaza Governorates

Methods: A case control study conducted from five Gaza strip governorates and consisted of 132 child divided in two groups (44 cases who had confirm of childhood leukemia and 88 controls had not). Controls and cases

were matching by age, sex and residency. The cases distributed on Gaza Governorates. The cases were matching as 1 case: 2 control

Finding: The results of the study showed 54.5% were males and 45.5% were females, and the risk factors associated with childhood leukemia were as follows: Family history (P value= 0.001), child admitted to hospital with infection (P value= 0.027) and drug giving during pregnancy stages (P value= 0.005), also, there was association between child hood leukemia and pregnant exposed to passive smoking as (P value = 0.009), child beverage intake (P value= 0.013), and additive in artificial juices (P value= 0.001), while the study found child age, birth weight and child exposed to (passive smoking and X ray) were not association for childhood leukemia. Also, mother age, mother exposed to X ray, white phosphorus and explosive material were not relevant for childhood leukemia. Likewise, live status and additives in food were not associated with childhood leukemia.

Interpretation: The main of the life styles and health status risk factors appeared are avoidable and can prevented.

Keywords: childhood leukemia, risk factors, Gaza Strip, life styles, health status factors.

■ Acute Lymphoblastic Leukemia

P-019 Abstract Reference: 67

THE COMPARISON OF OUTCOMES OF TBI AND NO-TBI CONDITIONING REGIMEN FOR ACUTE LYMPHOBLASTIC LEUKEMIA UNDERGOING ALLOGENEIC HEMATOPOETIC STEM CELL TRANSPLANTATION: A COHORT STUDY

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Allogeneic hematopoietic stem cell transplantation (Allo-HCT) is a potentially curative method for acute lymphoblastic leukemia (ALL) patients. Total body irradiation (TBI) is a standard backbone for myeloablative conditioning regimen in allo-HCT. In this study, we aimed to compare outcomes of TBI and no-TBI conditioning regimen for allo-HCT. The primary endpoint of study was overall survival (OS) and disease free survival (DFS). The number of patients of TBI group and no-TBI group was 23 and 58, respectively. According to conditioning regimen, CY/TBI is the most preferred regimen in TBI group (17/23, 73.9%). 36.3%, 32.8%, 22.4% of patients were received Bu/Flu/ATG, Mel/Flu and Bu/CY regimen in no-TBI group, respectively. According to the FISH and PCR results, 16/56 (28.5%) patients were pH positive ALL. The 1-year and 3-year OS rates were 87% and 67.6% in TBI group. The 1-year and 3-year OS rates were 76.1% and 56.3% in no-TBI group, respectively. There was no statistically significant difference among the groups (p=0.34). The 1-year and 3-year DFS rates were 76.2% and 66.7% in TBI group. The 1-year and 3-year DFS rates were 63.1% and 48.9% in no-TBI group, respectively (p=0.16). 8 patients were died in TBI group. 23 patients were died in no-TBI group. In conclusion, although there was an improvement in allo-HCT results with TBI, there was no significant difference in OS and DFS among TBI and no-TBI groups.

Keywords: Acute lymphoblastic leukemia, conditioning regimen, hematopoietic stem cell transplantation.

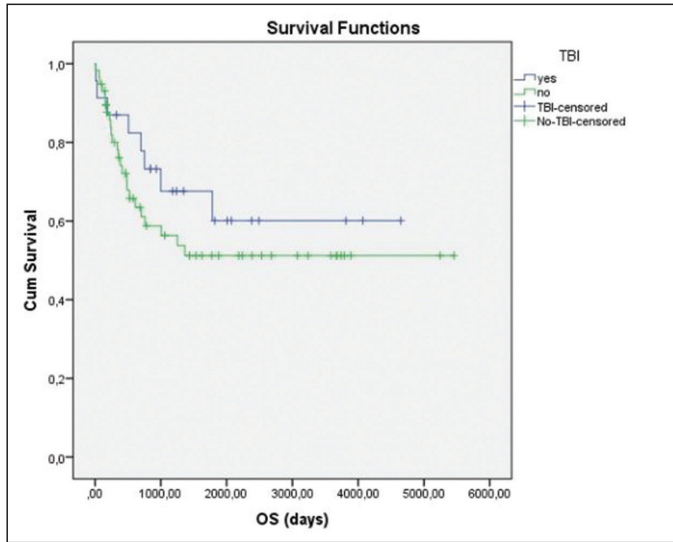


Figure 1. Overall Survival in TBI and no-TBI groups

Table 1. Baseline clinical characteristics of the groups.

	TBI-group (n=23)	no-TBI group (n=58)	p
Age (mean±SD)	29±9.5	33.7±10.2	0.05
Sex (M/F)	15/8	32/26	0.40
B cell ALL	18	42	
T cell ALL	3	11	0.47
Mix phenotype ALL	1	1	
Burkitt ALL	1	4	
Pre Allo-HCT CR disease	19	55	0.08
Pre Allo-HCT Refractory disease	4	3	

■ Acute Lymphoblastic Leukemia

P-020 Abstract Reference: 152

CAN NELARABINE RESCUE THE GRAFT AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN T-ALL?

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Introduction: Adult ALL is a rare disease, T-ALL accounts for nearly %20 of all ALL and T-ALL is more common in adults than children. The success of treatment is less than B ALL treatment for both children and adults. Survival for adult ALL is poor. The use of pediatric intensive chemotherapy regimens in AYAs improved outcomes and nelarabine for relapsed and refractory diseases has resulted in significant response and allogeneic SCT still remains an important component of treatment. Nevertheless relapse is inevitable. Aim of the study is to evaluate the effect of nelarabine as salvage therapy after ASCT, in terms of disease control, GVHD, PFS and OS.

Patients and Methods: Nine (F/M= 1/8; median age= 28 years (21-45)) patients are evaluated retrospectively. None of them received nelarabine, before ASCT. Transplantation characteristics are given in table 1. Between 2014-2018 nine patients from one center received nelarabine as salvage therapy. Patients were treated at the time of relapse with nelarabine alone 1.5g/M2/day on days 1, 3, 5 every 28 days.

Results: Among the 9 patients 67% achieved hematologic remission during 8.2 months (range; 2.9-19.2 mos) follow-up. The features of nelarabine based salvage therapy are shown in table 2. The main toxicity was neurological and involved 22% of patients. At 1 year, disease- free and overall survival rates were 66.7% and 50% respectively (Figure1). Only one patient (11%) received DLI and MRD was lost. On the other hand patients who had MRD and received nelarabine had a stable MRD disease those did not transform to hematologic disease.

Conclusion: The OS at 1 year for salvage treatment with nelarabine at first and secondary relapse is 28%. There is no data about interaction between immune reconstitution, relapse prevention and nelarabine after HSCT. Nelarabine is a well tolerated drug with minimal toxicity and can be considered for maintenance therapy post HSCT in both MRD positive, bulky and CNS disease. Even though it does not show graft versus tumor effect, it can just prevent T-ALL transform to an aggressive leukemia.

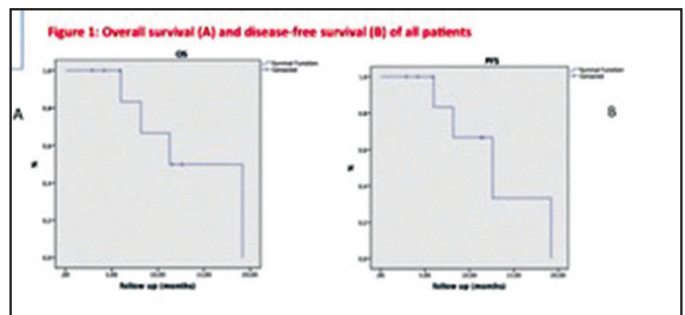
Keywords: T-ALL, nelarabine, allogeneic hematopoietic stem cell transplantation

Table 1: Transplantation characteristics

Characteristics	n (%)
Median date of transplantation	4/2016
CR1	100%
CR2	100%
CR3	100%
Median duration between transplantation and relapse	11 mos (2.3-37 mos)
Median age	34 mos
Median relapse	100%
Transplant CR	100%
Relapse type	100%
Source of stem cells	
HL	4
HL	100%
Type of the conditioning regimen	
Myeloablative	4
Reduced intensity	4
CR-ALL prophylaxis	
CR-ALL	4
Trans-ALL	100%
Median CR-ALL	4 mos (1-10 mos)
Trans-ALL	4 mos (1-10 mos)
Median CR-ALL	4 mos (1-10 mos)
Trans-ALL	100% (1-10 mos)
Response	4
Median time between transplantation and relapse, mo	11 mos (2.3-37 mos)
Median characteristics of relapse	
MRD positive in bone marrow	4 (100%)
Transplant time	100%
CR-ALL prophylaxis	100%
Transplantation procedure	100%

Table 2: Nelarabine-based salvage therapy

Characteristics	Number of incidences
Median duration between transplantation and nelarabine, days (range)	5.1 mos (3.7-42.6)
Median number of nelarabine cycles (range)	3 (2-5)
Response to nelarabine treatment	
CR	5 (56%)
PR	2 (22%)
SD	2 (22%)



■ Multiple Myeloma

P-021 Abstract Reference: 151

CAN THE DRUGS USED BEFORE AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (ASCT) HAVE IMPACT ON CMV REACTIVATION THAT RESULTS IN DECREASED OS IN MYELOMA PATIENTS AFTER ASCT?

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Introduction: The prevalence of active cytomegalovirus (CMV) infection is lower after conventional single autologous stem cell transplantation (ASCT) than after allogeneic stem cell transplantation; however, little is known about the overall incidence of active CMV infection in patients with multiple myeloma (MM) receiving more intensive treatment regimens, such as proteasome inhibitors (PI) and/or immunomodulatory (IMiD) agents.

Patients and Methods: This study involved a retrospective review of all patients with who underwent ASCT between January 2015 and November 2018 at our stem cell transplantation center. A total of 144 consecutive adult patients with a diagnosis of MM (median age at diagnosis: 58, range: 35-77) underwent ASCT following induction treatment with novel agents (PIs and/or IMiDs). All patients received antiviral prophylaxis with acyclovir 600 mg/day (n=104) or valganciclovir 1000 mg/day (n=36). CMV serostatus was determined for all patients before transplantation (Immulate CMV IgG; Siemens, Tarry-town, NY).

Results: Baseline patient characteristics, according to induction treatment, are summarized in Table-1. The study population was predominantly male (60.4%), and had a median age of 58 (range: 35-77). The majority of patients received PI-based induction treatment (97.2%) and IMiD+PI were administered 35.4% (n=51) of the patients before the ASCT. The entire group received a median number of one line (range;1-4) myeloma treatment before the ASCT. One hundred-five of the 144 patients (97.2%) were CMV IgG-positive before ASCT. Overall, 14.6% (n=21) of CMV-seropositive patients developed at least one episode of CMV viremia (CMV DNA >100 copies/ml) after a median 24 months (range; 3-48 mos) follow-up. Persistent CMV viremia (detectable CMV DNA load in more than 2 sequential plasma specimens) occurred in 4.9% (7 of 144) of the seropositive ASCT recipients and all of them were preventive treated with ganciclovir (n=5) or valganciclovir (n=2). The time from stem cell infusion to the development of CMV viremia ranged from 3 days to 48 days. None of the patients with untreated viremia developed identifiable CMV sequelae. No case of primary infection in seronegative patients at transplant was observed. Adding to that none of the patients developed CMV disease post ASCT. If we analyzed the subgroups of patients according to induction therapy (PI-based, IMiDs, PI+IMiD), the incidence of post-ASCT CMV reactivation was higher but not statistically significant, in patients who received only PI vs PI+IMiD (13 (61.9%) vs 8 (38.1%); p=1.00). In univariate analysis, we could not demonstrate the importance of induction therapy with novel agents the occurrence of a post-ASCT CMV reactivation requiring antiviral treatment. However, statistically significant association found between the disease <VGPR status at ASCT and CMV reactivation (61.1% vs. 38.9%; p=0.035). After a median follow-up 14.3 months (range; 1-45.9 months), there was no significant impact on PFS, however there was significant decrease in estimated mean OS who had CMV reactivation when compared to those without CMV reactivation (34.1±4.5 vs. 41.9±1.3; p=0.002) (Figure-1). **Conclusion:** Our data suggests that MM patients treated with PI-based induction regimens and immunological response <VGPR at time of ASCT seem to have higher risk of developing symptomatic CMV reactivation. However, further studies on a large number of patients are warranted to clarify these findings.

Keywords: Multiple myeloma, cytomegalovirus infection, autologous stem cell transplantation

■ Acute Myeloid Leukemia

P-022 Abstract Reference: 39

EVALUATION OF SURVIVAL IN MONOSOMAL KARYOTYPE IN ACUTE MYELOID LEUKEMIA

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Objective: Cytogenetic karyotype analysis is used to determine the risk stratification and prognosis of hematologic diseases such as Acute myeloid leukemia (AML), myelodysplasia or primary myelofibrosis. AML is a disease caused by uncontrolled proliferation and dismaturation of hematological precursors due to idiopathic or chromosomal anomalies. For this reason, cytogenetic assessment is particularly important in AML disease. Monosomal karyotype (MK) is defined as 2 or more monosomies, or a single monosomy in the presence of structural abnormalities and known as a poor prognostic indicator in AML. The aim of the present study is to analyze the survival of AML patients with monozygous karyotypes in a single center.

Methods and Results: A total of 181 AML patients who diagnosed and followed in the Hacettepe University department of hematology between 2000-2017, were enrolled . A cytogenetic anomaly was obtained in 58 of 181 patients. The overall survival of patients with cytogenetic disorders was 85 months (range 0-141), whereas those without cytogenetic disorders were 124.5 months. (1-136)(p:0.01). 6 of 58 patients with cytogenetic abnormalities had monozygous karyotype (10,3%). 4 of 6 patients with monosomal karyotypes were died within 15 months. 3 patients with monosomal karyotypes did not response the chemotherapy (idarubicin-ara-c) and 1 patient,despite showing response to chemotherapy,developed relapse after 5 months. Of 85 patients with cytogenetic disorder, 11 (18.9%) had complex karyotypes. Overall survival of these patients were 37 months (2-45), but no statistically significant difference was observed between complex and monozygous karyotype. (p: 0.7)

Conclusion: Monosomal karyotpe and complex karyotype are poor prognostic indicator for AML. In this study, overall survival were decreased in both of two groups but there was no significant difference between the two groups.

Keywords: monosomal, myeloid, leukemia

■ Chronic Lymphocytic Leukemia

P-023 Abstract Reference: 17

ASSOCIATION OF INITIAL PROGNOSTIC PARAMETERS AND REQUIREMENT FOR TREATMENT IN CHRONIC LYMPHOCYTIC LEUKEMIA

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Aim: B-cell chronic lymphocytic leukemia (CLL) is the most common haematological malignancy in advanced age. The clinical course of the disease is highly variable, therefore there is a need to investigate the various prognostic factors. The CLL cell typically expresses CD5, CD19, CD23 and a monoclonal surface Ig (K or λ) while CD20 is moderately/weakly expressed. We aimed to analyze the clinical, genetic and immunophenotypic features which might have prognostic value in CLL.

Materials and methods: Between February 2010 and June 2018, 87 cases diagnosed with CLL were retrospectively analyzed. Patients who were followed without treatment (T0 group) and who required at least one line treatment (T) were compared. Patients who required 1 line treatment (T1) were also further compared with patients who required >1 line treatment (T2). Statistical analyzes were performed using chi-square test using SPSS

version 16.0 (SPSS Inc., Chicago, IL, USA). A value of less than 0.05 was considered significant.

Results: The mean age of our patient population was 65 (±SD12,8) with Male/Female 56/31. At diagnosis, 68(78.2%) patients were at early stage (0, I, II) and 19 (21.8%) were at advanced stage (III,IV). Del17p, del13q and trisomy 12 were evaluated in 49, 41 and 31 patients and 5, 13 and 4 patients were found out to be positive, respectively. Anemia and thrombocytopenia were present in 25 (28.7%) and 16 (18.4%) patients, respectively. Twenty one (24.1%) patients had B symptoms. Splenomegaly, lymphadenopathy and hepatomegaly were present in 34(39%), 67(77%) and 21(24.1%) patients, respectively. Four of the 15 patients who had direct coombs positivity also had clinical evidence of hemolytic anemia. Four patients had immune thrombocytopenia, 2 of them had concurrent direct coombs positivity and one also had hemolytic anemia. The median Hb, leukocyte and platelet counts were 13.2 gr/dl (4.4-17.5 gr/dl), 23.6 x 10⁹/L (1,7-527 x 10⁹/L) and 200 x10⁹/L (10-345 10⁹/L), respectively. Follow up period was median 38 months (3-180 months). Twenty five (28.7%) patients were treated at the time of diagnosis. Thirty three (37.9%) patients had T1 and 6 (6.9%) patients required T2. The ratio of male patients in group T were significantly higher than female patients (p=0.038). All patients in group T2 were male. More patients in group T had CD38 expression than group T0 (p=0.04). There was no significant difference between the groups in terms of FMC7 and CD11c expressions. Of the 5 patients with del17p, 2 patients required treatment at diagnosis, 2 patients required treatment after 13 and 48 months of follow up, respectively.

Conclusion: In our CLL patients, requirement for treatment was associated with CD38 expression, del17p positivity at diagnosis and male gender.

Keywords: chronic lymphocytic leukemia,

■ Chronic Myeloid Leukemia

P-024

Abstract Reference: 47

SIGNIFICANCE OF LYMPHOCYTE COUNT, MONOCYTE COUNT, AND LYMPHOCYTE-TO-MONOCYTE RATIO FOR PREDICTING MOLECULAR RESPONSE IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA: SINGLE CENTER EXPERIENCE

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Background: Chronic myeloid leukemia (CML) is a neoplastic disease characterized by the translocation of chromosome 9 and 22 to form BCR-ABL fusion gene. Currently, it is possible to quantify the efficacy of CML treatment by molecular monitoring of BCR-ABL via advanced techniques. However, there is need for more simple and rapid biomarkers to assist follow-up of patients with CML. Lymphocyte-to-monocyte ratio (LMR) is a popular and simple marker which is shown to be associated with prognosis in various neoplasms. In this study, we aimed to evaluate the significance of absolute lymphocyte count (ALC), absolute monocyte count (AMC), and LMR in relation with molecular response status in patients with chronic phase CML.

Methods: Samples from chronic phase CML patients admitted to our hematology laboratory for BCR-ABL quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) between April 2012 and October 2018 were retrospectively reviewed and concurrent hemogram testing were noted. Data were grouped according to the molecular response status: absence of major molecular response (MMR), presence of MMR and presence of deep molecular response (DMR). Then, the groups were compared for ALC, AMC and LMR.

Results: A total of 224 samples from 95 patients were included. For each sample, the molecular response status of the corresponding patient together with the values of ALC, AMC and LMR are summarized in table 1. Analysis

revealed significant difference between groups when results from newly diagnosed patients are compared with the patients on treatment regardless of response status (p< 0.05). However, when the samples from patients on treatment are grouped according to molecular response status (without MMR, with MMR and with DMR) analysis failed to reveal difference between groups considering ALC, AMC or LMR (p > 0.05).

Conclusion: ALC, AMC or LMR are not potential biomarkers projecting the molecular response status in patients with chronic phase CML. Different studies with larger scales are needed to find simple markers which will aid follow-up of these patients in the future.

Keywords: chronic myeloid leukemia, lymphocyte, monocyte, lymphocyte-to-monocyte ratio

Table 1. Data of ALC, AMC and LMR relative to molecular response status

Response	n (%)	ALC (k/mm ³) Median (Min-Max)	AMC (k/mm ³) Median (Min-Max)	LMR Median (Min-Max)
Newly diagnosed	29 (13)	5.18 (1.13-67.96)	3.29 (0.03-15.91)	2.07 (0.74-135)
Without MMR	94 (42)	2.02 (0.75-28.76)	0.42 (0.01-19.42)	5.33 (0.56-358)
With MMR	36 (16)	2.05 (1.12-10.43)	0.36 (0.16-1.10)	5.65 (2.11-20.58)
With DMR	65 (29)	1.85 (0.85-7.34)	0.38 (0.20-1.38)	4.82 (1.32-10.83)

■ Chronic Lymphocytic Leukemia

P-025

Abstract Reference: 86

17P AND 13Q DELETION FREQUENCY IN OUR CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS

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Introduction: Deletions 17 p and 13q14 are associated with prognosis in CLL. The data in our country is limited. In a national thesis study at 2010 (Dr Canan Belin Cirit, et al), among 45 CLL patients, there was a percentage of 71% in 13q14 deletion (32 patients) and 31.1% of 17 p deletion (14 patients). Based on the literature, 13q14 deletion percentage is about 55% and 17p deletion is about %7. In our study we aimed to evaluate the frequency of 17 p and 13q14 deletions and their demographic data among 72 patients.

Material and Method: Seventy two patients who have been diagnosed of CLL based on the International Working Group (IWG) criteria were included in the study. Thirty of them were female. Forty two patients were Binet B and 2 patients were Binet C stage. The positivity level of deletions was determined as 15% and above. Four patients who had inadequate interphase were excluded from the study.

Results: The mean age of our study was 66 ±10. Deletions of 17p and 13q14 were evaluated with FISH method. Mean lymphocyte count was 46365 ± 8910 , hemoglobin value was 12.1 ± 1.5 gr/dl and platelet count was 203647 ± 94508 /mm³ Deletion 17 p ratio was 5.6 % (4 patients) and 13q ratio was 27% (20 patients). Two deletions were both positive in 1 patient. Only 5 patients (3 of them were blood type A and 2 of them were type B) didn't have Rhesus(Rh) antigen (Rh negative). There was no relation between 17p and 13q14 deletions and the stage. All of the patients who have the associated deletions were Binet B stage.

Discussion: There was no relationship between 17 p and 13q14 deletions and the lymphocyte count. CLL was dominantly present in the Rh(+) group. The treatment hasn't been initiated any of the patients with deletion 17 p positivity, known as the poor prognosis, at the time of their diagnosis. The patient who had both 13q14 and 17p deletions is being followed as Binet A stage. The life curve analysis of the patients is planned and deletion 11q results are awaited.

Keywords: lymphocyte, del 17p, del 13q14,

■ Stem Cell Transplantation

P-026 Abstract Reference: 43

MESENCHYMAL STEM CELL INFUSION IN GRAFT VERSUS HOST DISEASE: A SINGLE CENTER EXPERIENCE

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Background: Human mesenchymal stem cells (MSC) are non-hematopoietic multipotent cells which may differentiate in osteogenic, adipogenic and chondrogenic series. Steroid refractory graft versus host disease (GvHD) remains to be an important therapeutic challenge in allogeneic hematopoietic stem cell transplantation (HSCT) recipients. Although corticosteroids have been considered as first-line therapy for acute and chronic GvHD, salvage treatment options are limited in refractory cases. Several studies demonstrated that MSC infusion may be a feasible alternative for steroid refractory GvHD. The aim of this study is to determine the therapeutic efficacy of MSCs in acute and chronic GvHD cases who did not respond to several treatment lines including corticosteroids and combined immunosuppressive approaches.

Methods: A total of 16 allogeneic HSCT recipients [median age: 51(19-68) years; male/female: 9/7], who had received MSC infusions for steroid refractory GvHD, were included in this study. Medical records of the participants were retrospectively evaluated.

Results: Of 16 patients, 5 patients (31.3%) were diagnosed as acute myeloid leukemia, 4 patients (25%) as acute lymphoblastic leukemia, 2 patients (12.5%) as Hodgkin lymphoma, 2 patients (12.5%) as myelodysplastic syndrome, 1 patient (6.3%) as primary myelofibrosis and 1 patient (6.3%) as aplastic anemia. Fourteen patients (87.5%) were in complete remission, while 2 patients (12.5%) had progressive disease at the time of MSC infusion. A total of 11 patients (68.8%) had acute and 3 patients (18.8%) had chronic GvHD whereas 2 patients (18.8%) had overlapping features. Eleven patients (68.8%) had gastrointestinal GvHD, 1 patient (6.3%) cutaneous GvHD, 2 patients (12.5%) hepatic GvHD and 2 patients (12.5%) had concomitant cutaneous and pulmonary GvHD. Median day of GvHD onset was +105 (30-2155) and median GvHD grade was found to be 3(1-4). Corticosteroids were the first-line treatment in all patients. All patients were refractory to multiple immunosuppressive and monoclonal antibody combinations including steroids, calcineurin inhibitors, mycophenolate mofetil, ruxolitinib, ibrutinib and rituximab. Standard MSC dose was 1×10^6 /kg for the first and recurrent infusions. Median 4(1-13) infusions were performed based on treatment response. Infusion related side effects were vasovagal syncope and headache which were observed in 2 patients (12.5%). Cytopenia was seen in 4 patients (25%) and infections in 8 patients (50%). Optimum clinical response was achieved on day 15(7-60) of the first MSC infusion. Six patients (37.5%) were evaluated as complete response, 5 patients (31.3%) as partial response and 5 patients (31.3%) as refractory (Table 1). At the end of median 366(100-3325) days of follow-up, overall survival was found to be 35% in the study population (Figure 1). GvHD related mortality was observed in 9 patients (56.3%) and relapse related mortality in 1 patient (6.3%).

Conclusions: Our retrospective results in a limited number of cases demonstrated that MSC therapy may be considered as a feasible option for the treatment of steroid-refractory GvHD with its acceptable toxicity profile in short term follow-up.

Keywords: Mesenchymal Stem Cells, Graft versus Host Disease, Allogeneic Hematopoietic Stem Cell Transplantation

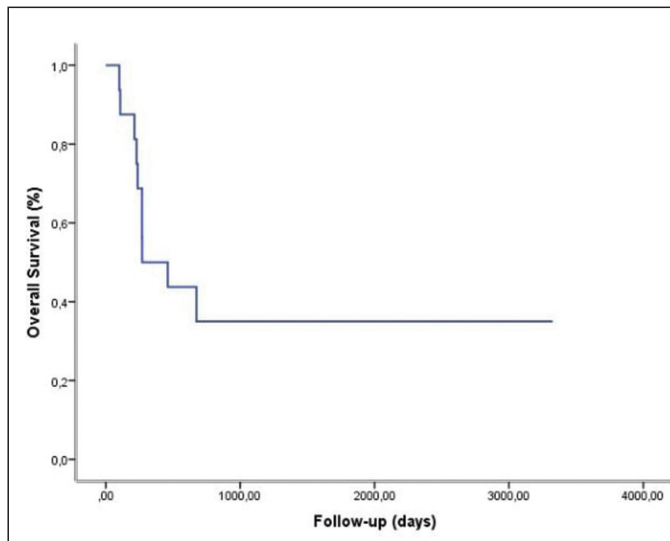


Figure 1. Overall survival was 35% at the end of median 366(100-3325) days of follow-up

Table 1. Mesenchymal Stem Cell Therapy Responses Based on Graft versus Host Disease Type and Localization

		Response			Total
		Complete Response	Partial Response	Refractory	
Type	Acute	4	3	4	11
	Chronic	0	2	1	3
	Overlap	2	0	0	2
Total		6	5	5	16
Localization	Cutaneous	0	0	1	1
	Hepatic	1	0	1	2
	Gastrointestinal	5	3	3	11
	Cutaneous+ Pulmonary	0	2	0	2
Total		6	5	5	16

■ Stem Cell Transplantation

P-027 Abstract Reference: 112

THREE-YEAR EBV PCR RESULTS IN ALLOGENEIC STEM CELL TRANSPLANTATION

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Epstein-Barr virus (EBV) associated posttransplant lymphoproliferative disorders (PTLD) is a major morbidity in patients undergoing hematopoietic stem cell transplantation, and is a cause of mortality. The incidence of EBV DNA-emia and EBV-PTLD varies according to transplant centers. EBV DNA positivity was reported between 0.1-63% according to the type of transplant. According to the donor family donor types of data EBMT 1.2%, or incompatible family donors haplo 2.8%, 4% matched unrelated donor, mismatched unrelated donor was reported to be 11.2%.

Materials and Methods: The EBV PCR results, which were sent once a week between 2016-2018, were retrospectively screened. The files of patients with EBV PCR positive were examined and clinical features were evaluated during positivity.

Results: When evaluated according to years, 216 cases were requested from 38 patients in 2016 and 6 patients (16%) had positive results at 14

tests (6.4%). In 2017, 238 patients were requested from 48 patients, and 11 patients (22%) were positive in 24 (10%) patients. In 2018, 217 investigations were requested from 47 patients and positivity was found in 8 cases (3,68%) in 1 patient (2%)(Table1). Of 18 cases with EBV PCR positive, 5 (27%) were haploidentic and 3 (16%) were transplant. In patients with thalassemia who had positive EBV PCR, Pesaro-class 3 had hemorrhagic cystitis due to BK viremia. Some of our patients had CMV PCR positivity at the same time. EBV Ig G values of all our patients and donors were positive before transplantation. None of our patients had lymphoproliferative disease. We did not receive rituximab treatment except CD27 deficiency and our patient who was positive for EBV PCR before transplantation.

Result: In high-risk (haploidentic, second-line) transplantations, it is useful to perform EBV PCR with CMV PCR.

Keywords: EBV PCR, Children, Allogeneic Stem Cell Transplantation

Table 1. EBV-PCR results by year

	Number of EBV PCR test	Number of positive tests	Number of Patient	Number of Patients with EBV PCR+
2016	216	14 (6,4%)	38	6 (16%)
2017	238	24 (10%)	48	11 (22%)
2018	217	8 (3,68%)	47	1 (2%)

■ Stem Cell Transplantation

P-028 Abstract Reference: 109

CAN ELTROMBOPAG TREAT THE THROMBOCYTOPENIA AFTER STEM CELL TRANSPLANTATION?

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Statement: None

Introduction and Aim: Eltrombopag is an oral nonpeptide thrombopoetin receptor agonist, approved by the Food and Drug Administration for immune thrombocytopenia and aplastic anemia. It is common for the stem cell transplant patient to experience delayed thrombocyte recovery and thrombocytopenia due to poor graft function, and many of them require thrombocyte suspensions throughout this process due to severe and deep thrombocytopenia Here, we present our center’s experience with this molecule in post-hematopoietic stem cell transplantation settings.

Methods: We have retrospectively analyzed our list of HSCT patients shown in the table 1. The patients who failed to achieve adequate graft functioning were given eltrombopag between 25- 75 mg/ day (except 150 and 175 mg/ day in two consecutive patients).

Results: Female to male ratio was 4: 11 and the median age at transplant was 50. The median platelet count was 9000/ mL (3000 to 15000/ mL) at the beginning of treatment and 43000/ mL (6000/ mL in one patient who is reported to be eltrombopag refractory, to 80000/ mL) at the end. The median duration of treatment was 82 days and the median platelet count increase was 38000/ mL and found statistically significant (p= 0.026). The median eltrombopag dose was 50 mg per day. No serious adverse effects such as hepatotoxicity or myelofibrosis related to eltrombopag were seen and the treatment cost was acceptable.

Conclusion: As thrombocytopenia is closely associated with transplant related mortality and overall survival, eltrombopag is an eligible option in posttransplant thrombocytopenia management

Keywords: Hematopoietic cell transplant, eltrombopag, primary isolated thrombocytopenia, secondary failure of platelet recovery, post transplant thrombocytopenia

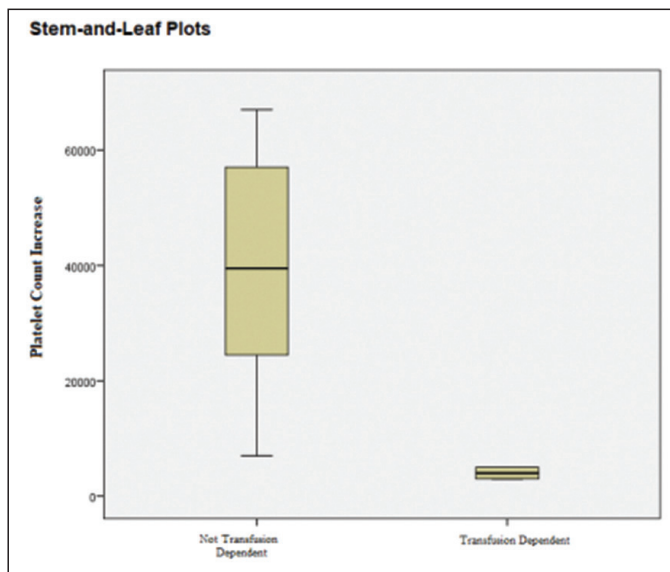


Figure 1. Platelet increase count and transfusion dependency

Table 1. Patient Characteristics

Age (median)	21- 62 (50)
Sex	
F: M	4: 11
Disease	
AA	6 (40 %)
AML	2 (13.3 %)
MF	1 (6.6 %)
CLL	1 (6.6 %)
ALL	1 (6.6 %)
Blastic plasmacytoid dendritic cell neoplasia	1 (6.6 %)
MM	3 (20.3 %)
Donor (Allogeneic)	
Related	6
Unrelated	6
Conditioning	
Myeloablative	12
Reduced intensity	3
Stem cell source	
Peripheral blood	10
Bone marrow	5
Platelet count before starting eltrombopag, median (range), per mL	9000 (3000- 15000)
Platelet count increase, median per mL	38500
Median time from transplant to eltrombopag	145
Median eltrombopag use duration (days)	82

■ Non-Hodgkin's Lymphoma

P-029 Abstract Reference: 129

BORTEZOMIB FOR TREATMENT OF NON-HODGKIN'S LYMPHOMAS; A SINGLE CENTER EXPERIENCE

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Introduction:Bortezomib, an ubiquitin proteasome system inhibitor, is used for multiple myeloma treatment, usually in a combination with other agents. Several aggressive lymphomas such as activated B-cell subtype of diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL) are characterized substantially also NF-kB pathway activation. Considering that, this activation is sensitive to proteasome inhibitors, so bortezomib may be effective for treatment of aggressive lymphomas. In this poster, we present eight relapsed NHL patients treated with bortezomib.

Materials and Methods: We reviewed patients with relapsed and refractory Non-Hodgkin's Lymphoma (NHL) treated during 2000-2019, retrospectively, using patient files and computerized documents. Descriptive and demographic data, type of NHL, treatment sequence of bortezomib, number of totally cure and of complete response, survival after bortezomib treatment and overall survival were analyzed by IBM SPSS version 22.

Results: The median age of the patients was 61.4 ± 9.4 (49-81), number of patients with MCL, DLBCL and marginal zone lymphoma (MZL) were 6 (%75), 1 (%12,5) and 1 (%12,5) respectively. Mean survival after bortezomib treatment was 22.8 ± 16.2 (7-46) months, and overall survival was 79.3 ± 37.2 (35-152) months. Half of the patients were responsive to bortezomib, and 50 percent of these were still alive. Comparison of response to bortezomib between the sub-type of lymphomas was not analyzed due to inadequate number in each of groups.

Discussion: Aggressive lymphomas such as DLBCL and MCL often relapsed after first and subsequently remissions throughout treatment. Several study of combination/single agent bortezomib for sub-type of NHL shows that response rates including CR and PR are up to %50 of patients as our study. Because of limited number of patients and therefore comparative analysis cannot be done, our study may be evaluated as case experience.

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Keywords: Non-Hodgkin, Lymphoma

■ Acute Myeloid Leukemia

P-030 Abstract Reference: 144

DEMOGRAPHIC FEATURES AND CLINICAL CHARACTERISTICS OF MYELOID SARCOMAS : SINGLE-CENTER EXPERIENCE

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Aim and objective: Myeloid sarcoma (MS), also known as granulocytic sarcoma, is an extramedullary tumor mass composing malignant blastic myeloid cells. MS generally presents as the first finding of AML at the time of diagnosis or at the time of relapse. Myelodysplastic syndrome and myeloproliferative neoplasms can also transform into MS less commonly. MS prognosis generally entails poor outcomes. In case of isolated MS, there is myeloblastic infiltration of single or multiple extramedullary organs without any evidence of leukemia in bone marrow and peripheral blood. The diagnosis of isolated MS is very difficult. Here in we report the clinical features and survival outcomes of our MS patients.

Materials and methods: Patient records of the hematology department from September 2011 to October 2011 were screened for myeloid sarcoma. Overall, 10 cases MS were identified and included into this study. Clinical and pathological presentations, demographic features, survival outcomes were reviewed retrospectively.

Results: There were 5 females (50 %) and 5 males (50 %) with a median age of 60 ± 13.8 years (34-75 years). The primary involved sites of MS could be classified into 5 groups as follows: head and neck (N=2, 20%), skin (N=3, 30%), gastrointestinal (GI) tract (N=2, 20%), lymph node (N=2, 20 %), and muscle-skeletal (N=1 10%). 6 patients (60%) had solitary lesion and 4 patients (40%) had multiple MS lesions at the time of diagnosis. 3/10 patients had also bone marrow infiltrations. 9/10 patients had normal karyotype, one patient had complex karyotype. Nine patients were treated with systemic AML therapy (3+7 induction and ara-C consolidation). One patient

were treated with hypomethylating agent due to older age. Complete remission was obtained in seven patients (70%). Partial remission was obtained in two AML with MS patient. One of them was referred to allogeneic bone marrow transplantation. Progression free survival was 11.8 (1-59 months), overall survival was 22 months (1-60). Local radiotherapy was not used in any patients.

Conclusion: MS is rare and unique entity of myeloid neoplasm which diagnosis is difficult. There are not large prospective studies to determine optimal therapy. In our study, systemic chemotherapy seems to be acceptable for fit patients. But to identify novel and selected therapies, larger prospective studies are needed.

Keywords: Myeloid sarcoma, granulocytic sarcoma, acute myeloid leukemia

■ Acute Lymphoblastic Leukemia

P-031 Abstract Reference: 34

LEVEL OF SENSITIZATION BY LEUCOCYTE ANTIBODIES OF PATIENTS WITH ACUTE LEUKOSIS

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Introduction: Ensuring immunological safety of blood transfusion remains one of the most important problems of transfusion medicine. In its decision, the main importance belongs to measures aimed at preventing allosensitization of recipients and the prevention of posttransfusion complications, including refractoriness to therapy with blood components.

The aim: To study the dynamics of the increase in the level of sensitization of patients receiving blood platelet hemotransfusions in Kazakhstan.

Materials and methods: In scientific-production center of transfusiology of Astana city, 23 patients with hematological diseases receiving platelet transfusions were examined for the level of sensitization level. Samples of sera were examined for the presence of antibodies directed to leukocyte antigens of the first class of the HLA system. A flow cytometry method was used on the LABScan 3D analyzer (One Lambda, USA).

Research results: Research of blood serum of patients performed prior to the initiation of transfusion therapy with platelets showed the presence of leukocyte antibodies to class I of HLA in 14 patients (61%), 9 patients (39%) of leukocyte antibodies were not detected.

Further detection of antibodies in 9 patients with initially negative status showed that in 7 of them antibodies appeared within 2 weeks from the beginning of blood transfusion therapy. Antibodies were detected in the remaining 2 patients in study conducted 4 weeks after the onset of platelet transfusions. Two- and four-week monitoring of antileukocyte antibodies among 14 patients with an initially positive status revealed an increase in the level of sensitization available at the beginning of treatment.

Keywords: Acute leukosis, transfusion, patients, antibodies, donors

■ Acute Lymphoblastic Leukemia

P-032 Abstract Reference: 45

METHOTREXATE, VINCRISTINE, L-ASPARAGINASE AND DEXAMETHASONE FOR ADULTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN BRIDGING BEFORE AND SALVAGING AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Despite recent developments in the treatment options, relapsed/refractory acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) are still worse diseases in adults with low salvage and cure rates compared to childhood. L-asparaginase is one of the mainstay differences in the back-bone of multidrug regimens used in children. In our center, we have been using an L-asparaginase integrated combination of methotrexate, vincristine and dexamethasone (MOAD protocol) as a salvage regimen since 2017. In this study, we aimed to summarize our experience with this combination and to the best of our knowledge, there are only limited studies reporting MOAD protocol in the relapsed/refractory disease setting.

Materials and Methods: The adult patients followed at our institution over the course of 2 years (2017-2018) with a diagnosis of relapsed/refractory ALL or LBL were retrospectively reviewed and cases treated with MOAD protocol were enrolled for the study. One treatment cycle of our protocol was 28 days and it combined methotrexate 200 mg/m² intravenously (IV) on days 1 and 15; vincristine 1.4 mg/m² IV on days 1, 8 and 15; L-asparaginase 10 000 IU/m² IV twice in a week; and dexamethasone 40 mg given IV or orally (PO) on days 1 to 4 and 15 to 18 of each cycle. Demographic and clinical characteristics of the patients, response to treatment and adverse events related to therapy were analyzed.

Results: A total of 8 patients included in the study are summarized in table. The median age was 37 years (range: 21-58 years). Half of them have had a history of HSCT and MOAD was used for salvaging after transplantation. The lineage of ALL was B-cell in 4 patients, but all were negative for Philadelphia chromosome. Complete remission (CR) was obtained in 38% after the first cycle and for two of them MOAD protocol worked as a bridging regimen for allogeneic HSCT. Another 2 patients with lymphomatous disease had PR after the first cycle and one of them has also had a successful allogeneic HSCT. All of the 3 patients proceeded to allogeneic HSCT had T-cell disease. No clinically evident hypersensitivity reactions were seen with L-asparaginase and the most common adverse events associated with MOAD protocol were hypofibrinogenemia, anemia and febrile neutropenia.

Conclusions: The MOAD protocol is found to be an effective and tolerable regimen which enables bridging before and salvaging after HSCT, particularly in the setting of relapsed/refractory T-cell ALL and LBL. Yet, the issue warrants more studies with large-scale patient populations.

Keywords: Acute lymphoblastic leukemia, Lymphoblastic lymphoma, L-asparaginase

Table 1. Summary of the patients' clinical course

Patient	Sex/ Age (years)	Lineage	HSCT before MOAD	Response to MOAD	Cycles of MOAD	HSCT after MOAD	Follow-up after MOAD	Outcome
1	M/26	T	Allogeneic	PR after first cycle	3	No	Progression following the 3rd cycle	Exitus
2	M/50	B	Allogeneic	CR after first cycle	3	No	Progression following the 3rd cycle	Continuing treatment with inotuzumab
3	F/21	T	Autologous	CR	1	Yes	Progression at the 123rd day of HSCT	CR after liposomal vincristine
4*	F/58	T	No	CR	1	Yes	Progression at the 90th day of HSCT	Exitus
4*			Allogeneic	NA	1**	No	NA	Exitus
5	F/58	T	No	PR	1	Yes	Keeping PR at the 4th month of HSCT	Keeping PR
6	M/21	B	No	RD	1	No	NA	Exitus
7	M/43	B	No	NA	1**	No	NA	Exitus
8	M/22	B	No	NA	1**	No	NA	Exitus

NA: not applicable; CR: complete response; PR: partial response; RD: refractory disease;
 * The patient has taken MOAD protocol twice at different time points of her follow up: before and after HSCT; ** Exitus before completing the cycle

■ Multiple Myeloma

P-033 Abstract Reference: 7

IMPACT OF BONE MARROW PLASMA CELLS PERCENTAGE ON SURVIVAL AT DIAGNOSIS AND PRE-TRANSPLANT PERIOD IN NEWLY DIAGNOSED MULTIPLE MYELOMA

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Background and Aim: The current definition of complete remission (CR) in multiple myeloma (MM) includes negative serum and urine immunofixation (IFE) tests and <5% bone marrow plasma cells (BMPCs). The aim of this study was to examine the impact of BMPCs percentage on survival at diagnosis and pre-transplant period in newly diagnosed multiple myeloma.

Materials and Methods: One hundred and forty eight patients with newly diagnosed MM who received an autologous stem cell transplantation (ASCT) in our HSCT (hematopoietic stem cell transplant) center at Hacettepe University Hospital between the years of 2008 and 2018 were evaluated retrospectively.

Results: The median follow-up period was 27.4 months (range, 4.5-122) for the entire group. The 3-year OS was 87% in pre-transplant BMPCs <5% group when compared to pre-transplant BMPCs ≥ 5% group as 92% with no statistically significant difference. The 5-year OS for pre-transplant BMPCs <5% group and pre-transplant BMPCs ≥ 5% group were 73% and 70%, respectively (p=0.50). The 3-year the PFS in pre-transplant BMPCs <5% group and pre-transplant BMPCs ≥ 5% group were 77% and 57%. The 5-year PFS in pre-transplant BMPCs <5% group and pre-transplant BMPCs ≥ 5% group were 43% and 13%, respectively. There was statistically significant difference between two groups on PFS (p=0.04).

Conclusion: In conclusion, this study focuses on determination of survival outcome based on the best response obtained before ASCT and particularly highlights the significance of reaching <5% plasma cell pre-transplant period. OS and PFS were better in patients who had pre-transplant BMPCs <5% than pre-transplant BMPCs ≥ 5%.

Keywords: Autologous stem cell transplantation; bone marrow plasma cell; multiple myeloma

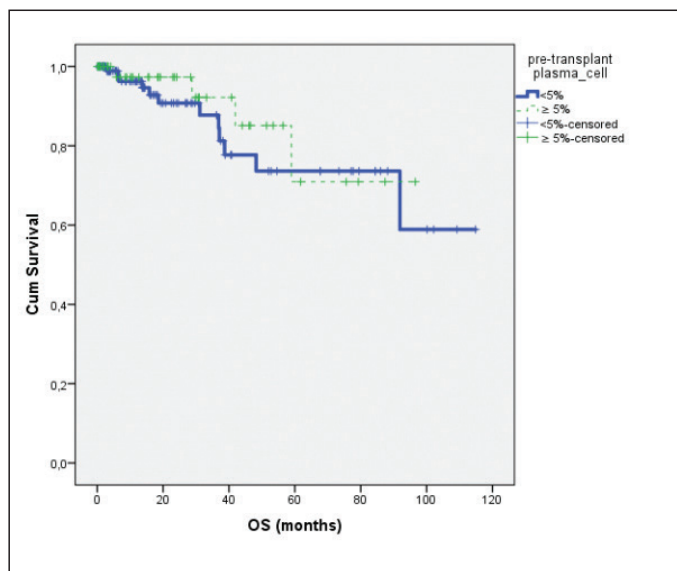


Figure 1. Overall survival according to the pre-transplant bone marrow plasma cells (p=0.50)

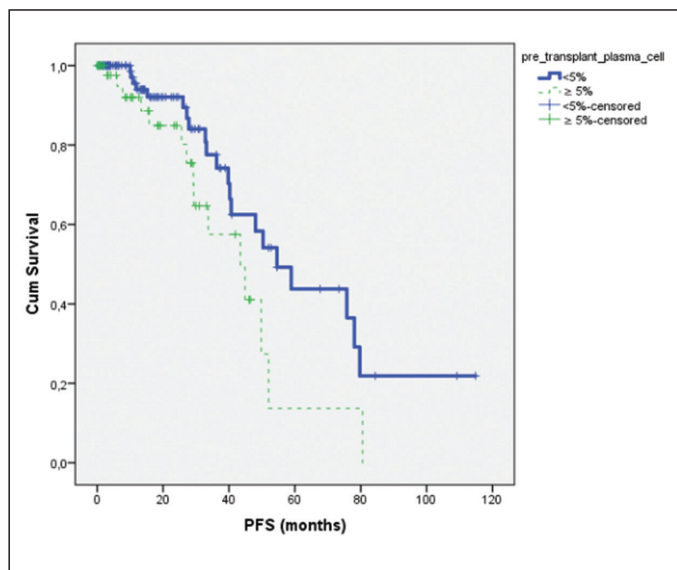


Figure 2. Progression free survival according to the pre-transplant bone marrow plasma cells (p=0.04)

■ Multiple Myeloma

P-034

Abstract Reference: 6

COMPARISON OF BORTEZOMIB-CYCLOPHOSPHAMIDE-DEXAMETHASONE (VCD) VERSUS BORTEZOMIB-DEXAMETHASONE (VD) BASED REGIMENS AS INDUCTION THERAPIES IN MULTIPLE MYELOMA

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Background and Aim: The treatment landscape and clinical outcome of multiple myeloma (MM) patients have changed in the last decades, with an improved median survival of 8-10 years. This study aimed to evaluate the VCD regimen versus bortezomib and dexamethasone (VD) in patients with newly diagnosed MM.

Materials and Methods: This study has been performed in a retrospective manner. One hundred and three patients with newly diagnosed MM who received IT at Hacettepe University Hospital between the years of 2009 and 2018 were evaluated.

Results: A total of 103 patients were included. The 5-year overall survival for patients who received VD regimen and patients who received VCD regimen were 75 % and 83 %, respectively. The OS for VD patients was 113.1±12.5 versus 122.2±9.5 months for VCD patients with no statistically significant difference (p=0.47). The 5-year PFS for patients who received VD regimen and patients who received VCD regimen were 66 % and 75 %, respectively. The PFS for VCD patients was higher than the PFS for VD patients (99.3±13.6 versus 72.4±8 months), but no statistically significant difference was observed (p=0.59). Relapse rate (p=0.002) and mortality rate (p=0.01) were higher in VD group than VCD group and they were statistically significant.

Conclusion: The OS and PFS were clinically longer in patients receiving VCD regimen than in patients receiving VD regimen, although not statistically significant. Cyclophosphamide should given to patients at physician discretion and depending on patient’s frailty function.

Keywords: Multiple myeloma, VD regimen, VCD regimen

Figure :

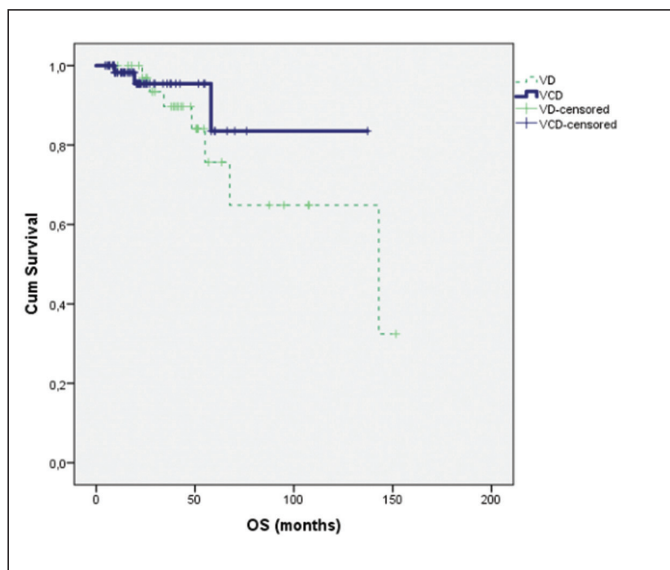


Figure 1. The overall survival for VD and VCD patients (p=0.47)

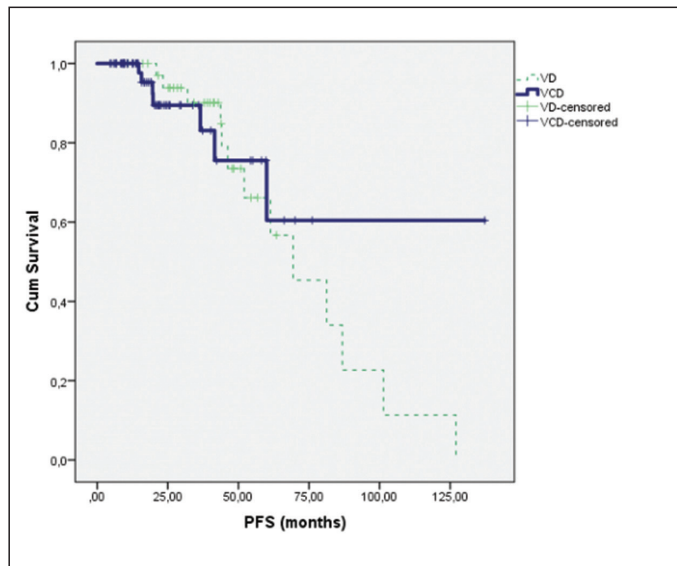


Figure 2. The progression free survival for VD and VCD patients (p=0.59)

■ Non-Hodgkin's Lymphoma

P-035 **Abstract Reference: 95**

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLPD)-CENTRAL NERVOUS SYSTEM (CNS) INVOLVEMENT IN A CASE WITH LIVER TRANSPLANTATION: CASE REPORT AND REVIEW OF THE LITERATURE

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Post transplant lenfoproliferative diseases (PTLPDs) are generally seen in cases with solid organ transplantation (SOT) and related with EBV infection in 70-90% of the cases. PTLPDs are classified as polymorphic, monomorphic, early lesion and classical Hodgkin lymphoma like type. Here a case with PTLPD with CNS involvement has been reported and literature has been reviewed.

Case: 55 year-old-man admitted to the hospital with one week of fever, cough, sputum, headache and difficulty in writing. He had the history of liver transplantation from related living donor and had been treated by mycophenolate mophetile for 18 months, everolimus a few months and then tacrolimus for 2 years. Physical exam showed fever (37.8°C) and he had been treated by tazobactam piperacillin and moxifloxacin combination. Cranial MRI showed bilateral parietal and left cerebellar lesions compatible with metastatic lesions. Systematic evaluation including CT scanning and PET/CT scanning did not show extracranial lesion. Hydrocephalus developed in a short time and ventriculo-peritoneal shunt was performed and cerebellar mass was excised. Histopathologically mass was reported as PTLPD-polymorphic type. Immune-histochemically LMP-EBV, CD20, LCA, Pax5 and CD30 were found to be positive and CD15 was negative. Rituximab and methotrexate containing regimen was planned but he died due to opportunistic infection.

Discussion: The majority of PCNS-PTLDs are B-cell non-Hodgkin lymphomas, 20- to 120-fold higher incidence of lymphomas/PTLD have been reported in cases with SOT. Age, type of transplantation and intensity of immunosuppression are the most significant risk factors. Although PTLDs typically occur in the first year post-transplant period, late recurrences of EBV+ PTLPD are common and 40% of cases are diagnosed later than 6 years after SOT. PTLPD in our case was detected at 4th year of transplantation. Isolated CNS involvement of PTLD is uncommon, about 100 patients have been reported so far. Presenting signs and symptoms of PCNS-PTLD are similar to intracranial mass lesions as in our case. MRI is the preferred imaging

as in our case. Multifocal supratentorial involvement is more frequent but periventricular region may be involved and may cause to hydrocephalus as in our case. Diagnosis is based on biopsy to confirm the diagnosis and also to exclude opportunistic infections. Surgical resection is the treatment of choice but this may be possible in the minority of the cases. Surgery can not be performed in cases with multicentric disease as in our case and poor prognostic indicator. Other treatment options are reduction of immunosuppression, whole-brain radiotherapy, and systemic chemotherapy and/or monoclonal antibody therapy. Although reduction of immunosuppression alone is useful in cases with early systemic polyclonal PTLPD this is not sufficient in cases requiring rapid disease control as in our case. Rituximab-containing regimens and/or cranial radiotherapy are frequently used. Autologous or allogeneic EBV-specific cytotoxic T-lymphocytes (CTL) may be useful but it requires time and is not appropriate in cases requiring urgent treatment.

Keywords: Post transplant lenfoproliferative diseases, EBV, solid organ transplantation

■ Acute Lymphoblastic Leukemia

P-036 **Abstract Reference: 21**

SUCCESSFUL TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA DURING PREGNANCY RESULTING IN A SAFE DELIVERY: CASE REPORT

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Introduction: Acute leukemia is a rare event during the course of pregnancy. There is almost always a dilemma between optimal maternal treatment and fetal well-being. The maternal interest favors the immediate initiation of leukemia. However, possible teratogenic effects may result in the delay of leukemia treatment.

Case: A 22-year-old female primigravida at 20 weeks gestation presented to the emergency department with a 2 week history of progressive fatigue and dyspnea. Complete blood count showed a white blood cell count of 12000/mm³, hemoglobin 3.9 g/dl and platelets 95000/μl. Bone marrow biopsy revealed precursor B-cell Acute Lymphoblastic Leukemia (ALL). Bone marrow cytogenetic analysis showed 46 XX karyotype and RT-PCR analysis revealed the expression of MLL-AF4 fusion. Ultrasound revealed a single living fetus at 20 weeks with weight corresponding to the 39th percentile and normal amniotic fluid. The decision was made to wait until at least 30 weeks to deliver the baby via caesarean section. As remission induction treatment, HyperCVAD regimen was initiated. Intrathecal treatment was not planned due to possible risk of induction of labor due to lumbar puncture. For initial prophylaxis, acyclovir and fluconazole were given. Bone marrow biopsy on day +25 of HyperCVAD1A showed hematological remission. HyperCVAD1B and HyperCVAD2A were initiated at 24th and 27th week of gestation, was initiated. The fetal follow-ups showed no abnormality. HLA matched sibling donor was identified. It was planned that the patient undergoes caesarean section after completion of HyperCVAD2B and subsequently undergoes allotransplantation due to high risk ALL. At 31st week of gestation, HyperCVAD2B was started. On day +6 of HyperCVAD2B, her birth contractions began and the patient gave birth to a 1250 mg female following caesarean section. The baby required transient respiratory assistance for 36 hours post delivery due to cyanosis and poor respiratory effort. One month after delivery, the patient has now been hospitalised for allogeneic stem cell transplantation from her matched related donor. The baby continues to do well as well.

Discussion: Each pregnant patient with malignancy represents a peculiar challenge requiring the treating physician to take into consideration the gestational age at presentation, the type of malignancy and the chemotherapy regimen and its doses while focusing on optimal outcome for both the mother and the infant. Treatment of acute leukemia during pregnancy remains an even greater challenge than treating solid tumors or lymphoma due to the requirement of using much higher doses of induction chemotherapy. Our

case represents the feasibility of treating ALL with HyperCVAD during the second trimester of pregnancy with optimal outcomes.

Keywords: acute lymphoblastic leukemia, pregnancy

■ Non-Hodgkin's Lymphoma

P-037

Abstract Reference: 87

EXCEEDINGLY RARE PATHOLOGIC EVOLUTION AFTER ALLOGENIC STEM CELL TRANSPLANTATION: FOLLICULAR HELPER T CELL TYPE NODAL PERIPHERAL T CELL LYMPHOMA

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T cell lymphomas are rare and heterogenous types of lymphomas and development of follicular T helper phenotype T cell lymphoma after the treatment of B cell lymphomas are exceedingly rare. Here we present a case, which autologously transplanted years ago because of diffuse large B cell lymphoma (DLBCL) and relapsed, then treated with chemotherapy and allogeneic stem cell transplantation (ASCT), and relapsed early and showed characteristically T cell lymphoma phenotype.

Fourty one year old male patient was diagnosed DLBCL (stage 4 A, International prognostic Index:2) from axillary lymph node biopsy at year 2014 and received 8 cycles of R-CHOP-21 chemotherapy. While he was being followed up at remission, at 2015, he developed back pain and cervical lymphadenopathy (LAP) and PET-CT was performed, new developing retroperitoneal (SUV max:4) and cervical LAP (SUV max:4.9) were detected. (Deauville-3) Cervical lymph node biopsy was performed and relapsed DLBCL diagnosis was confirmed. R-ESHAP-28 protocol was begun. After 2 cycles, autologous stem cell transplantation was performed at May 2016. The patient was followed up in remission without treatment until September 2017, but relapsed again as new developing axillary, mediastinal, mesenteric and peripancreatic LAP (SUV max:6). Donor screening for allogeneic transplantation and lenalidomide treatment was initiated. After 6 cycles, repeat PET-CT at June 2018 showed progression of abdominal and retroperitoneal LAP (SUV max:5.7, size:2.1). Lenalidomide treatment was changed with GDP-21 (gemcitabine, dexamethasone, cisplatin) regimen. After 2 cycles, although new PET showed progression of present LAP, the patient received allogeneic stem cell transplantation with myeloablative conditioning regimen from his full match (10/10) healthy sister at November 2018. He was discharged from hospital with no obvious sign of graft versus host disease to be followed at outpatient clinic. After 2 months from the transplantation, a persistent axillary LAP was detected by physical examination, and excisional biopsy showed nodal peripheral T cell lymphoma, phenotyped as follicular helper T cell type. The biopsy showed CD19, CD 20 and cyclin D1 positivity and EBV (EBstein Barr Virus encoded RNA) negativity. Ki-67 index was 70%. He admitted to hospital again and received donor lymphocyte infusion (DLI) as one single CD3 dose of 1×10^7 /kg from his sister, 2 additional DLI infusions are planned in the future. Brutinib monotherapy was started for the relapsed lymphoma. Control PET-CT showed regression of previous involved abdominal and complete remission of supraclavicular, axillary and cervical LAP (Deauville 4).

De novo CD20 (+) T cell lymphomas are rare malignities, but pathological evolution from B cell lymphoma after ASCT is extremely rare. We want to emphasize careful examination of treatment resistant B cell lymphomas and the importance of DLI's at early phase of post-ASCT.

Keywords: lymphoma, DLI

■ Stem Cell Transplantation

P-038

Abstract Reference: 117

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH CD27 DEFICIENCY

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CD27 deficiency, also known as lymphoproliferative syndrome 2, is an autosomal recessive immunodeficiency disorder. Persistent symptomatic EBV viremia, hypogammaglobulinemia and T cell dependent B cell response are associated with impairment of specific antibody formation and T cell dysfunction. The clinical presentation ranges from symptomatic, borderline hypogammaglobulinemia, to EBV-associated life-threatening systemic inflammatory response, to hemophagocytic lymphohistiocytosis and malignant lymphomas.

In this article, we present allogeneic hematopoietic stem cell transplantation in advanced CD27 deficiency was detected in the advanced investigation of two siblings diagnosed as Hodgkin lymphoma and Burkitt lymphoma.

Case-1: A 9-year-old female patient was diagnosed with CD27 deficiency in advanced investigations due to stage 3 Burkitt lymphoma 6 years ago and nodular sclerosing Hodgkin lymphoma 5 years ago. She received rituximab treatment 2 times before transplantation; because of EBV PCR was high titer positive. Conditioning regimen was consisted of rituximab, fludarabine, busulfan, thiotepa and ATG. A bone marrow-derived stem cell transplantation containing 2.75×10^6 /kg CD34+ cells, 3.98×10^9 /kg nucleated cells was performed from the HLA 10/10-compatible cousin. Graft versus host prophylaxis was consisted of Cyclosporine + short MTX. Neutrophil engraftment was on day +17, thrombocyte engraftment was on day +35. During follow-up, EBV PCR was negative. The patient who completed the 12th month after transplantation had no acute or chronic GVHD. The first year of chimerism was 99% donor.

Case-2: A 13-year-old female patient was treated 6 years ago with the diagnosis of mixed cellularity classic Hodgkin lymphoma. In further investigation, she was diagnosed with CD27 deficiency and allogeneic stem cell transplantation was performed by a HLA 10/10 cousin. The preparation regimen included fludarabine, busulfan, thiotepa and ATG. A bone marrow-derived 2.3×10^6 /kg CD34 + cells were given. Neutrophil engraftment was on day +14, thrombocyte engraftment was on day +52. She received defibrotide for sinusoidal obstruction syndrome on day +32. The patient who completed the 4th month after transplantation had no acute or chronic GVHD. The third month resulted in chimerism as 99% donor.

Discussion: Treatment with CD27 deficiency varies according to clinical presentation. Allogeneic cord stem cell transplantation has been reported in 3 patients who developed lymphoma in the literature with a reduced intensity preparation regimen (Bu-Flu-ATG / Bu-Cy-ATG / Cy-Flu-TBI). In these cases, HHV6, CMV and EBV reactivation were post-transplanted. In our first case, EBV PCR was decreased with rituximab, and EBV PCR was decreased. The EBV PCR results were negative during and after transplantation and post-transplant lymphoproliferative disease free. No viral infection or reactivation was observed in the second case.

Keywords: CD27 deficiency, Allogeneic Hematopoietic Stem Cell Transplantation, Hodgkin lymphoma, Burkitt lymphoma.

■ Chronic Lymphocytic Leukemia

P-039 Abstract Reference: 49

LATE ONSET LEFT VENTRICULAR DYSFUNCTION AND CARDIOMYOPATHY INDUCED WITH IBRUTINIB

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Bruton tyrosine kinase is an important part of B cell receptor and is very essential for B cell survival, proliferation and differentiation. We report a case with left ventricular dysfunction and cardiomyopathy developed 1 year after treatment with ibrutinib for relapsed CLL.

In our case, a 66-year-old, presented with widespread itching in her body and lymphocytosis. Bone marrow biopsy was performed in July 2011, pathology was diagnosed as CLL. The del17p mutation was negative. She (Stage 1 CLL- according to Rai staging) was followed up for 2 years without treatment. R-FC treatment was started in January 2013, due to the fact that lymphocyte doubling time decreased below 6 months. She received 4 courses of R-FC and 4 courses R-bendamustine. She complained of palpitations in April 2015 and did not have any cardiac history other than hypertension (HT). Atrial fibrillation (AF) was detected on electrocardiography (ECG). Echocardiography (ECHO) was performed and the ejection fraction (EF) was 60%. The patient was evaluated as Grade 2a AF and sinus rhythm was achieved with medical treatment. In October 2017, because she was unresponsive to 2 treatment, ibrutinib 420mg po was initiated to the patient by obtaining non-indication, due to the fact that the lymphocyte doubling time was below 6 months. The patient received ibrutinib 420mg between October 2017 and October 2018 and applied to the cardiology department on October 2018 due to dyspnea, exertional dyspnea and pretibial edema. ECG revealed normal sinus rhythm, transthoracic ECHO revealed EF 15%, left ventricle and atrium dilated and systolic dysfunction. The patient's low EF status was noted after 1 year of ibrutinib use and ibrutinib treatment was discontinued. In the control transthoracic ECHO performed 1 month after cessation of treatment, the patient's EF was 41%.

Clinical study data show only two main cardiac side effects, HT and AF by this time. AF is frequently observed with the use of ibrutinib and 5% -6% with 18 months follow-up and up to 16% in longer follow-ups. In HELIOS study; 7% patients in the ibrutinib group, 2% patients in the placebo group, AF observed. Median time until beginning of AF, was 3-10 months in the ibrutinib group and 2-4 months in the placebo group. In our patient, there was a history of grade 2a AF and heart failure was detected in the 12th month of ibrutinib treatment. The development of cardiomyopathy with ibrutinib is reported with two cases. In these 2 cases left ventricular dysfunction and cardiomyopathy was presented with arrhythmia which was not present in our case. One of the routes regulated by BTK is the phosphoinositide 3-kinase (PI3K)-Akt pathway. PI3K-Akt path is important for prevention of stress-induced cardiomyopathy. Ibrutinib irreversibly inhibits BTK and causes blocking of a pair of pathways. It has been hypothesized that blocking PI3K-Akt pathway is mainly involved in atrial fibrillation development. Similar to this, inhibition of tec protein tyrosine kinases pathway with ibrutinib may be the reason AF. Even though both mechanisms are involved, the exact cause of atrial fibrillation and heart failure development by ibrutinib have not yet been fully clarified. Particular attention should be paid to the emergence of AF and other unexplained cardiac complications in patients treated with ibrutinib and other agents acting on the PI3K-Akt pathway inhibiting PI3.

Keywords: ibrutinib atrial fibrillation cardiac failure

■ Non-Hodgkin's Lymphoma

P-040 Abstract Reference: 84

PRIMARY SKELETAL MUSCLE DIFFUSE LARGE B CELL LYMPHOMA WITH SEVERE NECROSIS SUCCESSFULLY TREATED WITH CHEMOTHERAPY: CASE REPORT

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Introduction: Diffuse large B cell lymphoma is the most common form of non-Hodgkin lymphomas. Twenty to 30% of them are presented as extranodal disease. Primary skeletal muscle presentation is a very rare form of the disease [1]. Patients typically present with a painful and swollen mass.

Case report: A 71-yo woman was presented to the dermatology clinic with pruritus in the right thigh area. No overt lesion was present and symptomatic medications were prescribed. In the follow-up, a diagnosis of abscess was made and, antibiotherapy was prescribed. However, the antibiotherapy did not improve the mass and it continued to become larger and deeper. Six months after the initial presentation, the MRI reported a mass of 10cmx12cm in the rectus femoris muscle and in the soft tissue anterior to the muscle.

Biopsy was performed and diffuse neoplastic infiltration on a desmoplastic area with extensive coagulation necrosis was described. The tumoral cells were CD20+, CD3-, Bcl6+, CD10-, MUM1-, Bcl2+ and, Cmyc+, with a Ki67 proliferation index of 90-95%. The findings were reported to be consistent with double expressor high grade B cell lymphoma.

Our patient was presented to our outpatient clinic with an open wound of 10cmx4cmx5cm (Figure 1a), with an extensive malodorous discharge. She was a frail elderly patient, with a severe walking disability due to muscle loss in the right thigh, using crutches. In her past medical history, she had a cerebrovascular accident probably related to the atrial fibrillation. In her CBC, she had neutrophilic leucocytosis, with a WBC of 18600/mcl. The serum LDH level was within normal limits. In the PET/CT scan, the only area involved was the anterior thigh, with a mass of 10.3x6.3x15.3 cm (Figure 2a). We could not perform bone marrow biopsy due to her physical condition.

Considering her fragility and her cardiac problems, we initiated the treatment with three cycles of rituximab 375mg/m², cyclophosphamide 750 mg/m² and oral methyl-prednisolone 80 mg/day D1-5 q21d. Her wound was improved (Figure 1b) and her physical performance was better, we switched to R-miniCHOP regimen (Rituximab 375mg/m², cyclophosphamide 400mg/m², doxorubicin 25mg/m², vincristine 1mg and methylprednisolone po 80mg D1-5). Following 4 cycles q21d, the wound was almost totally closed (Figure 1c), with a concordant complete response on the PET/CT (Figure 2b). Curative radiotherapy for the primary involved area is planned for our patient.

Discussion: The common clinical symptoms of primary skeletal muscle lymphoma are related to extremity pain, muscle swelling and, edema. They may occur as isolated lesions. The thigh muscles, which were involved in our case, constitute an atypical area for this type of presentation. The initial lesion was confused firstly with dermatitis, then with abscess. Although it is a very rare type of DLBCL, it should be kept in mind especially in elderly patients presenting to the orthopedics clinics with related symptoms. The choice of treatment may be challenging as it is an aggressive disease which presents in the elderly patients and which develops its own disabilities due to muscle necrosis. Our patient responded well to R-mini CHOP treatment and we need long term follow-up to evaluate the durability of response after radiotherapy.

1. Swerdlow SH, Campo E, Pileri SA et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016;127:2375-2390.

Keywords: Primary skeletal muscle lymphoma diffuse large B cell lymphoma, elderly



Figure 1: The open wound on the right thigh of our patient.
A: at the time of presentation to our clinic
B: After 3 cycles of R-CP
C: After 4 cycles of R-miniCHOP

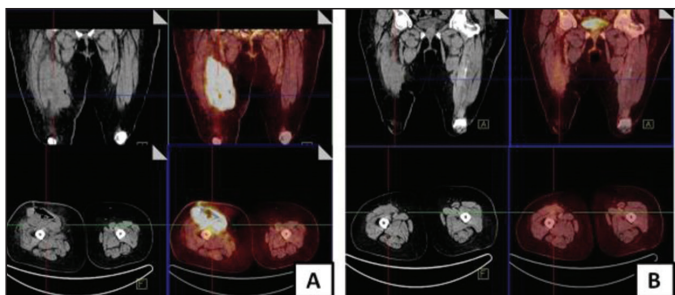


Figure 2: The open wound on the right thigh of our patient.
A: Initial PET/CT scan
B: End-of-treatment PET/CT scan

■ Acute Myeloid Leukemia

P-041 Abstract Reference: 124

ACUTE MYELOID LEUKEMIA ASSOCIATED WITH NON LANGERHANS CELL HISTIOCYTOSIS, CHALLENGING CASE

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Introduction: Necrobioticxanthogranuloma (NXG) is a rare, chronic, progressive granulomatous disorder, it is also a subgroup of non langerhans cell histiocytosis (NLH). It manifests as cutaneous papules and nodules that evolve to form infiltrated plaques. Extra-cutaneous involvement is also known. A systemic association in the form of serum monoclonal gammopathy and there is also an increased risk of hematological and lymphoproliferative malignancies. We represent NXG with multiple organ involvement and associated with acute myeloid leukemia.

Case: A 59-year-old woman presented with complaints of yellowish brown swellings around both the legs since 3 years. These lesions were mostly asymptomatic other than the occasional itching. During the follow-up, the punch biopsy result is compatible with 75% of necrobiotic xanthogranuloma which is a subgroup of non langerhans histiocytosis. Lesions were gradually progressive in nature and both upper eyelids and face were also involved with plaques and nodules. During the follow up she also complained of total restriction of her field of vision, which was worse on the left side. Uveitis like lesion detected and she was treated with methylprednisolon successfully. After 1 month treatment of methyl prednosolon the lesions were relapsed and massive stiff leg edema was detected. Her blood count was WBC:20,670 /mm³, Neut:13,500/ mm³Monocyte: 4,140/ mm³ Hb: 8,8 g/dL, Plt: 260.000/ mm³ creatinin: 1,2 mg /dl, LDH: 462 IU (N: 125-220IU), üric acid:10,2 mg/ dL (N: 2,6-6,0 mg/dL) Ca:9,54 P:3,5 AST: 17, ALT: 13 ALP: 262 GGT: 379 total bilirubin: 0,54 mg/dL direct bil: 0,31 mg/dL, and hepatosplenomegaly was revealed at physical examination. On the peripheral smear examination myeloid blast cells was seen. Liver biopsy showed the myeloid infiltration of liver tissue. She was diagnosed as acute myeloid leukemia with spontaneous tumor lysis syndrome and liver involvement. Acute myeloid leukemia was confirmed with the bone marrow biopsy and hyper cellular bone marrow with grade 3 reticular fibrosis and diffuse infiltration of CD61 (+) myeloblasts

was detected. She was treated with the 3+7 chemotherapy protocol. After the chemotherapy treatment cholestasis and stiff leg edema was resolved. Complete remission was detected with bone marrow biopsy at the 27th day of the treatment. Eye, liver, muscle and skin lesions are also in remission. She was referred to allogeneic stem cell transplantation with secondary acute myeloid leukemia.

Discussion: NXG is a very rare disease and can presented with variable systemic involvement. This patient also had liver and possibly musculoskeletal tissue involvement but we could not performed muscle biopsy. Liver and muscle tissue involvements are also extremely rare. Non Langerhans cell histiocytosis may be transform into acute myeloid leukemia and have a very poor prognosis. This transformed patients should be treated with stem cell transplantation.

Keywords: Histiocytosis, Leukemia, Langerhans

■ Chronic Lymphocytic Leukemia

P-042 Abstract Reference: 25

LONG-LASTING REMISSION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A VERY REFRACTORY CLL PATIENT

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Allogeneic hematopoietic stem cell transplantation (AHSCT) in chronic lymphocytic leukemia (CLL) is particularly considered in younger patients with either a high risk of refractoriness or actual refractory disease to targeted therapy.

A 42-year-old female with heavily pretreated refractory CLL was referred to our transplantation unit for allogeneic stem cell transplantation evaluation. Her history dates back to 2009 after when she had several relapses of CLL requiring multiple lines of treatment, including FCR, R-bendamustin and ibrutinib. Her physical examination in January 2015 revealed bulky cervical and axillary lymph nodes (Figure 1). CT scan revealed right cervical 48x27 mm, left cervical 43x20 mm, right axillary 49x12 mm, left axillary 58x38 mm, infracarinal 43x20 mm, paraaortocaval 38x32 mm, perihiler 39x25 mm, mesenteric 34x57 mm, right external iliac77x49 mm, left external iliac 65x45 mm lymph nodes. Deletion of 17p was detected by FISH analysis (25%). She underwent a matched related peripheral blood SCT (13.02.2015) from her 46-year-old male sibling donor with a myeloablative conditioning regimen (fludarabine, busulfan and cyclophosphamide). Graft-versus-host disease (GVHD) prophylaxis included cyclosporine (starting day -1) and methotrexate 15 mg/m² on day 1 and 10 mg/m² on days 3, 6 and 11. Neutrophil and platelet engraftment occurred on day +10 and +12. Acute GVHD grade II (stage 3) with skin involvement was diagnosed on day +20. She was treated with methylprednisolone, cyclosporine, mesenchymal stem cells and extracorporeal photopheresis. Mixed donor chimerism (75% donor) was detected on day +28. She was diagnosed with progressive chronic GVHD (cGVHD) with lichenoid skin involvement on day +87. She was treated with methylprednisolone, mycophenolate mofetil and ECP. On day +100, her bone marrow showed patchy CLL infiltration and CT scan showed right cervical 29x11 mm, left axillary 23x15 mm, right axillary 30x13 mm and left paraaortocaval 14x12 mm lymph nodes. Deletion of 17p and mixed donor chimerism persisted. He was in partial remission. On day +125, ibrutinib 420 mg/day was started to obtain complete response (CR) and to treat cGVHD. On day +180, the patient's peripheral blood chimerism showed 100% donor engraftment. A repeat bone marrow biopsy showed no evidence of CLL. Subsequent CT scans showed no lymph nodes. On repeat FISH analysis, 17p deletion was negative. CR was obtained. She remained free of cGVHD for 1 year under ibrutinib. She subsequently had multiple flares of cGVHD involving the skin, mucosa and liver. Multiple agents including bortezomib, methotrexate and rituximab were used. During the treatment course, she was complicated with hypogammaglobulinemia, recurrent bacterial infections and recurrent CMV viremia. She continued to remain in CR for about 25 months when she

succumbed to her disease 31 months after AHSCT due to cGVHD induced immunosuppression and E.coli septicemia.

AHSCT may enable longer-lasting progression-free survival especially in patients who achieve MRD-negativity. The results of AHSCT is better in patients with responsive disease. Herein, we report a refractory CLL patient with bulky disease in whom CR was obtained 180 months after AHSCT in the concomitant presence of cGVHD and post-transplantation ibrutinib treatment. Her remission period was long-lasting but immunosuppression in the setting of recurrent cGVHD and E.coli septicemia were the causes of late mortality after AHSCT.

Keywords: Allogeneic hematopoietic stem cell transplantation, chronic lymphocytic leukemia

Figure:



Figure 1. On physical examination bulky servikal and axillary lymph nodes were detected before transplantation

■ Myeloproliferative Disorders

P-043

Abstract Reference: 42

THE VERY RARE MAST CELL LEUKEMIA PRESENTING WITH ANASARCA EDEMA

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Mast cell leukemia represents a rare and aggressive subtype of malignant mastocytosis characterized by the presence of atypical mast cells in the peripheral blood and/or $\geq 10\%$ of total WBC count in blood, mast cells $\geq 20\%$ of hematopoietic cells in bone marrow aspirate.

It is usually characterized by leukemic spread of mast cells with multiple organ involvement such as the liver, peritoneum, and spleen.

Here we present an unusual case with mast cell leukemia referred to our clinic via hypervolemia and edema.

Case: A 64-years-old male presented with shortness of breath, abdominal discomfort and weakness. Physical examination revealed rhonchi and anasarca edema. The laboratory results revealed albumin: 2,93 g/dL LDH: 268 U/L ALT: 21 creatinine: 0,92 mg/dL Total bilirubin: 0,47 mg/dL Hb : 7,9 g/dL WBC 28,69 x 10e3/uL (differential count of 54.5% monocytes, 15.5% lymphocytes) and platelet count 27 x 10e3/uL. There was an infiltration of monotypic myeloid cells with bold-violet large granules both in the cytoplasm and the nucleus. There were no myeloblasts but this picture was alarming for mast cell neoplasias. We performed bone marrow aspiration and biopsy. The bone marrow aspirate smear showed 60% of the hematopoietic myeloid cells similar to the ones we found in the peripheral smear.

Evaluation of bone marrow biopsy revealed diffuse leukemic infiltration. These cells were widespread-to-moderate cytoplasmic expression of CD45, CD117 and mast cell tryptase was positive. (Picture 1) No pathology was detected in caryotype.

The patient was diagnosed as mast cell leukemia and cladribine protocol was initiated. He is still on follow up in remission.

Discussion: Mast cell leukemia (MCL) which is one of the rarest myeloid malignancies, presents with severe clinical symptoms but our patient was investigated for isolated monocytosis and anasarca edema with no sign of organ metastasis.

MCL was relatively rare (1%) in the previous series; the prognosis in most cases was dismal with median survival of only 2 months.

In addition to WHO systemic mastocytosis subtype, a significant and independent association between inferior survival and advanced age ($P < 0.0001$), history of weight loss ($P < 0.01$), anemia ($P < 0.007$), thrombocytopenia ($P < 0.0008$), hypoalbuminemia ($P < 0.0008$), and excess BM blasts ($> 5\%$; $P < 0.004$) has been shown in the literature.

We suggest, therefore, patients with monocytosis and edema should be considered for mast cell leukemia.

Current therapy in systemic mastocytosis is largely palliative and directed at degranulation symptoms (e.g., pruritus, urticaria, angioedema, flushing, nausea, vomiting, abdominal pain, diarrhea, episodic anaphylactoid attacks), symptomatic skin disease (e.g., urticaria pigmentosa) and/ or organ dysfunction from mast cell tissue infiltration (e.g., hypersplenism or pathologic fracture).

Treatment options range from observation, to symptom management (e.g., managing pruritus or diarrhea), to supportive measures (e.g., red blood cell transfusion or osteoporosis treatment), to cytoreductive therapy for debulking in the setting of aggressive, advanced, or treatment-refractory disease. In our patient we planned to perform cytoreductive treatment for his aggressive disease.

Keywords: mast cell leukemia, edema, myeloproliferative neoplasms

■ Multiple Myeloma

P-044

Abstract Reference: 20

SIMULTANEOUS MANIFESTATION OF CHRONIC MYELOMONOCYTIC LEUKEMIA AND PLASMA CELL DYSCRASIA

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Introduction: Multiple myeloma (MM) is characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin.

Chronic myelomonocytic leukemia (CMML) is a malignant hematopoietic stem cell disorder with clinical and pathological features of both a myeloproliferative neoplasm (MPN) and myelodysplastic syndrome (MDS) and it is characterized by a peripheral blood monocytosis accompanied by bone marrow dysplasia.

Patients with MM have a significantly high risk of developing MDS, CMML, or acute myeloid leukemia (AML) compared with healthy controls.

Here we present 59-year-old man with synchronous diagnosis of both CMML and MM.

Case: A 59-year-old male patient was admitted to our center with symptoms of B and abdominal pain. Physical examination revealed massive splenomegaly and moderate hepatomegaly with skin and mucous paleness. Biochemical evaluation revealed macrocytic anemia, thrombocytopenia, monocytosis and 1300 mg/day proteinuria. The monocyte value was 5620/mm³ on the hemogram. M spike in serum protein electrophoresis, IgG / Lambda monoclonal band in serum immunoelectrophoresis, and free monoclonal lambda band in urinary immunofixation were detected. Bone marrow biopsy showed 20% in lambda monoclonal plasma cells and increase of monocyte population with erythroid dysplasia. No bone lesion involvement was observed in PET / CT. In the cytogenetic analysis, 48, XY, +8, +8 (4) / 46, XY (6) were observed. Based on all these findings, the patient was diagnosed with MM and CMML.

Six cycles of azacitidine treatment for CMML was administered. After treatment with azacitidine, bone marrow biopsy revealed 30-40% lambda monoclonal plasma cells and 2% monocytic cells. Serum protein electrophoresis revealed M spike. We obtained IgG/Lambda monoclonal band in serum immunoelectrophoresis, and free monoclonal lambda band in urinary immunofixation. Velcade-cyclophosphamide-dexamethasone (VCD) chemotherapy protocol for MM was started and 4 cycles were applied. After 1 month of last VCD treatment AML developed in the patient. Standard remission induction therapy was administered but he died due to the development of septic shock in the later period.

Discussion: The risk of development of AML and MDS due to cytotoxic agents in the treatment of MM is increasing. The risk of development of AML and MDS increases by 2.4 -8.1 fold even if no cytotoxic treatment is applied in MM. Simultaneous manifestation of CMML and MM are very rare. When we made a literature review, we encountered only one case. Lenalidomide would be another treatment option for both CMML and MM. Clinical trials with combination therapy of lenalidomide and azacitidine for myeloid neoplasias and plasma cell dyscrasias have been reported which includes %44 with complete response.

Keywords: Multiple myeloma, Chronic myelomonocytic leukemia

■ Stem Cell Transplantation

P-045 Abstract Reference: 15

CNS TOXOPLASMOSIS IN HAPLOIDENTICAL BONE MARROW TRANSPLANT RECIPIENT: CASE REPORT OF SUCCESSFUL TREATMENT

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Central nervous system (CNS) toxoplasmosis is a rare and frequently fatal complication of stem cell transplantation (SCT). Definitive diagnosis of this infection requires detection of *Toxoplasma gondii* in histologic sections. Since biopsy of the brain is associated with serious risks, the diagnosis based on neuroradiologic imaging, positive serologic tests and typical lesions, which resolve after appropriate therapy. Polymerase chain reaction (PCR) of cerebrospinal fluid and blood is sensitive and specific non-invasive methods for detection.

Case report: In our 27-year-old patient with diagnosis of the Hodgkin's lymphoma after three lines of chemotherapy, autologous SCT and anti CD 30 antibody treatment, refractory disease is pointed. Haploidentical SCT had been performed. In pre transplant phase because of serological positivity for *Toxoplasma gondii* he had been treated with antibiotics therapy until negativity of finding. He also received post transplant prophylaxis. Three months after transplant procedure patient presented with tremor and pain of arms, thereafter clinical status rapidly got worse until quadriplegia. Magnetic resonance imaging (MRI) of brain and cervical spine pointed numerous cerebral hemispheres and cervical spinal cord lesions. Biopsy of the lesions was associated with high risks. MRI lesions match to toxoplasma infection, PCR showed positive signal for *Toxoplasma gondii* in CSF. Therapy approach was pyrimethamine and sulfadiazin. After 6 months of treatment patient, MRI of involved area showed complete resolution of lesions, with significant improvement of patient clinical state. After we stopped antibiotic therapy he had recidivism of Toxoplasmosis, but retreatment with the same antibiotics resolved disease again. We continued prophylactic treatment with sulfadiazin and clindamicin, his findings and status are stable two years after haploidentical SCT.

Conclusion: CNS toxoplasmosis is a rare complication of BMT. Beside adequate antibiotic treatment, absence of immunosuppressive treatment and graft-versus-host disease in our patient at the time toxoplasmosis developed were probably major contributors to the favorable outcome.

Keywords: CNS toxoplasmosis, Hodgkin lymphoma, haploidentical SCT

■ Other

P-046 Abstract Reference: 80

ROSAI-DORFMAN DISEASE DIAGNOSED WITH THE NASAL CAVITY INVOLVEMENT: CASE REPORT

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Introduction: Rosai-Dorfman Disease (RDD) is a rare disease with unknown histiocyte origin. The clinical course of the disease has a wide range from spontaneous remission to vital organ involvement leading to morbidity and mortality. RDD is frequently involves the head and neck region. It is frequently seen in childhood and young adulthood. Extranodal involvement is seen in 43% of all cases. Head and neck involvements are observed in 22% of the patients. In this article, the clinical follow-up of a young male patient with a diagnosis of RDD involving the nasal cavity is presented.

Case Report: A 43-year-old male patient was admitted to the otorhinolaryngology clinic with left sided nasal obstruction for about 7 months. Otorhinolaryngology examination revealed a 25 cc mass formation in the left nasal passage. The mass was excised. The patient was referred to our clinic after the pathology result reported as RDD. His physical examination revealed left submandibular semimobil, painless, non-fluctuating lymphadenopathy and 1 cm palpable splenomegaly. There were no significant findings in laboratory tests. At this stage, systemic screening was performed for visceral and nodal involvement. The neck, thorax, abdomen CT imaging was performed. In CT results; multiple lymph nodes with oval configuration in both submandibular and submental regions and splenomegaly (140 mm) were observed. Because of complete removal of the mass and lack of pathological lymphadenopathy and visceral involvement, it was decided that the patient did not require treatment and clinical follow-up was appropriate.

Discussion: RDD usually occurs in the first two decades with massive painless bilateral cervical lymphadenopathy. The etiology is not fully known. It is characterized by leukocytosis, elevated erythrocyte sedimentation rate, fever and polyclonal hypergammaglobulinemia. Diagnosis of the disease is made by histological examination of the biopsy materials taken from the lymph nodes or the involved organs. In the microscopy, the normal organization of the lymph gland is disrupted. Lymph sinuses have a large number of lymphocytes, plasma cells and histiocytes with large vesicular nuclei and clear cytoplasm with neutral lipid. Most of these histiocytes have a large number of intact lymphocytes, red blood cells and few plasma cells in their cytoplasm. This feature is called "emperipolesis" and it's pathognomonic for RDD. The clinical course of the disease varies according to the affected area. After diagnosis, the involvement areas of the disease should be evaluated. The majority of cases show a benign course and do not require treatment. Those with extranodal disease affecting vital organs and life-threatening nodal disease require treatment.

Conclusion: Patients described in the literature are usually patients with a large mass in the neck. In our patient, an involvement originating from the nasal cavity and affecting the nasal passage was observed. Therefore, RDD should be kept in mind in the differential diagnosis of head and neck masses. We would like to emphasize the role of RDD in the differential diagnosis of head and neck lesions since early diagnosis will affect the management of the disease in patients with visceral involvement.

Keywords: Rosai-Dorfman Disease

■ Non-Hodgkin's Lymphoma

P-047 Abstract Reference: 26

INDIVIDUALIZED MANAGEMENT OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER: CASE REPORT

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Introduction: Post-transplant lymphoproliferative disorder (PTLD), is seen in allogeneic hematopoietic stem cell and more commonly in solid organ transplantation. Risk is increased with increased immune suppression. Early lesions like infectious mononucleosis, polymorphic PTLD and more monoclonal monomorphic PTLD are subtypes. All the subtypes need different management options. Herein we aimed to present our management approach in a case with monomorphic PTLD after renal transplantation.

Case: Forty-two year old male admitted to our clinic with inguinal lumps. He had no complaints of fever, night sweats or weight loss. He had mechanical aortic valve replacement at 22 year old age and renal transplantation at 35 year old age. He also had an operation for papillary thyroid carcinoma. He was using warfarin and clopidogrel and also was heavily immune suppressed (prednisolon, mycophenolate mofetil and sirolimus). Computed tomographies of neck-chest and abdomen revealed 3 cm diameter pathological inguinal lymphadenopathies and incidentally discovered superior vena cava thrombosis and hypersensitivity pneumonitis. Excisional lymph node biopsy was consistent with CD 10, CD20 and bcl-6 positive monomorphic PTLD with Grade 1-2 Follicular Lymphoma. Positron Emission Tomography scan was done and left inguinal and left iliac lymph nodes had increased metabolic activity. Lymphoma involvement was not seen in bone marrow aspiration and biopsy. Radiation oncologists were consulted for possible local radiotherapy option. They recommended not performing radiotherapy as involved nodes were very close to transplanted kidney. Epstein-Barr viral load was negative. Nephrologists were consulted and de-escalation of immune suppression was planned. mycophenolate mofetil was stopped. It was decided to wait for response to reduced immune suppression and give immunotherapy or chemo-immunotherapy in case of progression.

Conclusion: Our case was monomorphic PTLD with Grade 1-2 Follicular Lymphoma histological subtype. Bone marrow aspiration and biopsy was recommended in Follicular Lymphoma in order to confirm early stage, so we performed it. Diffuse bcl-6 positivity is associated with poor response to reduction in immune suppression. Radiotherapy was not a good choice for our patient due to localization of the involved nodes. Our case had much comorbidity, so we decided to give a chance to wait a response to reduced immune suppression. Clinicians also should not forget that there were no studies showing overall survival differences between different treatment modalities in Follicular Lymphoma.

Keywords: Follicular Lymphoma, Post-transplant Lymphoproliferative Disorder

■ Acute Myeloid Leukemia

P-048 Abstract Reference: 110

EFFICACY OF GEMTUZUMAB OZOGAMICIN IN TREATING ISOLATED EXTRAMEDULLARY RELAPSED AML EVEN AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Gemtuzumab Ozogamicin (GO) is approved by FDA in the treatment of Relapsed/Refractory AML, but its efficacy in treating isolated

extramedullary relapse is not well defined. Here we present a case, who relapsed with extramedullary skin lesions, even after allogeneic hematopoietic stem cell transplantation and responded to the treatment of GO.

Case Report: 40-years-old woman admitted to our outpatient clinic with pain in her joints and redness in her back and stomach. She was diagnosed with CD33-positive Acute Myeloid Leukemia according to the immunophenotyping of bone marrow blasts. Idarubicin and ARA-C (7+3) combination initiated as a frontline induction therapy and morphological remission was achieved after the first cycle of induction. After the first cycle of consolidation chemotherapy with high dose ARA-C she has relapsed with skin myeloid sarcomas and diffuse bone marrow infiltration. Soon after the relapsing disease she was put on to idarubicin salvage chemotherapy and she responded well with the disappearance of skin lesions and morphological complete remission of bone marrow. After achieving response, an allogeneic stem cell transplantation (HSCT) was applied from her sibling donor with a myeloablative conditioning. Unfortunately patient had a relapsing extramedullary disease with reappearance of skin lesions even with an ongoing acute skin gvhd (Figures 1 and 2) soon after allogeneic HSCT. Bone marrow biopsy revealed no increase in blast count.

We have decided to initiate a novel targeted therapy to control the extramedullary disease. As her blasts infiltrating the skin were universally CD 33 positive we considered to put her on GO therapy with the approval obtained from health authority. GO was applied according to the dosage approved by FDA for relapsing disease. After the first cycle of GO she had a rapid disappearance of all skin lesions just complicated with a febrile neutropenic episode and re-activation of CMV infection which was easily controlled with Gancyclovir.

She is still in remission regarding both skin lesions and bone marrow after the first cycle of GO.

Conclusion: Our case demonstrated that GO can also be considered as a therapeutic approach in AML patients who relapses with isolated extramedullary sarcomas even after allogeneic HSCT.

Keywords: Gemtuzumab Ozogamicin (GO) , Acute Myeloid Leukemia, Extramedullary relapse

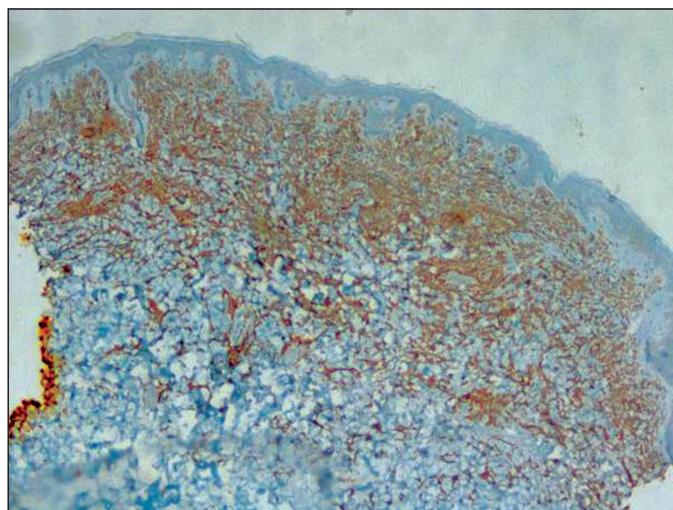


Figure 1. Relaps extramedullary disease of skin lesions

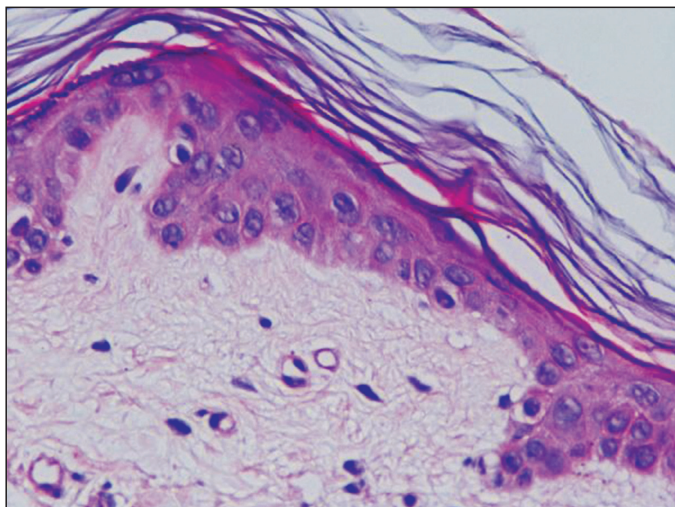


Figure 2. Skin GVHD

■ Other

P-049 Abstract Reference: 118

EVALUATION OF SYRIAN REFUGEE CHILDREN WITH HEMATOLOGIC CANCERS BETWEEN 2016-2018 : SINGLE CENTER EXPERIENCE

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Turkey is the leading country among the countries that accept Syrian refugees. We surveyed the demographic data, treatment and the outcome of the refugee children with leukemia and lymphoma that were treated in our clinic between 2016-2018. There were 28 patients; 25 boys and 3 girls. Median age was 94 months (min 24mos-max 194 mos). Of the twelve children who were diagnosed with leukemia one had AML, three had T cell leukemia, three had pre-B cell ALL, five had B cell leukemia. Sixteen children had lymphoma; eight of them were Hodgkin's lymphoma and the other eight were non-Hodgkin lymphoma. One patient with non-Hodgkin lymphoma progressed despite therapy. Eighteen patients were alive, five patients died and five were lost to follow up.

Keywords: refugee children, leukemia, lymphoma

■ Myeloproliferative Disorders

P-050 Abstract Reference: 92

CO-OCCURRENCE OF MULTIPLE THROMBOPHILIC FACTORS WITH A POPLITEAL ARTERY EMBOLISM HISTORY: A CASE REPORT

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Factor V Leiden mutation is the most common cause of hereditary thrombophilia. Co-occurrence of prothrombin gene mutation, MTHFR C677T and Factor V Leiden mutation is a rare condition. Prefibrotic myelofibrosis (pre-PMF) is a distinct entity among chronic myeloproliferative neoplasm defined by the revised 2016 WHO classification. Although clinical features of pre-PMF patients is heterogeneous, the incidence of thrombotic events is similar to essential thrombosis.

A 37-year-old male patient was admitted to the hematology outpatient clinic with leukocytosis, polycythemia and thrombocytosis without any complaints. He had a history of right popliteal artery embolectomy in 2009 and ischemic, cyanotic changes and amputation in his right toes. He also had a 20 pack-year smoking history. There was no specific trait in his family history. The patient was examined for thrombophilia during the period of popliteal arterial thrombosis, and Factor V Leiden heterozygous, prothrombin G20210A heterozygous and MTHFR C677T heterozygous mutations were determined. On examination, only w 4 cm palpable splenomegaly (SM) was found. In his blood test: WBC: 20.200 u/L, hemoglobin: 18.7 g/dL, platelet : 688.000 u/L were showed, his biochemical parameters were normal. Antiphospholipid syndrome and systemic lupus erythematosus antibodies were not revealed. The patient's liver structure were normal; the diameter of the portal vein was considered to be within normal limits (10 mm) and the spleen size was increased (164 mm) in his portal doppler USG. The patient was considered as myeloproliferative disease due to SM and JAK2V617F mutation positivity. He was diagnosed with pre-PMF as a result of bone marrow biopsy and described as a low risk (0 points) patient by DIPSS plus score. Besides he had leukocytosis, thrombocytosis, SM and a history of thrombosis, Hydroxyurea 500 mg/day was added to the current acetylsalicylic acid treatment. Phlebotomy was performed at regular intervals. He was advised to quit smoking. The patient does not have a newly developed history of thrombosis and is in a clinically stable condition.

We have found it worthy of presenting our case because there is no case previously reported in literature with 4 thrombophilic markers (Factor V Leiden heterozygous, prothrombin G20210A heterozygous, MTHFR C677T heterozygous and JAK2V617 mutation) involved together. We believe that thrombophilia should be approached with a wider perspective, especially in patients with atypical thrombosis, and that the JAK2V617F mutation should be screened as a thrombotic marker in addition to hereditary thrombophilic factors. The presence of multiple thrombophilic risk factors not only determines the increased risk of thrombosis but also change the treatment approach.

Keywords: Factor V Leiden Mutation, Prefibrotic Myelofibrosis, Hereditary Thrombophilia

■ Other

P-051 Abstract Reference: 63

A CASE OF APLASTIC ANEMIA AFTER SHORT-TERM ISOTRETINOIN USE

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Isotretinoin is an effective treatment that is widely used in acne treatment. There are various side effects affecting many systems. We would like to present a case of aplastic anemia after short-term isotretinoin use.

A 20 year old female patient had been using isotretinoin tablets for acneiform lesions on her face for a month. She was referred to our hematology outpatient clinic because her blood values were low during routine controls. The patient did not have a known chronic disease and was not taking any medication other than isotretinoin tablet. There was no addiction to alcohol or cigarette or any other substance. Hemogram values were found to be normal before the initiation of the drug. About 1 month after taking the drug in the laboratory; white blood cell $0,87 \times 10^3 / \mu\text{L}$, neutrophil $0,39 \times 10^3$, hemoglobin 7,2 g/dl and platelets: $31 \times 10^3 / \mu\text{L}$. Peripheral smear was compatible to the hemogram and there was no atypical cell. Tests on the patient's etiology of pancytopenia; serum level of LDH, BUN, creatinine, cyanocobalamin, folic acid were normal. The patient's procalcitonin and CRP levels were normal. There was no feature in the detailed viral serology (in the hepatitis panel, toxoplasma, rubella, CMV, herpes virus type 1 and type 2, EBV and parvovirus infections). Brucella IgM and IgG were negative. Antinuclear antibody and dsDNA were negative. Peripheral lymphadenopathy and splenomegaly were not detected in physical examination. Abdominal, neck and superficial ultrasonography confirmed the physical examination and no lymphadenopathy

or splenomegaly was detected. For the etiology bone marrow aspiration and biopsy were performed. Bone marrow aspiration was hypocellular by age. No blast or other atypical cells found in bone marrow smear. The patient's bone marrow biopsy was consistent with aplastic anemia. The patient was hospitalized in our hematology clinic and followed-up. The medication he had used was discontinued.

Oral isotretinoin has been used in the treatment of severe acne for more than 25 years. The use of isotretinoin is becoming increasingly widespread, however, several case reports are presented which are not previously reported on the side effects and new studies are being carried out. Depending on the use of isotretinoin in the literature; Side effects such as anemia, lymphadenopathy, neutropenia, thrombocytopenia have been reported but hematological parameters generally do not show any deterioration in the studies. There was no data about the development of aplastic anemia due to isotretinoin use when the literature was reviewed.

Severe aplastic anemia is a life-threatening hematological disease characterized by suppression of bone marrow. The diagnosis is made in the context of pancytopenia associated with a permanent hypocellular cellular marrow without major dysplastic symptoms or marrow fibrosis. The treatment includes patients having anti-thymocyte globulins and cyclosporin or immunosuppressive therapy with allogeneic stem cell transplantation, in particular a donor.

In our case, it was seen that aplastic anemia may be possible due to the use of isotretinoin when Naranjo adverse drug reaction scale is applied. Chloramphenicol is one of the best known drugs to cause hematologic dyscrasias. Although the cause of chloramphenicol-related aplastic anemia has been described in the literature, we believe that more studies are needed to explain the development of isotretinoin-induced aplastic anemia.

Keywords: Pancytopenia, aplastic anemia, isotretinoin

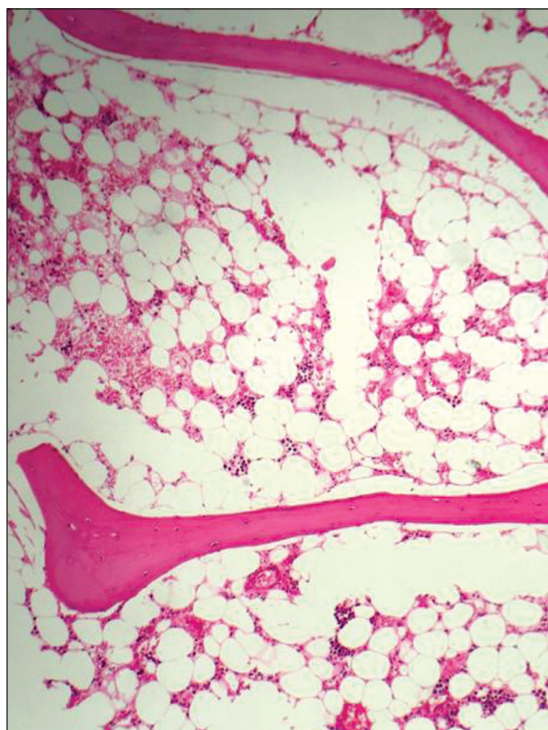


Figure 1. Bone marrow biopsy section

■ Non-Hodgkin's Lymphoma

P-052

Abstract Reference: 76

PRIMARY INVOLVEMENT OF THE BREAST IN DIFFUSE LARGE B-CELL LYMPHOMA: TWO CASE PRESENTATIONS AND REVIEW OF THE LITERATURE

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Introduction: Diffuse large B-cell lymphoma (DLBCL); is an aggressive lymphoma of B cell origin, which constitutes 50% of all non-hodgkin lymphomas (NHL). Lymph node excisional biopsy is the gold standard in the diagnosis. DLBCL, which is characterized by rapidly developing lymphadenopathy (LAP), is frequently associated with the involvement of extranodal organs such as central nervous system (CNS), gastrointestinal tract (GIS), kidneys and lung. However, primary involvement of the breast in DLBCL, are quite rare. In this presentation, we report 2 cases that were diagnosed with primary involvement of breast in DLBCL with the opinion that they would contribute to the literature

Case 1: A 66-year-old female patient with a known history of diabetes mellitus, hypertension and heart failure, was referred to our hospital with a mass in the upper quadrant of the left breast when magnetic resonance imaging was performed. In the computed tomography (CT) images, a mass lesion (87x42 mm) with irregular borders was found in the left breast retromammarian area. The tru-cut biopsy of this mass was reported as DLBCL which myc and bcl-2 negative, bcl-6 positive, and a Ki-67 score of 90%. PET-CT images showed elevated metabolic involvement of soft tissue mass defined in the proximity of the pectoral muscles and in left axillary, interpectoral, retropektoral, internal mammarian lymph nodes. Due to the lack of involvement in bone marrow biopsy, the patient was accepted as stage II E and IPI score was considered as 1. Because of the patient's comorbidities and poor performance, it was decided to give him R-CHOP treatment instead of R-EPOCH. The patient received 8 cycles of R-CHOP treatment and radiotherapy. Prophylactic intrathecal chemotherapy was given. At the end of the treatments, the patient received the complete response (CR) in the PET-CT scan and the patient is still under follow-up in the second year after CR.

Case 2: A 63-year-old male patient with known HT and hypothyroidism was diagnosed with DLBCL as a result of tru-cut biopsy from the mass detected in the left chest. Ki-67 score of tumor is 80%, myc negative; bcl-2 and bcl-6 were positive. In the CT images of the patient, periferic LAP was not detected. Bone marrow biopsy revealed disease involvement and the patient was accepted as Stage 4 E. The patient's IPI score was evaluated as 2. 6 cycles of R-EPOCH chemotherapy regimen were received with prophylactic intrathecal chemotherapy. Complete response was obtained after PET-CT imaging at the end of treatment. In order to perform autologous stem cell transplantation if patients will have relapse, stem cells were successfully collected by mobilization with Endoxan + GCSF protocol. Follow-up of the patient at the 8th month following the treatment is continued under complete response.

Discussion: DLBCL is an aggressive NHL and in some cases, extranodal involvement can also be seen. Although especially CNS, GIS, pulmonary and renal involvement are detected, it is rarely seen primary breast tissue involvement and can be diagnosed with breast biopsy.

Result: Although primary breast DLBCL cases are rare, it should be kept in mind in the differential diagnosis to avoid unnecessary mastectomy and axillary lymph node dissections. These two case presentations show that; breast DBBHL is should be included in the differential diagnosis of breast malignancies and it can be seen in both sexes and can be treated successfully with early diagnosis.

Keywords: breast, lymphoma, rare

■ Stem Cell Transplantation

P-053 Abstract Reference: 153

SUCCESSFUL TREATMENT OF GRAFT FAILURE WITH SECOND ALLOGENEIC STEM CELL TRANSPLANTATION WITHOUT CONDITIONING REGIMEN

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Here we report a case of secondary graft failure that was effectively treated with second allogeneic hematopoietic stem cell transplantation (Allo-HSCT). A 49-year-old female patient with Philadelphia-positive acute lymphoblastic leukemia obtained first complete remission with BFM protocol and subsequently underwent unrelated allogeneic bone marrow transplantation (BMT). After confirming successful engraftment and achieving complete remission with incomplete blood count recovery, she was subsequently followed up at an outpatient clinic. A routine test performed by day 80 after BMT revealed the presence of pancytopenia. A bone marrow aspirate did not reveal any evidence of disease relapse or hemophagocytic syndrome but demonstrated hematopoietic insufficiency. Donor chimerism also declined over time; thus, the patient was diagnosed with secondary graft failure. Supportive treatment, including granulocyte-colony stimulating factor, eltrombopag and blood transfusion, failed to improve the blood parameters. The patient developed Gram-negative sepsis and invasive fungal infection. After CRP has started to decline and the patient's general condition has improved, we performed a second Allo-HSCT without conditioning regimen on day 120 after BMT (CD34+ cells: 3.45x106/kg). Consequently, the blood cell count improved promptly and dramatically without adverse events.

Keywords: allogeneic hematopoietic stem cell transplantation, Philadelphia-positive acute lymphoblastic leukemia, graft failure

■ Non-Hodgkin's Lymphoma

P-054 Abstract Reference: 75

PRIMARY THYROID MARGINAL ZONE LYMPHOMA CASE REPORT

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Introduction: Marginal zone lymphomas (MZL) are low-grade (indolen) lymphomas that classified among non-hodgkin lymphomas (NHL). It is seen in the 3rd frequency among the NHLs, and it is more common in women than in men. The average age is 60 years. MZL has 3 subtypes. Extranodal MZL, splenic MZL and nodal MZL. Extranodal MZL constitutes 65% of MZL and is most commonly seen in the stomach, but it can also be seen in the eye, brain, breast, intestine, skin, bladder, kidney, salivary glands. Primary thyroid MZL is an extremely rare extranodal MZL. We concluded that MZL cases with primary thyroid involvement are rare and may contribute to the literature

Case Report: A 49-year-old female patient who was under follow-up for known MNG; has an USG scan and revealed a 13x13x17 mm isohypoechoic, predominantly cystic nodule with no apparent blood flow to the right lateral lobe in may 2018. Primarily parathyroid adenoma was considered and parathyroid scintigraphy confirmed that no evidence of parathyroid adenoma. Posterior localized focal activity involvement in the left inferior lobe of the thyroid gland was detected in the SPECT screening. Fine needle aspiration biopsy (FNAB) was performed but resulted in nondiagnostic. In June 2018, right thyroid lobectomy + bilateral inferior parathyroidectomy + left central region exploration was performed. The pathology results were reported as low Ki-67, negative Bcl-2, low grade B cell lymphoma, compatible with MZL. PET-CT was performed on the patient who with no B symptoms such as fever and night sweats. PET-CT revealed pathological involvement in the left lobe

of the thyroid gland and left lobectomy was performed too. Postoperative pathology results were reported as chronic lymphocytic thyroiditis consistent with hashimoto thyroiditis. Bone marrow biopsy revealed no lymphoma. Patient was accepted as stage 1E. The evaluation was made according to the GELF / BNLI criteria and the patient was planned to be followed up without any treatment. The patient is being followed up without treatment for 5 months from the diagnosis.

Conclusion and discussion: In primary thyroid lymphomas, which usually constitute only 2% of all thyroid malignancies, usually as NHL, women are 4 times more risky than men and the average age is between 65-75. In primary thyroid lymphomas, extranodal MZL is at the 2nd place with a rate of 30% and it is frequently associated with hashimoto thyroiditis which is considered to be one of the most important risk factors for the development of all thyroid lymphomas. In more than 90% of patients who were diagnosed with thyroid lymphoma, have the fast growing goiter which is the main symptom however as seen in this case, slow-growing thyroid nodules in the follow-up of hashimoto thyroiditis are among the rare symptoms. As a result, primary thyroid lymphomas are rare; it can also occur in the background of hashimoto thyroiditis. Therefore, it should be kept in mind that in the presence of slow-growing thyroid nodules as well as accompanying indolen lymphoma. On the other hand, Hashimoto association in primary thyroid lymphomas also suggests that autoimmunity may have an effect on lymphoma development.

Keywords: thyroid, lymphoma

■ Other

P-055 Abstract Reference: 126

A CASE OF HL WITH A RARE EXTRANODAL INVOLVEMENT OF HODGKIN LYMPHOMA (HL) WITH LIVER INVOLVEMENT AND RESPONSE AFTER TREATMENT

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Introduction: Classical Hodgkin lymphoma is a malignant disease of lymphoid tissue, often derived from germinal centered B cells. Its specific cellular structure and immunotypic properties are characterized by the presence of Reed-Sternberg cells. The annual incidence of hodgkin lymphoma is 2-3 / 100.000 and it is observed more frequently in men than in women (1.4 / 1). 11% of all lymphomas constitute. The disease has a bimodal distribution, 15-34 and above 60 years of age.

Case: A 61-year-old female patient was admitted to our hospital with complaints of weakness, loss of appetite, weight loss and fever for 3 months. LDH: 1311U / L, AST: 316U / L, ALT: 138U / L, ALP: 1150U / L; GGT: 293U / L; T.BIL: 3.4mg / dl,D.bil:2,4 mg/dl.

In the abdominal section of the abdomen bt 2 cm hypodense lesion in the liver segment 4, 17 mm LAP in the portal hilus, a few LAPs in the spleen hilus 19 * 29 mm in size,multiple paraaortic in the parakaval LAPs, in the thorax bt mediastinal Multiple LAPs were detected ,and 14 mm LAP in the right axilla. In the abdomen usg of the patient with multiple LAPs, hypoechoic metastatic mass in multiple number and size lesions in the parenchyma of the liver were detected.During the follow-up period, liver enzyme elevation continued increasing bilirubin levels (t.bilirubin 17.94 mg / dl, d .bilirubin14.42 mg / dl) In order to reduce increasing bilirubin levels of the patient made excessive day to day plasmapheresis.Minimal regression of the knowledge after plasmapheresis.Classic HL from the right axillar 1.5 cm LAP obtained from trucut bx.

Reduced Bleomycin-Vinblastine-Dakarbazine (BVD) to the patient with elevated liver enzyme and bilirubin levels.In the follow-up, adriamycin was added to the treatment of ABVD and 6 cycles were completed.After 6 cycles of ABVD, liver enzymes and biliubin levels were completely normal.

Discussion: This case is uncommon in the literature, however, because of the improvement in liver enzymes and bilirubins after 6 cycles of ABVD, and as a result of complete recovery, Classical HL considers liver involvement.

Conclusion: It should be kept in mind that HL liver involvement may be present in patients with weakness, lack of appetite, weight loss and fever, lymphadenopathy and plasmapheresis response with elevated liver enzyme and bilirubin.

Keywords: Hodgkin lymphoma

■ Non-Hodgkin's Lymphoma

P-056 Abstract Reference: 111

PERIPHERAL T-CELL LYMPHOMA IN A CHILD WITH PULMONARY INVOLVEMENT

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Introduction: Peripheral T-cell lymphoma (PTCL) is rare in pediatric patients and is associated with worse outcome compared with other pediatric non-Hodgkin lymphomas. pulmonary non-Hodgkin's lymphoma is a rare diagnosis. Most of the cases originate from B cell lineage and arise from mucosa associated lymphoid tissue of the bronchus. Few cases of pulmonary T-cell lymphoma have been reported. We report here on an rare case of pulmonary peripheral T-cell lymphoma not otherwise specified (PTCLN), and we present the CT and Radiation therapy for oncological emergencies (airway obstructions).

Case Presentation: A 8-year-old man was hospitalized on October, 2018, for an lower respiratory tract infection and weakness, shortness of breath. Physical examination was; no hepatosplenomegaly or lymphadenopathy was noted. Hematologic studies, including complete blood counts and marrow biopsy, were normal. Blood chemistries were unremarkable except for slightly elevated serum lactic dehydrogenase. Abdominal and cervical tomography normal. The contrast enhanced chest CT scan revealed variable sized masses in the right upper lobe and and both lower lobes, big mediastinal mases and the masses displayed central necrosis. A small fluid collection was seen in the left hemithorax. (Figure 1, 2) A CT-guided percutaneous transthoracic needle biopsy (PTNB) was done for the mass in the left lower lobe. Pathological diagnosis was primary pulmonary T-cell precursor lymphoblastic lymphoma. Patient received external beam radiotherapy 400 Gy / day in 2 fractions total 800 Gy with 3D planning tools. Patient continuing chemotherapy

Discussion: PTCLs have been the "poor step-child" of the diseases we refer to as lymphomas. The aggressive PTCLs were lumped in clinical trials with the aggressive B-cell lymphomas. PTCLs are uncommon and heterogeneous malignant lymphoproliferative disorders that originate from post-thymic (peripheral) T cells or mature natural killer (NK) cells. PTCL seem to be somewhat less radiosensitive than the aggressive B-cell lymphomas, and higher radiation doses may be needed, although still lower than for most solid tumours. Our patient has got superior vena cava syndrome and airway obstructions. We recieved high doses radiation therapy. Results; Peripheral T-cell lymphoma (PTCL) is rare in pediatric patients. Because histopathological findings and staging of the disease are necessary for diagnosis and treatment plans, we should carefully perform strategic examinations with the knowledge of this rare malignant disease.

Keywords: Peripheral T-cell lymphoma, pulmonary, Child

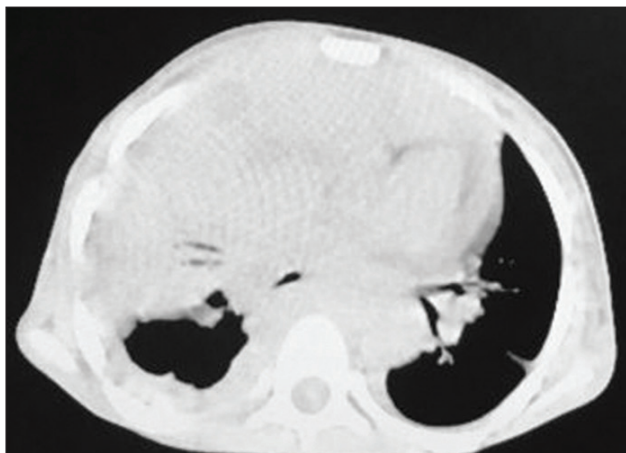


Figure 1. CT scan revealed variable sized masses in the right upper lobe and and both lower lobes, big mediastinal mases and the masses displayed central necrosis

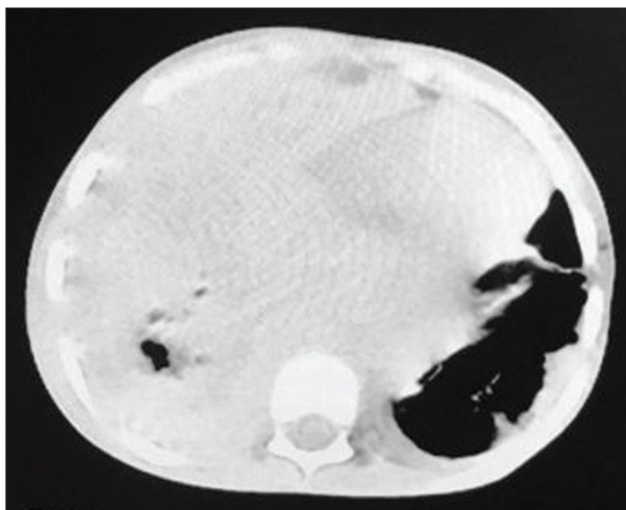


Figure 2. CT scan revealed variable sized masses in the right upper lobe and and both lower lobes, big mediastinal mases and the masses displayed central necrosis

■ Multiple Myeloma

P-057 Abstract Reference: 96

HEMATURIA AND HEMATOCHEZIA; COULD IT BE THE FIRST ADMISSION TO A CASE OF MULTIPLE MYELOMA?

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Introduction: Multiple myeloma (MM) is a monoclonal plasma cell disease accounting for about 10% of hematological malignancies. The most common causes of admission are anemia (%73) and bone pain (58%). Rarely, bleeding resulted by hemostatic abnormalities due to high serum paraproteinemia may also be the first reason for admission. We present a case diagnosed as MM, who was admitted initially with hematochezia and hematuria.

Case: A 69-year-old male patient was admitted to the emergency department in November 2018 with lower abdominal tenderness, macroscopic hematuria and hematochezia.

Radical prostatectomy was performed in 2007 and in 2014 he received 72 Gy RT for relapse disease. In December 2017 prostate specific membrane antigen (PSMA)-PET revealed, multiple lytic lesions in bones. Also MRI revealed 25% height loss in the sacral and lumbar vertebrae. With suspicion

of metastasis he was ordered six courses of docetaxel and zoladronic acid by radiation oncology.

In September 2018,PSMA-PET showed progression with additionally lytic characteristics in new areas.Upon this,abirateron and prednisolone were started in medical oncology,when PSA was 0.003.

When admitted to our emergency room,sonographically there was no ectasia/dilatation in the renal collecting system.Laboratory test results were shown in Table 1.Because of acute postrenal/renal injury and hematuria the patient has been hospitalized.The nephrologist indicated an emergency hemodialysis.Macroscopic hematuria regressed after bladder irrigation. Urine culture was sterile.

Simultaneously the patient underwent colonoscopy due to rectal bleeding,in which giant solitary rectal ulcers were observed.

The patient, whose anemia and thrombocytopenia progressed,had in routine examination: Albumin:2.3g/dL, total protein:9.2 g/dL; M protein in serum protein electrophoresis:3.7g/dL(Figure 1). Monoclonality of IgG Kappa was in immunofixation electrophoresis (Table 1).

The biopsy showed hypercellular bone marrow containing 80% IgG kappa monoclonal plasma cells.CyBorD protocol was started to the patient with MM.The patient did not need routine hemodialysis.

In his second course he developed hematuria,which we considered to be secondary to cyclophosphamide and therefore protocol was changed to VRD(bortezomib-lenalidomide and dexamethazone).

After the second cure with VRD:(Table 1)(Figure 2)

As a result of bone marrow biopsy,the plasma cell ratio was <10% and the patient was directed to autologous stem cell transplantation.

Discussion:MM is associated with bleeding diathesis in about 15% of patients. In our case, aPTT and PT were initially and latterly normal.Thrombocytopenia was not enough to explain spontaneous gross bleeding.Because of the recuren radiotherapyprotocols ,radiation-related hemorrhagic cystitis was also considered in the differential diagnosis.Gross hematuria after the second course with CyBorD was thought to be associated with cyclophosphamide and hematuria did not recur after the treatment was changed to VRD.He has been referred to autologous stem cell transplantation without complication.

Here we would like to memorize the different spectrum of clinical features for plasma cell neoplasias,presenting with bleeding either from gastrointestinal or urinary system.We should remember the possibility of co-existing malignancies and/or genetical predisposition for malignancies after the first diagnosis in elderly patients.

Keywords: multiple myeloma, hematuria, lytic bone lesions

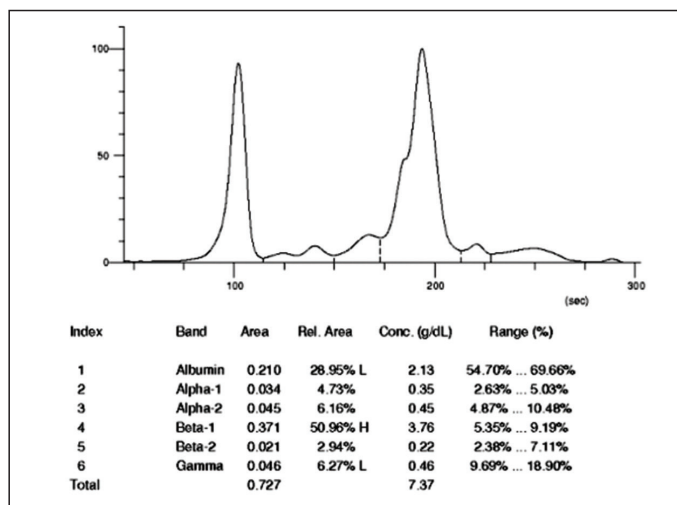


Figure 1. Serum protein electrophoresis at admission with monoclonal band in the beta region

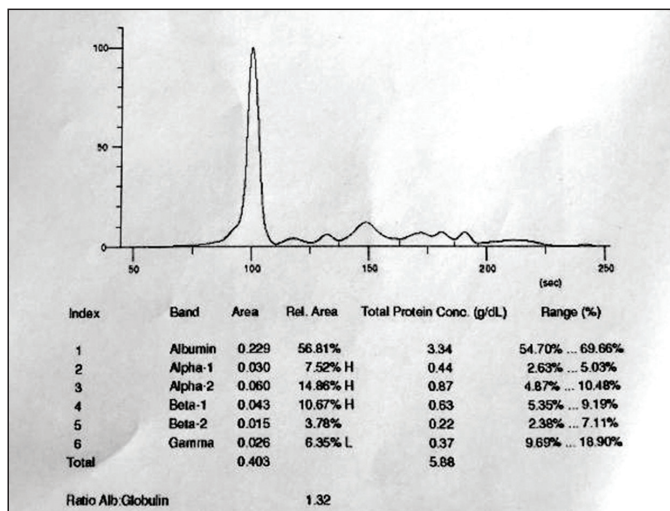


Figure 2. Serum protein electrophoresis-the second cure with VRD

Table 1.

	Reference values	Initial	Postchemotherapy
Hemoglobin (g / dL)	12,9-15,9	7,1	10,7
Leukocytes (10e3/uL)	3,7-10.1	5,9	6,9
Platelets (x109/L)	155-366	75	47
Activated partial thromboplastin time (sec)	31	32,2	30
Prothrombin time (PT) (sec)	11,6	13,2	12,9
Fibrinogen (mg/dL)	200-400	363	385
Urea (mg/dL)	10-50	199	68
Creatinine (mg/dL)	0,7-1,2	12,3	1,07
Calcemia (mg/dL)	8,6-10,6	7,1	7,2
Lactate dehydrogenase (U/L)	135-248	246	204
Albumin (g/dL)	3,5-5,2	2,3	3,6
Total Protein (g/dL)	6,4-8,3	9,2	6,1
AST/ALT (U/L)	0-50	21/16	21/49
M protein (g/L)	0,30-0,74	3,7	0,58
Serum free kappa/lambda light chain(g/L)	1,7-3,7/0,9-2,1	5,45/0,63	1,58/0,48
Urine Immunofixation kappa/lambda light chain(mg/L)	0,012-32,71/<4.9	955,8/6,1	410/6,1

■ Chronic Lymphocytic Leukemia

P-058 Abstract Reference: 147

ATYPICAL PRESENTATION OF MYCOBACTERIUM TUBERCULOSIS IN CHRONIC LYMPHOCTIC LEUKEMIA (CLL)

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Introduction: The main cause of hospitalization in CLL patients is infections, mainly pulmonary and urinary. The causes of infections in CLL patients is multifactorial including immunosuppression mediated by the disease itself as well as the drugs used to treat the disease. Patients with CLL have defects mainly in humoral immunity characterized by defective immunoglobulin synthesis. Here we describe a CLL patient who is followed up without specific therapy and presented with tuberculous peritonitis.

Patient: A 67-year-old male patient with the diagnosis of Rai Stage 1 CLL who had been followed up without any treatment was admitted to hospital with fever, abdominal pain and fatigue. His complete blood count revealed a WBC of $38700 \times 10^3/\mu\text{L}$, consisting of %90 lymphocytes. Hb level was 9,8 g/dl and platelet count was $291000 \times 10^3/\mu\text{L}$. His biochemistry findings were consisted with Lactate Dehydrogenase 219 U/L, Protein/Albumin 6,1/2,7 mg/dl, AST/ALT 265/191 U/L, ALP/GGT 214/157 U/L, Urea/Cre 54/1,0 mg/dl. He had an elevated ESR (104 mm/hr) and CRP (322 mg/L). The patient did not have a past medical history of tuberculosis. He did not report any recent tbc infection in the family. His physical examination showed an elevated body temperature and ascites which was confirmed by an ultrasound exam. Computerized tomography of the abdomen revealed enlarged lymph nodes (paraortic, hepatogastric, hepatoduodenal, paraceliac, parailiac, pararectal, retrocrural, epicardial areas and at the hilus of the spleen) and a thickened omentum. Ascetic fluid was exudative and cytological exam showed rare atypical cells but no real sign of malignancy. Polymerase chain reaction performed on ascitic fluid sample for Mycobacterium Tuberculosis was negative. However, omentum biopsy showed granuloma formations with necrosis and EZN stain detected bacilli in the necrotic zones. With these findings the patient was diagnosed as tuberculous peritonitis and anti-tbc therapy was started with 4-drug regimen (Isoniazid, Rifampin, Ethambutol and Pyrazinamide). After the start of therapy, the patient's symptoms quickly started to relieve. He has been on anti-tbc treatment for 4 months without symptoms and his ascites also resolved significantly.

Conclusion: Patients with CLL may experience a variety of infections due to profound immunosuppression. Tuberculosis should be considered in any CLL patient who has fever of unknown origin and atypical presentations. Sometimes, molecular investigation of the ascetic fluid may fail to demonstrate the bacillus DNA and a tissue biopsy may be required for definitive diagnosis.

Keywords: Chronic Lymphocytic Leukemia, CLL, TB, Mycobacterium Tuberculosis, Peritonitis, Ascites

■ Other

P-059 Abstract Reference: 114

WHAT IS THE BEST TREATMENT OPTION IN A LYMPHOMA PATIENT WITH CARDIAC THROMBUS: THROMBOLYTIC THERAPY OR SURGERY?

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Introduction: The basis for the strong association between cancer and thrombosis is a well known issue. Primary mediastinal large B-cell lymphoma (PMBCL) is the most common type of B cell lymphoma leading to thrombosis. Some risk factors may potentiate the development of thromboemboli such as central venous catheters (CVC). Catheter-related right arterial thromboiss (CRAT) is a rare but potentially life-threatening complication of CVC.

Case : A 32-year old woman with PMBCL and on chemotherapy(R-EPOCH) through an-indwelling catheter was referred for echocardiography due to dyspnea and tachikardia at the end of the fourth cycle. Echocardiography revealed 27 X28mm and 17X14mm in diameter, mobile thrombus. Thorax CT also supports .Shown in the Picture(pic 1)

Treatment: This mass was removed by videoassisted surgery without any complications. The patient has been on LMWH and antiaggregan therapy for 6 months.

Conclusion: Minimally invasive surgery and anticoagulation is a safe alternative option when compared to thrombolytic therapy. The patient is in methobolic complete remission at the end of one year without any comorbidity.

Keywords: lymphoma, cardiac thrombus, surgery

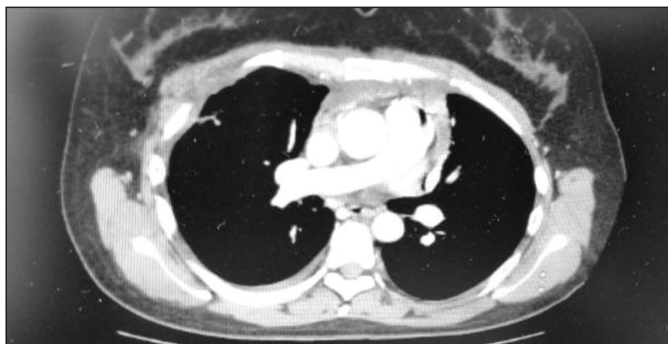


Figure 1. Cardiac thrombus

■ Other

P-060 Abstract Reference: 71

COEXISTENCE OF INTRAABDOMINAL AND INTRATHORACIC MASS DUE TO EXTRAMEDULLARY HEMATOPOIESIS IN A PATIENT WITH BETA THALASSEMIA INTERMEDIA

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Extramedullary hematopoiesis is an uncommon condition characterized by the formation of blood cells outside the bone marrow as a compensatory process in several hematological diseases such as thalassemia. EMH is common in non-transfusion-dependent thalassemia patients. In patients with thalassemia intermedia, the incidence of EMH increases up to 20% while the incidence is below 1% in patients with multiple blood transfusion thalassemia major. The most common sites of EMH are liver and spleen, Less frequently the retroperitoneal, and mediastinal regions may be involved. We report a 48-year-old woman with beta-thalassemia intermedia who coexistence of intra-abdominal and intrathoracic extramedullary hematopoietic masses due to poor clinical follow-up. Imaging workup showed intrathoracic and intra abdominal masses. The extramedullary hematopoietic focus was confirmed by biopsy from the thoracic mass. Radiotherapy planned for extramedullary masses. The patient refused radiotherapy treatment. Hydroxyurea was started. This case raises the question of whether or not blood transfusion can be performed in some patients with non-transfusion-dependent beta thalassemia intermedia. We want to emphasize the importance of blood transfusion replacement in case of need and close clinical follow-up in patients with beta thalassemia intermedia by presenting a patient who developed multiple extramedullary hematopoietic foci.

Keywords: extramedullary hematopoiesis, thalassemia, intrathoracic and intraabdominal mass, blood transfusion

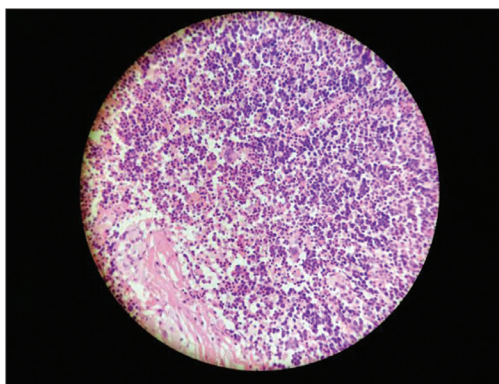


Figure 1. An extramedullary hematopoietic focus. This micrograph shows megakaryocytes and the other hematopoietic cells (H&E x100)



Figure 2. Abdominal computed tomography shows a mass of 155 x 85 mm in the abdomen.

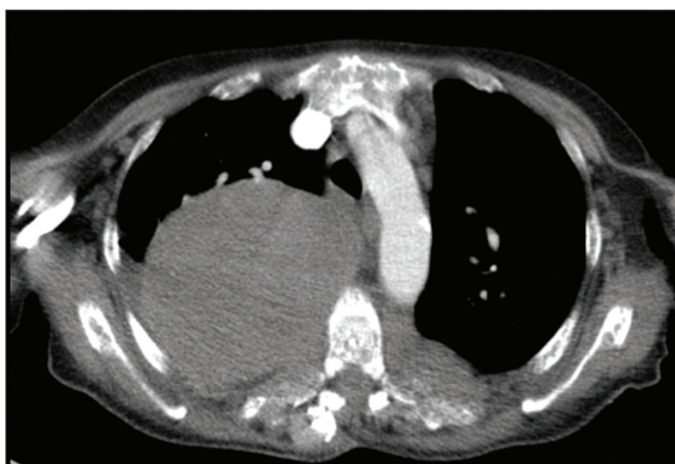


Figure 3. Thoracic computed tomography shows homogeneous mass with anterior-posterior diameter of approximately 100 mm and a lateral diameter of 110 mm in the right thoracic region.

■ Chronic Myeloid Leukemia

P-061 Abstract Reference: 70

SUCCESSFUL TREATMENT OF A CHRONIC MYELOID LEUKEMIA PATIENT WITH INTRACRANIAL HEMORRHAGE

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Introduction: Bleeding and thrombosis are frequent complications in myeloproliferative disorders (MPD) and are associated with severe organ damage and a high mortality. A patient with CML who has a bleeding complication will be presented.

Case report: 33 years old male patient was referred to our clinic as leucocytosis on complete blood count 8 years ago. Bone marrow aspiration biopsy was performed that reported as hypercellular bone marrow compatible with myeloproliferative neoplasia with showing an increase basophils and megakaryocytes. Bone marrow examination showed a positive BCR-ABL/t(9;22) (q34;q11) chromosomal translocation detected by FISH and RT-PCR and he was diagnosed as chronic myeloid leukemia (CML) in the chronic phase (CP).

Imatinib therapy was started as 1x400 milligram. After about 6 years of regular follow-up, the patient has not come to visit for the last 1 year. The patient was brought to the emergency clinic 1 month ago by his relatives with syncope and a change in consciousness. It was learned that the patient did not

use the treatment regularly. The brain MR showed focal intracerebral hemorrhage of the frontal, temporal, and parietal regions. On CBC, haemoglobin 6.7 mg/dl, leukocyte 409.000 neutrophile 353.000 and thrombocyte 140.000. The differential counts tested in our hospital were blasts 2%, promyelocytes 5%, myelocytes 15.5%, metamyelocytes 8.5%, bands 14.5%, segments 40%, eosinophils 2%, basophils 4%, lymphocytes 7%, and monocytes 1.5%. dasatinib was started as 2x70 mg, hydroxyurea 2x1000 mg. Leukocyte apheresis was performed. Emergency surgery was not performed by the neurosurgeon. He was followed up in the intensive care unit. It was observed that the intracerebral hematomas resolved in the control computerized tomography of the patient 1 week later. Patient's consciousness and orientation improved. The patient was discharged with a 1x100 mg dasatinib treatment.

Discussion: Hyperleukocytosis is associated with an early morbidity and mortality due to potential complications, including intracranial haemorrhage, pulmonary leukostasis syndrome, and tumour lysis syndrome. Leukostasis can affect every organ or system, symptoms generally arise from the involvement of pulmonary and cerebral microvasculature, and most early deaths are due to the intracerebral haemorrhages. Although complications of leukostasis-associated haemorrhage are common in acute leukemia and chronic myeloid leukemia accelerated and blastic phase, they can be observed in the chronic phase. It should be kept in mind that haemorrhage may develop without thrombocytopenia on patients with leukocytosis. Early leukocyte apheresis and cytotoxic treatment can be life saving for these patients.

Keywords: Chronic, myeloid, leukemia

■ Non-Hodgkin's Lymphoma

P-062 Abstract Reference: 77

ILEUM INVOLVEMENT IN DIFFUSE LARGE B-CELL LYMPHOMA: AN ATYPICAL EXTRANODAL PRESENTATION

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is an aggressive lymphoma which is originated from B cell lymphocytes. Although DLBCL usually presents as lymphadenopathy (LAP), the involvement of extranodal organs can also be seen. The most common areas of extranodal disease are stomach, skin, small intestine and tonsil. In this report, we wanted to present our case who was diagnosed with DLBCL from ileum.

Case: A 56-year-old male patient was admitted to the emergency department with nausea, vomiting, abdominal pain and jaundice. In the examinations of the patient who had no stool discharge for 3 days, elevation of cholestasis enzymes, air fluid levels on the abdominal X-ray of the abdomen, and 8x10 cm mass in the mesentery of the abdominal CT were detected. He was operated for ileus. Intraoperative examination showed that the mass originated from the small intestine mesentery and invaded the surrounding tissues and superior mesenteric artery. The mass was accepted as unresectable. Palliative operation was completed and wedge biopsy was performed for diagnostic purposes. Pathology result was reported as DLBCL. Ki 67 was detected 80%. PET-CT for staging showed increased FDG involvement in the neck, bilateral axillary, mediastinal, hilar, intraabdominal, pelvic, inguinal lymph nodes, consistent with lymphoma infiltration. Bone marrow biopsy revealed no lymphoma infiltration. There was no atypical cell in the cerebrospinal fluid in the patient who underwent lumbar puncture. Patient was diagnosed as stage 3EB and was evaluated as medium-high risk. The IPI score was calculated as 3. As the patient had stage III EB and the IPI score was 3, prophylactic intrathecal chemotherapy (methotrexate + ARA-C + dexamethasone) was planned in each cure with R-EPOCH (rituximab + etoposide + vincristine + adriamycin + cyclophosphamide + prednisolone) chemotherapy regimen. In the evaluation of the disease after the third cycles of chemotherapy, significant regression was detected and treatment continued.

After the fifth cure, the patient developed LAP in the left inguinal region. Lymph node excisional biopsy was performed considering the disease progression and the pathology result was reported as DBBHL. R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin) chemotherapy regimen was planned as rescue chemotherapy because of refractory disease. Also autologous bone marrow transplantation was planned if full remission can be achieved. The patient is currently taking the first course of R-DHAP chemotherapy.

Discussion: DBBHL is the most common lymphoid malignancy in adults. Although these high-grade lymphomas usually show aggressive course, but they are also curable malignancies. Extranodal involvement is also common in this disease with rapidly developing LAP. It should be kept in mind that lymphomas should be considered in the differential diagnosis of intraabdominal masses and may be aggressive.

Keywords: extranodal, ileum, lymphoma

■ Non-Hodgkin's Lymphoma

P-063

Abstract Reference: 115

ANAPLASTIC LARGE T CELL LYMPHOMA ARISING FROM CASTLEMAN DISEASE IN A PEDIATRIC PATIENT: CASE REPORT

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A nonclonal lymphoproliferative disorder, Castleman disease is not a malignant condition, and is very rare in childhood. These condition is usually a great mimic of both benign and malignant abnormalities, because of its diverse manifestations and ability to affect any body region. But also an association with concurrent or subsequent malignancy may occur in CD. In this case report, we describe a pediatric case developing anaplastic large cell lymphoma three years after diagnosis of a hyalin vascular type unicentric Castleman's disease.

Case Report: A 11 years old healthy female was admitted with a painless right axillar mass. At presentation she had no major health complaints or disease history and has been in good general condition. On the physical examination, there was right axillar lymphadenopathy. It was firm, nontender, mobile and was of 3x2 cm in its maximum diameter. Clinically there was no palpable lymph node enlargement in any of the various lymph node sites. In addition, she had no significant abnormalities detected by blood tests, included complete blood count, C-reactive protein, erythrocyte sedimentation rate, serum biochemical analysis, serum viral analysis. Ultrasonography of the right axillar region confirmed the adenopathy of 32x18 mm diameter. A chest computed tomography scan revealed that the paratracheal lymph nodes sized 1 cm in diameter. An excisional biopsy of the axillary lymph node showed morphological features suggestive of hyaline vascular type of CD. Serological test for HIV was negative in this patient. The patient received no further treatment and remained under follow-up care with no signs of recurrence for three years after her operation. After three years she admitted to our clinic because a supraclavicular mass. Physical examination revealed an adenopathy in the supraclavicular area of up to 4x3 cm in size. Complete blood count, CRP, serum biochemical and viral analysis were normal. Radiological examination of neck with ultrasound showed conglomerate nodal mass in the supraclavicular area with a round configuration of several lymph nodes (2 cm in size). Chest X-ray and abdominal ultrasound were all normal. An excisional biopsy was performed from the cervical lymph node. The pathological diagnosis was identified as anaplastic large cell lymphoma (ALK+). A staging with 18FDG-PET/CT scan showed metabolically active lymph node enlargement, especially in right supraclavicular, bilateral jugular, axillary, iliac regions, and detected 15 mm sized lymph node that abnormal high uptake in medial side of the ascending colon. Bone marrow aspiration and biopsy had no evidence of lymphoma cell infiltrate. Finally, we diagnosed our patient with stage III ALCL, associated with Castleman disease

in unicentric hyaline vascular variant. She was treated with ALCL-99 protocol. She had been followed up without any complications after the treatment

Result: Although Castleman disease is not a malignant condition, an association with concurrent or subsequent malignancy may occur in both types of CD. Lymphoma may have been present all along, or the CD may transform into lymphoma. This occurs most often with the multicentric/ PC variant, and is exceptionally rare in unicentric/ HV variant in general, and in childhood CD in particular. A regular medical surveillance is necessary in patients with Castleman's disease, because they are at a high risk for the development of malignant lymphomas.

Keywords: Anaplastic Large T cell Lymphoma, Castleman Disease, childhood

■ Chronic Myeloid Leukemia

P-064

Abstract Reference: 141

NEUTROPHILIC LEUKOCYTOSIS IN A PATIENT WITH LIVER TRANSPLANTATION: DIAGNOSED AS CHRONIC NEUTROPHILIC LEUKEMIA; A RARE CASE REPORT

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Chronic neutrophilic leukemia (CNL) is a rare, BCR-ABL1-negative myeloproliferative neoplasia with a poor prognosis. It is characterized by peripheral neutrophilic leukocytosis, hepatosplenomegaly and hypercellular bone marrow with less than 5% myeloblast, predominant neutrophilic maturation without dysplasia. In 2016, the World Health Organization (WHO) recognized the CSF3R T618I mutation of the colony-stimulating factor 3 receptor (CSF3R) as one of the diagnostic criteria. We report a rare case of CNL with CSF3RT618I positive, 65-year-old patient with liver transplantation due to hepatocellular carcinoma (HCC).

A 65-year-old male patient with a history of liver transplantation due to HCC secondary to chronic hepatitis C was evaluated because of neutrophilic leukocytosis. On his laboratory examination; WBC: 93,7 x 10³/uL, Neutrophil: 89 x 10³/uL, platelet: 218 x 10³/uL Hb: 6,1 g/dL MCV: 91,3 fL. Peripheral smear was revealed mature neutrophils as 90%, 5% metamyelocyte, 5% lymphocytes. There was no dysgranulopoiesis and blast. His bone marrow was hypercellular with granulocytic proliferation and minimal dysplasia at erythroid and myeloid series that may be due to liver cirrhosis, HCC and older age. Conventional cytogenetic was normal. To exclude myeloproliferative neoplasia, we studied JAK 2 mutation and bcr/abl (p210,230) from peripheral blood by PCR. All were negative. But we started hydroxyurea due to rapidly progressive neutrophilic leukocytosis. Then CSF3R mutational analysis by NGS was studied in another center. NGS analysis was revealed CSF3R T618I mutation. The patient was diagnosed as CNL. At the second month of hydroxyurea, malleolus ulceration was developed while hematological remission was got. Therapy was changed to ruxolitinib. At the 6.month of ruxolitinib, the patient transformed to acute myeloid leukemia.

In case of neutrophilic leukocytosis, CNL should be in mind and CSF3R mutation should be studied also. Molecular data are very important to decide the therapeutic intervention. But unfortunately still prognosis is very poor and there is no standart therapeutic algorithm.

Keywords: Neutrophilia, chronic neutrophilic leukemia, liver transplantation, CSF3R

■ Multiple Myeloma

P-065 Abstract Reference: 108

PLASMA CELL LEUKEMIA: A CASE REPORT

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Seventy years old male patient admitted to our hospital with worsening back pain and difficulty in walking. On physical examination there was a mass settled on the back in the midline. Blood tests revealed anemia, leucocytosis and renal insufficiency. Also serum lactate dehydrogenase and uric acid levels were very high. The patient diagnosed with spontaneous tumour lysis syndrome and serum protein electrophoresis revealed monoclonal M spike. Plasma cells were detected on peripheral blood smear, and bone marrow aspiration and biopsy was performed. Bone marrow aspirate specimen showed 100% atypic plasma cell infiltration. The spinal mass was compatible with extramedullary plasmocytoma on MRI scanning and PET/CT revealed multiple extramedullary masses. The patient was diagnosed with plasma cell leukemia and PAD/VCD regimen was started concurrent with irradiation of spinal mass. During the first course of treatment the patient worsened with newly generating skin lesion on the chin and biopsy from skin revealed plasma cell infiltration. No response to treatment achieved and the patient died on the 47th day of diagnosis.

Keywords: Plasma cell leukemia, tumour lysis syndrome

■ Other

P-066 Abstract Reference: 148

AN UNUSUAL CAUSE OF SPLENOMEGALY IN A THROMBOCYTOPENIC ADULT PATIENT: NIEMANN-PICK DISEASE

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Introduction: Niemann-Pick disease (NPD) is a rare autosomal-recessive lysosomal storage disorder characterised by the deficiency of acid sphingomyelinase activity resulted in the accumulation of sphingomyelinase in hepatocytes, reticuloendothelial cells and neurons. Types A and B are associated with mutations in the ASM gene (*SMPD1*) while type C results from mutations in either the NPC1 and NPC2 gene. The age of presentation ranges from the neonatal period to adults over 50 years with an extreme clinical heterogeneity. Here we report an adult patient who presented with thrombocytopenia and splenomegaly and diagnosed with NPD with the typical findings of bone marrow examination.

Case: A 34-year-old female patient who was scheduled for operation due to nasal septum deviation by ENT (ear-nose-throat) department was consulted us due to thrombocytopenia. She did not have any clinical complaints and no previous medical history. Complete blood count and peripheral smear did not show any pathological findings except moderate thrombocytopenia and leukopenia (WBC:3870/mm³, Neu:2250/mm³, Hb:14.3 gr/dl, PLT:87000/mm³). All biochemical parameters and coagulation tests were normal. On physical examination spleen was not palpable but percussion of Traube's space was dull. In abdominal ultrasound, liver craniocaudal length was 160 mm and echogenicity was normal. The spleen length was approximately 200 mm, and a 30 mm accessory spleen was present. Bone marrow aspiration and biopsy were planned for the patient to clarify the current findings. In the bone marrow aspiration, significant increase in macrophages including dense basophilic granulation like sea-blue histiocytes and a number of foam-cells were noted. The appearance was consistent with the typical morphology for hereditary lysosomal storage disease, Niemann-Pick. Biopsy was also revealed hypercellular (%70) bone marrow with marked hyperplasia of histiocytes and grade 2 reticulin fibrosis. Blood samples of the patient

were sent to the laboratory to measure the acid sphingomyelinase activity. It was decided to investigate the possible gene mutations as the next step. Cranial MRI and EEG were planned to evaluate the neurological involvement although the patient has normal neurological examination without any neurological complaints. HRCT and ecocardiography were also planned to evaluate the possible lung and cardiovascular involvement. The patient's investigations and follow-up are still continuing in our clinic.

Conclusion: This is an unusual case of a young adult woman with NPD with striking bone marrow findings, suggesting the diagnosis. Although sea blue histiocytes can be found in bone marrow that is rapidly turning over, typical morphological appearance of intense sea blue histiocyte infiltration suggests the diagnosis of NPD, which should be confirmed by demonstrating the enzyme deficiency and/or gene mutations. It should be kept in mind that the cause of splenomegaly may be an inherited lysosomal storage disease like NPD in an asymptomatic adult patient and may be recognized clearly from bone marrow examination.

Keywords: Niemann-Pick Disease, splenomegaly, thrombocytopenia

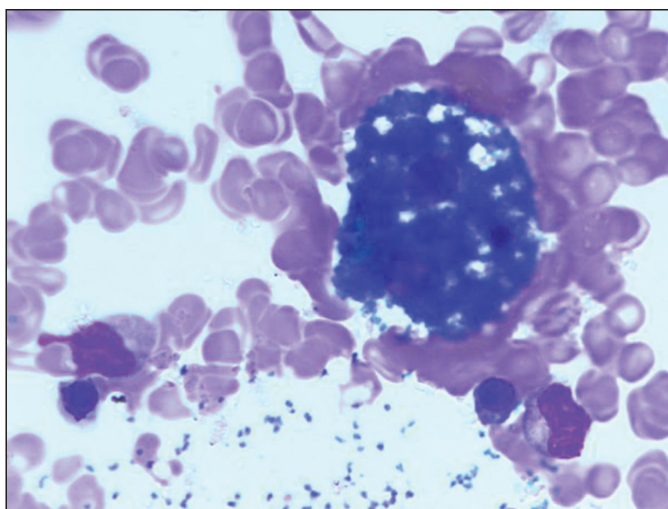


Figure 1. Sea-blue histiocytes in bone marrow aspiration

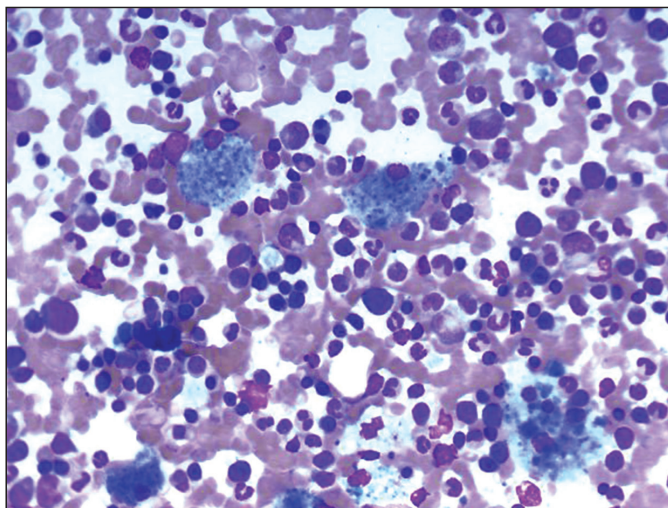


Figure 2. Sea-blue histiocytes in bone marrow aspiration

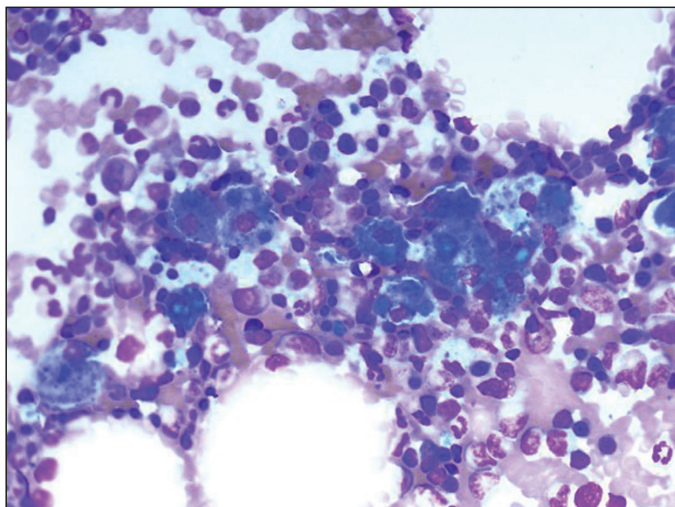


Figure 3. Sea-blue histiocytes in bone marrow aspiration

■ Multiple Myeloma

P-067

Abstract Reference: 146

SUCCESSFUL TREATMENT OF POEMS SYNDROME WITH COMBINATION BORTEZOMIB ,LENALIDOMIDE AND DEXAMETHASONE THERAPY.

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Introduction: POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal [M] protein and skin changes) syndrome is a rare plasma cell disorder. The standard therapy for patients with POEMS syndrome is high-dose chemotherapy followed by autologous stem cell transplantation (ASCT). But still has no standart treatment for relaps after ASCT. Combination Bortezomib ,Lenalidomide and Dexamethasone therapy is one of the treatment option for relaps patient.

Case presantions: A 47-year-old manwith history of type 2 diabetes mel-litus who was admitted to the neurology department with a complaint of inability to walk ,muscle weakness erectile dysfunction. Results from electrodiagnostic studies were compatible with sensorimotor polyneuropathy with predominantly demyelinating features and severe degree of secondary axonal loss.Endocrine evaluation revealed hypothyroidism, hyperpigmentation and hypogonadism. He was diagnosed with partial empty sella syndrome in pituitary MRI. At the moment of admission, the laboratory tests displayed the presence of IgG λ monoclonal gammopathy. Bone marrow aspiration and biopsy revealed normocellular marrow with 2% plasma cells. Morphological examinations by computer tomography (CT) detected osteo-sclerotic bone lesions of the left femur and right iliac bone at the same time hepatosplenomegaly. This findings including polyneuropathy, monoclonal gammopathy, organomegaly, endocrinopathy, monoclonal protein and skin changes led to the diagnosis of (POEMS) syndrome. The patient was started therapy with dexamethasone and cyclophosphamide for 4 cycles followed by autologous stem-cell transplantation after Melphalan 200 mg/ m2 as conditioning regimen.we obtained a hematologic partial remission. with the persistence of serum M-protein detected by immunofixation and a consistent improvement of the neuropathy with ability to walk.He was followed for 3 years as outpatient. Then he relapsed with complaints of inability to walk , loss of libido and erectil disfonction.We started Bortezomib - Lenalidomide –Dexametasone , with Len administered at a dose of 25 mg per day on 21 consecutive days of a 28-day cycle and Dex administered at 40 mg weekly, bortezomib administerd 1,3 mg/m2,together with a throm-boembolism prophylaxis therapy. He has received 8 months therapy anda

Within months, could walk comfortably. At last follow-up, he was well and continued improvement and haematologic partial remission with absence of monoclonal protein (M-protein) detectable by serum and urine protein electrophoresis sPEP.

Result: There are currently no standard treatments for patients with POEMS syndrome. there are several options for treatment of POEMS syndrome including melphalan, lenalidomide. bortezomib and transplantation. ASCT eradicates the underlying plasma cell clones more completely than Lenalidomide plus Dexamethasone or Melphalan plus Dexamethasone for first-line treatment regimens(1). Novel regimens including daratumumab may become the treatment options for relaps and multidrud resistans patients (2). We believe that Bortezomib, lenalidomide and dexamethasone combination therapy is good option for relaps POEMS, however, more research is needed to understand to define best options of thretments.

Keywords: POEMS, M protein