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ABSTRACT BOOK

EHOD
EGE HEMATOLOJİ VE ONKOLOJİ DERNEĞİ

FREQUENCY OF RAYNAUD'S DISEASE, VARICOSE VEINS AND FIBROMYALGIA IN PATIENTS WITH METHYLENETETRAHYDROFOLATE REDUCTASE MUTATION

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Fibromyalgia, Raynaud's phenomenon and varicose veins are widespread health problems in the general public. Etiology and pathophysiology of these conditions has not been fully elucidated. Varicose veins can be defined as the expansion of vessels in especially lower extremity. That occurs as a result of a variety of precipitating factors cyanosis, pallor or discoloration in fingers called Raynaud's phenomenon. Fibromyalgia is characterized by fatigue and widespread body pain. Debilitating fatigue, sleep disturbance and joint stiffness are also could be seen in fibromyalgia. Methylenetetrahydrofolate reductase (MTHFR) is an enzyme encoded by the MTHFR gene. Biochemically this enzyme converts 5-10-methylenetetrahydrofolate to 5-methyltetrahydrofolate as irreversible. Two crucial mutations including 677CT and 1298AC were identified in this gene locus that results a decrease in enzyme activity. Patients who admitted to internal medicine, hematology and obstetric polyclinic between January 2012 - April 2013 ranging from 21 to 83 years old (mean age 38.16 ± 13.1) were enrolled the study. Eighty-five (21,9%) of all 388 patients were male and 303 (78,1%) were female. MTHFR mutation was assessed in all patients; 57 (17,7%) of all patients has not MTHFR mutations, 269 (69,3%) were heterozygous positive and 62 (16%) were homozygous positive. Fibromyalgia, Raynaud's phenomenon and varicose veins was distinguish in 92 (23,7) ,56 (%14,4), 101 (26%) patients respectively. Plasma homocysteine levels were measured in all patients and all three pathologies were found significantly higher in patients with elevated plasma homocysteine. In addition serum uric acid levels were significantly higher in patients with MTHFR mutation. Frequency of Raynaud's phenomenon and fibromyalgia were significantly higher in patients with MTHFR mutation but there was not any difference varicose vein frequency. Genetic factors should be considered in etiologies of Fibromyalgia and Raynaud's phenomenon.

FEBRIL NEUTROPENIC EPIZODES IN AKUT MYELOID LEUKEMIA PATIENTS

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Objective Infections in febrile neutropenic patients is the most important cause of morbidity and mortality. Therefore, in patients with neutropenic fever infection until proven empirical antibiotic therapy should be initiated immediately. Methods In this study Bozyaka Izmir Training and Research Hospital between the years of 2012-2013 were followed in the Hematology Clinic, 46 acute myeloid leukemia (AML) developed in 112 patients with febrile neutropenia episodes were analyzed retrospectively. Results 19 of the patients were female and 28 percent male, respectively. The average of patients was 57 ± 15. The most common infection was pneumonia (41.4%). The most common

bacteria were gram negatives. The other febril neutropenic epizodes were upper respiratory infection (18%), sepsis (13.5%), urinary infection(9.9%), gastrointestinal infection (4.5%), perianal infection(4.5%), 2.7% skin infection(2.7%), tooth abscess(0.9%),pneumonia and gastrointestinal infection (0.9%), pneumonia and urinary infection (0.9%). Conclusion Every hospital should determine their infection agents and antibiotic therapy should be initiated immediately.

DEVELOPMENT OF SKIN NECROSIS RELATED TO AZASITIDIN THERAPY

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Objective: Chronic myelomonocytic leukemia (CMML) is a bone marrow disorder characterized by myeloproliferative and myelodysplastic features. It commonly presents with cytopenia,monocytosis, and splenomegaly. Azacitidine is a hypomethylating drug. This therapy can be administered at 75 mg/m2/day for 7 days or 100mg/m2/day for 5 days every 4 weeks. Methods We presented a patient who is 66 years old male, diagnosed with CMML. He had skin findings related to the use of azacitidine. Results 66 years old man was admitted to our center. He had been already diagnosed CMML by bone marrow aspiration ve biopsy in other center. He had no comorbitidy. He didn't use drug. He was operated and he had only a skin scar because of an accident .We have planned azasitidin therapy at 75 mg /m2/day for 7 days. After the third dose , some skin findings began on the injection regions. Dermatology physician considered necrosis.In the test, liver function test increased ten times at the same time. We stopped the therapy because of these findings.We applied hydration and acetyl cysteine therapy. Liver function test decreased until normal but necrosis is permanent. Conclusion Use of azacitidine therapy can develop some skin lesions should be known, especially the injection regions should be considered. Because some findings can be irreversible.

A CASE WITH CUTANEOUS ADVERSE EFFECT TO LENALIDOMIDE

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INTRODUCTION Multiple Myeloma(MM) is a systemic hematologic disease due to uncontrolled proliferation of monoclonal plasma cells. Lenalidomide is an oral immunmodulatory drug with direct antipro¬liferative and cytotoxic effects on the myeloma cells. Myelosupresion-Cytopenia, veneus thromboembolism, atrial fibrillation diarrhea,secondary malignancies and skin involvement such as eruptions-rash are the adverse events associated with lenalidomide. Stevens-Johnson Syndrome, erythema multiforme, toxic epidermal necrolysis, Skin eruptions are rare side effects of lenalidomide therapy. We present a case of adverse side effect of multiple myeloma.patient receiving lenalidomide therapy CASE: A 80 year-old man was followed with refractory multipl myeloma with lenalidomide therapy. After second cycle of lenalidomide therapy he admitted in hematology clinic with myalgie, and skin eruptions on his arms, legs and head. There was no other dermal disease history. Phisycal examination revealed dry skin with desquamation on arms, legs (four extremities) and face skin with mild erytema.No other important findings on physical examinition. Laboratory investigation revealed

haemoglobin Hb 9g/dL WBC 3220 mm3 and platelets 79.000 mm3.The patient was consulted to dermatologyst. Cutaneous punch biopsy revealed ichthyosis vulgaris. after diagnosis of ichthyosis vulgaris the patient was treated with local moisturising therapy and supportive care . After treatment, dermal findins progressed, increased and surrounded all body skin. At that time loss of consciousness and loss of motor function on bilateral legs and arms appeared. After MRI and CTs of cranium and neurology consultation we started enoksaparin sodyum for cerebrovasculary embolism. After 48 hours later patient died. CONCLUSION: In MM 5 to 10% of cases has skin involvement .In literature, dermatological side effects complication due to lenalidomide use with a frequency ranging from 12% to 43%. In literature there is a increasing risk of non-invasive skin cancers which used lenalidomide plus dexametasone. For our patient, no skin cancer finding detected. Adverse drug reaction for lenalidomide was defined fatal or life threatening status. We focused our attention on the cutaneous adverse reactions to lenalidomide. Important skin changes may be the poor prognostic factors for MM patients who therapied with lenalidomide.

RAPIDLY GROWING THYROID MASS AND NORMAL BLOOD COUNT: A RARE PRESENTATION OF ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Thyroid infiltration of acute lymphoblastic leukemia is very rare and fine needle aspiration is mandatory in patients whose symptoms are long lasting and do not resolve with steroid treatment. Patient Findings: A 53-year-old woman was admitted to endocrinology outpatient clinic with compressive symptoms and pain from a rapidly expanding thyroid mass. Thyroid tests and complete blood count results were normal. Thyroid ultrasonography showed moderate enlargement of bilateral thyroid lobes with altered echotexture with hypoechoic non-homogenous parenchyma. In thyroid scintigraphy, a hypoechoic nodularity was observed. Fine needle aspirates from thyroid revealed few lymphocytic and polymorphonuclearleukocytic infiltrations on a necrotic background with acute inflammation. She received steroid treatment with the diagnosis of subacute thyroiditis and she was cured by 1 mg/kg/day methyl prednisolone treatment. One month later, she was consulted for fever, weakness, enlarging painful thyroid lobes, multiple petechia and ecchymosis without hepatomegaly and lymphadenopathy by the hematology clinic. Complete blood count revealed Hg of 8.82 g/dL, RBC of 2.98 million/mm3, WBC of 8.170/mm3, neutrophilia of 2.100/mm3 and a platelet count of 22.300/mm3. In peripheral blood smear test, thrombocytopenia and blasts (52% of cells) were confirmed. Bone marrow biopsy showed 80% cellularity with a diffuse, uniform infiltration of lymphoblastic cells with prominent nucleoli. Normal cell lines were markedly decreased. Immunohistochemical (IHC) staining was positive for TdT, HLA-DR, CD19, CD20, CD22, CD10 and CD38; but negative for CD117, CD23 and myeloperoxidase. She was diagnosed with Precursor-B cell-ALL, and received induction chemotherapy with Berlin-Frankfurt - Munich (BFM) protocol. After one week, enlargement of thyroid was partially recovered with persistent pain on palpation. In the second FNA performed on Day 8, the pathology was consistent with malignant cytology and leukemic infiltration. Summary: A 53-year-old woman, diagnosed initially with subacute thyroiditis

was diagnosed with acute lymphoblastic leukemia infiltration in the thyroid gland after further investigations. Conclusions: The present case presentation emphasizes that fine-needle aspiration cytology should always be performed in clinical context if thyroid mass continues to grow rapidly, and symptoms are unresolved despite acceptable treatment.

ISOLATED RICHTER SYNDROME OF CENTRAL NERVOUS SYSTEM IN A REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA PATIENT; A CASE REPORT.

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INTRODUCTION: Chronic Lymphocytic Leukemia (CLL) ; is the most reported lymphoma subtype in adults. Richter syndrome (RS) is defined as the development of high grade non-Hodgkin'slymphoma (NHL) from low-grade NHL. Central nervous system (CNS) involvement of RS is a very rare condition with bad prognosis. CASE REPORT: 67 years old woman admitted with weakness. Her physical examination revealed splenomegalia, bilateral cervical lymphadenopaties, blood test indicated leucocytosis. She was referred to our clinic in September 2013. On admission complete blood count was as follows: Wbc:125x109/l, Lym:85 x 109 /l, Hgb:13,7 gr/dl, Plt:156x109 /l and LDH was 237 IU. Bone marrow biopsy revealed lymphoid cell infiltration of 70 % mostly consisted of medium or small sized cells. In immunohistochemical examination CD5, CD19, CD20, CD22, CD:25,CD:38, CD45, HLA.DR, IGM and KAPPA chain, ZAP 70, coexpression CD20/5(+) was detected as positive. 17P DEL was 10% positive. Biochemical serum analysis were all normal and HIV serological test was negative. With all above findings patient was diagnosed as Binet Stage B and RAI stage II CLL. Consequently COP regimen was administered. In first evaluation after 2 courses of chemotherapy her disease was stable so R-F-C was started. A cranial MRG was performed on 21th day of her therapy due to epileptic seizures and left hemiplegia. MRI indicated a 5 cm vasogenic edematous mass located in right frontal lobe which was significant in T1 hypointense and T2 hyperintense postcontrast images. Diagnostic CNS biopsy revealed diffuse large B cell non-Hodgkin lymphoma and the second bone marrow biopsy was reported as CLL. As an isolated RS in CNS we administered R- IDARAM. Patient died due to neutropenic fever and septisemia caused by pulmonary infection on the 18 th day of the treatment. DISCUSSION: Richter's Syndrome is the most dreadful complication of KLL which is reported in 1-10 % of the patients. It is mostly resistant to treatment. Especially refractory CLL cases should be closely monitored for CNS involvement of RS.

ALLOGENEIC AND AUTOLOGOUS HEMATOPOIETIC PERIPHERAL BLOOD STEM CELL MOBILIZATION: SINGLE INSTITUTION, 11 YEARS' EXPERIENCE

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Objective: Allogeneic and autologous hematopoietic stem cell transplantation is an important treatment option in most of malignant and some of benign diseases. We analyzed the last 11 years data of PBSC mobilization performed in patients and healthy donors in our center. Method: We analyzed the data of mobilization procedures of patients with hematological malignancies and healthy donors performed between January 2003 and June 2013 in Ege University Hospital, Department of Hematology retrospectively. Baxter CS3000, Amicus, COBE Spectra, Dideco and Fresenius aphaeresis systems were used for the PBSC mobilization procedures. The minimum number of collected CD34 + stem cell was accepted as 2x106/kg for adequate engraftment. Results: Total 3282 PBSC mobilization procedures were performed in 1210 healthy donors and patients. The indications of autologous stem cell transplantation were plasma cell dyscrasias 390 (41%), acute myeloid leukemia 119 (12,6 %), non- Hodgkin lymphoma 239 (25,1%), Hodgkin lymphoma 124 (13%), acute lymphocytic leukemia 20 (2,1 %), solid tumors 59 (6,2%). The median volume of the harvest was 125 (Range; 50-250cc). The patients and donors tolerated the procedures with acceptable side effects. The most common side effect was numbness around the mouth which was reported in 324 procedures (9.8 %). Median 4.76x106/kg (range; 2,3 - 32 x106/kg) CD34 + stem cell was collected from healthy donors. In subgroup analysis, the median number of the CD 34+ stem cells collected by CS 3000 was 8.79x106/kg (range; 2,3 - 32 x106/kg); and by Fresenius 5,91x106/ kg (3,18- 18,6x106/ kg) that is not statistically significant. Conclusion: We present our experience in collection of PBSC in both healthy donors and patients. We could not demonstrate a statistically significant difference in the harvesting of PBSC product between the types of the devices used. The mobilization procedures were safe for both health donor and patients with acceptable side effects.

A CASE DIAGNOSED AS MGUS DURING THE COURSE OF ESSENTIAL THROMBOCYTHEMIA

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Objective: Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm of multipotent hematopoietic stem cells characterized by thrombosis and high platelet levels. Here we want to represent a patient diagnosed as monoclonal gammapathy with unknown significance (MGUS) during the course of ET which is an uncommon entity. Case: A 58 year-old male was consulted to hematology department due to headache and high platelet level (Platelet: 600 000/mm3). Complete blood count revealed high platelet level and a slight leukocytosis (WBC: 10.900/mm3 Hb: 15.3 Hct: 45.8, Platelet: 971.000 mm3). Biochemistry results were normal. He had a heterogenous JAK 2 mutation and the bone marrow aspiration and biopsy was compatible with chronic myeloproliferative neoplasm, ET. Although the treatment consisted of anagrelide, allopurinol and aspirin was initiated,

optimal clinical or laboratory results could not be obtained. Cardiac tashiarthymia was devoleped during the treatment with anagrelid which was thought a related to drug. So we stopped the anagrelid treatment and hydroxyurea was initiated. During the course of the disease in January 2012, his routine laboratory test revealed a high globulin level. A IgG kappa monoclonal gammapathy was detected at serum protein electrophoresis and immunfixation tests (total protein: 8.2 (6.4-8.3gr/dl), albumin: 5.1(3.5-5.2 gr/dl),globulin: 3.7 (2.5-3.5 gr/dl), IgG: 1890 (700-1600 mg/dl), IgA: 190 (70-400 mg/dl), IgM: 92 (40-230 mg/dl), kappa:523 (138-375mg/dl), lambda:144(93-242 mg/dl), M- protein: 1398.32 mg/dl). There was no lytic lesion at bone X- rays. Bone marrow aspiration and biopsy revealed 8% plasma cells. In the light of these results, patient was diagnosed as MGUS. Conclusion: MGUS is characterized by monoclonal gammapathy without signs, symptoms and laboratory findings of multiple myeloma. Progressive B cell lymphoma or multiple myeloma can be developed during the course of MGUS but chronic myeloproliferative neoplasms diagnosed during the course of ET are not an excepted entity.

PRIMARY GASTRIC DIFFUSE LARGE B CELL NON- HODGKIN LYMPHOMA: SINGLE INSTITUTION EXPERIENCE

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Objective: Primary non- Hodgkin lymphomas are 3-4% of all gastrointestinal system malignancies. The most common subtype is diffuse large B cell lymphoma (DLBCL). It mostly affects the stomach. Methods: We retrospectively reviewed the data of 28 patients diagnosed as primary DLBCL of stomach and duodenum between 1998- 2013. The clinical characteristics of the patients are demonstrated at table 1. Results: The most common presenting symptom was epigastric pain (71.4%). The others were anorexia (14.2%), weight loss (32.1%), nausea and vomiting (17.8%), reflux symptoms (7.1%), malaise (7.1%). Only 1 patient (3.5%) was presented with hematemesis. Iron deficiency anemia is documented in 6 patients (21.4%). According to Lugano staging system, 16 (57.1%) patients were diagnosed at stage I, 5 (17.9%) patients at stage II1, 3 (10.7%) patients at stage II2, and 4 (14.3%) patients at stage IV. The data of treatments and survival time are documented at table 1. All the patients were treated with R-CHOP regimen (rituximab, adriamycin, cyclophosphamide, vincristine, prednisolone) as first line chemotherapy except 2 patients who were diagnosed before the era of rituximab. Radiotherapy is given none of the patients. One patient refractory to 4 cycles of CHOP therapy is treated with R-ICE (rituximab, ifosfomide, carboplatin, etoposide) as salvage therapy. Only 2 patients (7.1%) were relapsed after first line therapy. The first was treated with radiotherapy. Two cycles of R-ICE therapy followed by autologous peripheral stem cell transplantation was performed to the other patient. Complete remission was achieved in both of the patients. Conclusion: The treatment options in primary DLBCL of gastrointestinal system are radiotherapy, chemotherapy or surgery. After the effectiveness of rituximab treatment is proven in nodal DLBCL, rituximab is used for the treatment of DLBCL of the gastrointestinal system with CHOP like regimens. We also see that R-CHOP regimen is an effective treatment for these patients.

AUTOLOGOUS PERIPHERAL STEM CELL TRANSPLANTATION IN SOLID TUMORS: SINGLE INSTITUTION EXPERIENCE

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Objective: Patients with relapsed or refractory solid tumors are candidates for salvage therapy. Salvage chemotherapy consisted of cisplatin, ifosfamide, vinblastine, paclitaxel or high-dose chemotherapy with autologous stem-cell transplantation (ASCT) but the effectiveness of ASCT is not documented clearly. Method: We retrospectively analyzed patients diagnosed as solid tumor and treated with ASCT between January 2004 and November 2013. There were 28 ASCT transplantations of 21 patients, 7 of them were tandemly transplanted. Results: The characteristics of the patients and their response to chemotherapy before ASCT were shown at table 1. The median values of alfa fetoprotein (AFP), beta-human chorionic gonadotropin (β-hcg) were 9822,5 ng/ML (range 1,05- 86262), 162775 MIU/ML (range 0,5- 325536) respectively at the diagnosis. Median number of CD 34 + stem cell collected was 4,95x106 (range; 2,5 - 11,5x106 /kg). Carboplatin and etoposide was administered in 26 patients as a conditioning regimen. Two patients were underwent ASCT with conditioning of ICE chemotherapy. Complete and partial response was documented in twelve of patients after ASCT. There was progressive or stabile disease in seven patients. Two patients were died during transplantation procedure without response evaluation. Relapsed or progressive disease was documented in nine patients with complete or partial response after median of 5 (range; 2-13 months) months. 13 out of 21 patients (61.9 %) were died because of progressive disease in 12 patients and complication related to transplantation in one patient. The median overall survival was 21 months (range; 4-264 months) Conclusion: ASCT transplantation is a treatment option in relapsed and refractory solid tumors especially testis germ cell tumors. It is a relatively safe procedure in terms of both mobilization and transplantation. Results of long term follow up were still not favorable. The effectiveness of ASCT should be evaluated in prospective randomized studies with large cohorts.

JAK2V617F POSITIVE ESSANTIAL THROMBOCYTHEMIA DEVELOPINGIN A PATIENTWITH CHRONIC LYMPHOCYTIC LEUKEMIA

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Introduction: Coexistence of chronic lymphocytic leukemia (CLL) and essential thrombocythemia (ET) in a patient is extremely rare. Only 11 cases reported in literature. We report a patient with coexistence of CLL and ET. Case: A 60-year-old male patient was diagnosed with CLL in December 2009. There were no clinical symptoms. There was no lymphadenopathy, hepatomegaly or splenomegaly on clinical examination. The hemoglobin level was 14.2 g/dL, platelets 380×109/L, and white blood cells (WBC) was 19.5×109/L. The circulating lymphocyte was 62%. Serum biochemical parameters were normal. In the bone marrow, the cellularity was normal and an 20% infiltration by small lymphocytes were reported (Figure 1). The reticulin pattern was grade I. In flowcytometric

analysis CD5, CD20, CD23 were positive and CD3, CD10 were negative. Thrombocytosis was detected in March 2013. Platelets was 580×109/L. There was no thrombosis history. Furthermore, we identified JAK2 V617F mutation in the peripheral blood. (5-12.5%). BCR/ABL translocation was negative by RT-PCR analysis. Bone marrow biopsy was performed again and increased sellularity, megakaryocytes with staghorn nuclei, neighbouring the lymphoid infiltration was detected. Discussion: It is very rare to detect 2 different hematopoietic disorders in the same patient. Although it has relatively high frequency to occur 2 malignant hematopoietic disease at the same time, coexistence of CMPD and malignant disease has been reported very rare. There is a big question about this rare cases: Does CLL and ET originate at the level of the pluripotent hematopoietic stem cell and does it caused by the JAK2 V617F mutation? There was one case that reported JAK2 V617F mutation status in stem cells, myeloid cell lineages, and lymphoid cells in patients both diseases simultaneously occurred. It is possible that a common pluripotent cell can give rise to coexisting CLL and ET. In most cases reported in literature both the disorders developed simultaneously or ET preceded the development of CLL. But in our case CLL preceded the development of ET. It seems that there was no relationship between the diseases that developed sequentially.

ALK-NEGATIVE ANAPLASTIC LARGE CELL LYMPHOMA MIMICKING HODGKIN'S LYMPHOMA

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Introduction: Anaplastic large cell lymphoma (ALCL) and Hodgkin lymphoma (HL) are distinct entities. However, these entities have some same morphologic features responsible for diagnostic difficulties. A patient who diagnosed with HL from left axillary lymph node excisional biopsy in another hospital, re-evaluated in our hospital. The patient whose pathologic specimen reported as anaplastic lymphoma kinase (ALK)-negativeALCL with immunostaining is presented. Case: A 56-years-old male patient presented to a hospital with sudden swelling in right axillary. A mobile, painless, 2x3 cm lymphadenopathy was detected. Excisional lymp node biopsy was performed. HL was reported on conventional histopathological examination. Patient admitted to our hospital for treatment plan. There was 0.5 cm lympadenopathy on left servical region in physical examination. No splenomegaly and hepatomegaly was detected. Pathology department performed immunostaining. Immunohistochemically, lymphoid cells were positive for CD3, CD45RO, CD30 and CD4, but negative for CD20, CD79a and ALK. After immunostaining these case proved to be ALK-negative ALCL. Discussion: ALCL-ALK-negative is a provisional entity in the WHO 2008 classification that represents 2-3% of NHL and 12% of T-cell NHL. Usually, the architecture of involved organs is eroded by solid, cohesive sheets of neoplastic cells, with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) and HL being the main differential diagnoses. Characteristically, these lesions showed thick nodular fibrosing bands highly suggestive of NSHL. ALCL may mimic HL, and it is advisable to include EMA in the first line panel and to ask for ALK staining in EMA-positive, CD15-negative lesions with morphologic features suggestive of HL.

A RARE ENTITY: LEUKEMIA CUTIS ASSOCIATED WITH CHRONIC MYELOMONOCYTIC LEUKEMIA

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Introduction: Chronic myelomonocytic leukemia (CMML) is a clonal disorder of hematopoietic stem cells. It presents with peripheral monocytosis (>1 × 109/L) associated with single or multi-lineage dysplasia. Leukemia cutis (LC) is defined as cutaneous infiltration by myeloid or lymphoid leukemia, which includes acute myeloid leukemia (AML), chronic myelogeneous leukemia (CML), lymphoblastic leukemia/lymphoma, MDS, and MDS/MPN disease. Although LC is commonly associated with AML or CML, presence in CMML is very rare. Approximately 21 cases of skin infiltration with CMML was documented. Case: 62 years old male patient presented to Hematology department with thrombocytopenia at May 2011. He had a story of ankylosing spondylitis and metotrexat use. Complete blood count revealed a haemoglobin level 14,7 g/dl, Plt 107 x 109/L, WBC 7,41 x 103/mm3 and monocyte 0,78 x 103/mm3. Bone marrow biopsy was performed, hypercellularity and dismegakariopoiesis was reported with 2% blasts. On follow-up monocyte level was increased to 2.8 x 103/mm3 in one month and the patient was followed as CMML. He had no symptoms and physical examination was normal. At May 2013 patient presented with red non-pruritic plaques on the arms. Skin biopsy was performed and mononuclear and blastic cell infiltration on dermis was reported. Bone marrow biopsy was performed and 8% focal blastic cells and 18% CD34 positivity was reported. Four cycles of azasitidin (75 mg/m2, 7 days) was administered and skin lesions resolved and monocyte level was regressed to 1,5 x 103/mm3. Discussion:Although LC is commonly associated with AML or CML, presence in CMML is very rare and was shown as a risk factor for acute myeloid leukemia progression in CMML. In a review overall survival from LC to disease progression was reported as 7.8 months. Overall survival from diagnosis to the last follow-up in patients with LC was 28.2 months, shorter than patients without LC (44 months). LC and its equivalent could predict disease progression to AML. It is important to perform biopsy from skin lesions and to render a correct diagnosis. Close clinical follow up could potentially prevent further disease progression.

MALIGN MELANOMA IN THE COURSE OF SPLENIC MARJINAL ZONE LYMPHOMA

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Introduction: Malignant Melanoma is an immunogenic tumor that has been shown to have a worse prognosis in certain clinical settings of immunosuppression. A patient who was diagnosed with oral cavity malignant melanoma in the course of splenic marjinal zone lymphoma treatment was presented. Case: A sixty-seven years old female patient presented to Hematology department with fewer, abdominal pain and weakness at September 2012. Complete blood count revealed a haemoglobin level 6,7 g/dl, Plt 109 x 109/L, WBC 7,71 x 103/mm3. Spleen was 26 cm in ultrasonography. Bone marrow

biopsy was performed and splenic marginal zone infiltration was reported. Karyotype was 46,XX and tyrisomy 8 was 8% positive with CEP8 probe. Splenectomy was not performed due to patients comorbidities. Six courses of CHOP treatment was administered and rituximab was added after two courses. Multipl hyperpigmented lesions on upper palate and libs were developed after fourth course. (Fig 1, 2) A punch biopsy was performed and malignant melanoma was reported. Patient was followed without chemo or radiotherapy for malignant melanoma. Discussion: Underlying genetic associations in lymphoma patients, could correlate with the development of secondary cancers, including melanoma. Patients with a history of NHL have a risk of subsequent melanoma that is increased 1.8 to 2.4 times. Patients with NHL and melanoma had decreased overall survival compared with patients who had melanoma or NHL alone. Closer follow-up is needed for these patients.

RELAPS/RERAKTER MYELOMA AND CARFILZOMIB

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Introduction: Carfilzomib (CFZ) is a new generation proteosome inhibitor with significant activity among recurrent and/or refractory multiple myeloma patients. We evaluated our patients with myeloma and treated with CFZ in RR myeloma. Cases: In our clinic, 10 relapse/refractory multiple myeloma patients treated with CFZ, 4 of them female and 6 of them male, were examined. The mean age was found 63.7 ±6.5 years. The mean follow-up duration was 64.9±49 months. Time from diagnosis to CFZ was found 61.9±45.4 months. Response in all patients was refractory. CFZ was the fourth line therapy for 3 of them, the fifth line therapy for 2 of them, and in order of 3., 6., 7., 8. and 12. line therapy for the other patients. The mean of received lines of therapy was found 5.8±2.6. The mean dose of CFZ was 40.4±6.8 mg. The mean duration after starting to CFZ was found 2.9±2 months. During the treatment, no side effect was seen among 7 patients. Three patients had hematologic side effects, 2 of them with thrombocytopenia and 1 of them with neutropenia. Each of these three patients recieved in order of 6 cures, 4 cures and 1 cure CFZ. During the follow-up, 4 patients were assigned refractory MM and their treatment regimens were changed. One patient died due to neutropenia induced pneumonia. Four patients have been still treating with carfilzomib. Conclusion:Carfilzomib for relapse/refractory patients as the last line treatment may result in poor prognosis. Use in earlier steps may results with better progression-free and overall survival.

ATYPICALLY LOCALIZED HODGKIN LYMPHOMA

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Introduction: Hodgkin lymphoma (HL), malignancy of lymphoid tissue, is accounted for 25-40% of the all types of lymphoma. It is represented 90% with enlargement of peripheral lymph nodes. The nodular sclerosing type of HL, which is one of the 5 subtype of HL according to the classification of World Health Organization, usually represents with servical, mediastinal and paraaortic lymphadenopathies. Case: A 64 year-old man admitted to our clinic with the mass on his right

forearm. With the excisional biopsy, he was diagnosed with nodular sclerosing type HL. In his history, there was no B symptoms like loss of weight, fever or night sweats. During the examination, the lymphadenopathies without tenderness were palpated in the localizations of antecubital fossa about 3x1 cm sized and right axillary about 2x1 cm sized. His complete blood count, biochemical tests were normal. Viral infectious markers were negative. In the positron emission tomography (PET/CT), liver and spleen involvements and multiple hypermetabolic soft tissue mass that were derived from the right axillary fossa and were along with the right brachial arteria were detected. The biopsy materials from an another pathology department were consulted to our Pathology Department and were reported as nodular sclerosing HL. The patient was diagnosed as stage 4a and was begun to treat and to follow up. Discussion: Despite of mostly representation of supradiaphragmatic (i.e. servical, supraclavicular and mediastinal) lymph node enlargements, nodular sclerosing HL may start with atypical localizations as our patient.

MULTIPLE MYELOMA PRESENTING WITH CLIVUS PLASMACYTOMA

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Introduction: Multiple myeloma (MM) involves terminally differantiated plasma cells. MM can affect multipl organ systems; therefore, it may mimic different clinical syndromes at presentation and be found as an isolated lesion or as a part of MM. We report an extremely rare presentation of MM with clivus plasmacytoma. Case: A 66-year-old female presented with diplopia. Physical examination demonstrated 6th cranial nerve palsy. Magnetic resonance image (MRI) of the hypophysis revealed a heterogeneously enhancing expansile malign mass in clivus which extended into Meckel's cave. Neurosurgery was performed for resection of the mass. Mass speciemen showed extensive infiltration of kappa positive plasma cells. In laboratory examination; hemoglobin 6.6 g/dl, calcium 9.7 mg/dl, creatinin:1.43 mg/dl, kappa 141 mg/dl, eritrocyte sedimantation rate >140 mm, serum immunofixation electrophoresis kappa light chain monoclonal gammopathy was detected. Serum protein electrophoresis was normal. Skletal survey radiography showed multiple lytic lesions. Bone marrow biopsy showed diffuse (90%) plasma cells infiltration. Bortezomibe (1.3mg/m2), cyclophosphamide (500mg/day) and dexamethasone (40mg/day) was started. After two cycles control cranium MRI demonstrated residue polypoid solid particles. Whole brain cranial irradiation (30 Gy in 12 fractionated doses) was performed. After radiotherapy the patient has shown clinical improvement with disappearance of diplopia. DISCUSSION: Patients with MM present with a number of neurologic symptoms related to the involvement of the nervous system or the impact of cytokine or paraproteins on the nervous system. Brain, especially clivus involvement in MM is uncommon. Extramedullary involvement of MM has a poor prognosis. The sixth cranial nerve is the most frequent cranial nerve affected. Patients with MM and associated intracranial plasmacytoma are treated with localized radiotherapy followed by systemic chemotherapy. It is important to consider plasmacytoma in the differential diagnosis of all skull base tumors as it is a highly radiosensitive and potentially curable disease.

MEMBRANOUS NEPHROPATHY DEVELOPED AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR APLASTIC ANEMIA WITHOUT TYPICAL FEATURES OF GRAFT VERSUS HOST DISEASE

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Introduction: Nephrotic syndrome (NS) is a rare complication of a hematopoietic stem cell transplantation. (HSCT) Herein we report a case of aplastic anemia (AA), where the patient underwent HSCT from an HLA-identical sister and developed membranous glomerulonephritis (MG) without typical features of GVHD after discontinuation of immunosuppression. Case:A 36-year-old white female presented to our center with pancytopenia and complaints of fatigue, easy bruising and weight loss. After laboratory investigation and bone marrow biopsy she was diagnosed with aplastic anemia. She was failed to respond to immunsupresive and ATG treatment, we performed non-myeloablative bone marrow transplantation from an HLA-identical sister. Cyclosporine A (CsA) was used for GVHD prophylaxis. She developed a clinical nephrotic syndrome with marked edema of the lower extremities, a urinary protein excretion of 5,9 g/dl, hypoalbuminemia, hypercholesterolemia within 2 months after discontinuation of CsA. There were no apparent symptoms or abnormal laboratory data suggestive of chronic graft-versus-host disease. (cGVHD) A percutaneous renal biopsy was performed, renal histology demonstrated MG with glomerular basement membrane (GBM) thickening, granular GBM deposition of IgG on immunofluorescence, mild intimal fibrosis. There was no evidence of amyloid deposition. A bone marrow biopsy did not display any reccurence of aplastic anemia. The patient received prednisone 1mg/kg/d along with a loop diuretic and an angiotensin II receptor blocker. After 4 months of treatment her edema resolved, and her proteinuria decreased to normal range with normal serum albumin level. Prednisone tapered slowly and stopped. Discussion:Chronic renal impairment may occur in 20% to 60% of HSCT patients. MG is the most frequent renal complication observed in patients who develop NS. GVHD related glomerulonephritis should be considered in all patients with hypoalbuminemia following allogeneic HSCT, even if there is no clinical evidence of GVHD.

INVESTIGATION OF SEROUS EFFUSIONS WITH FLOW CYTOMETRY; SINGLE CENTER EXPERIENCE

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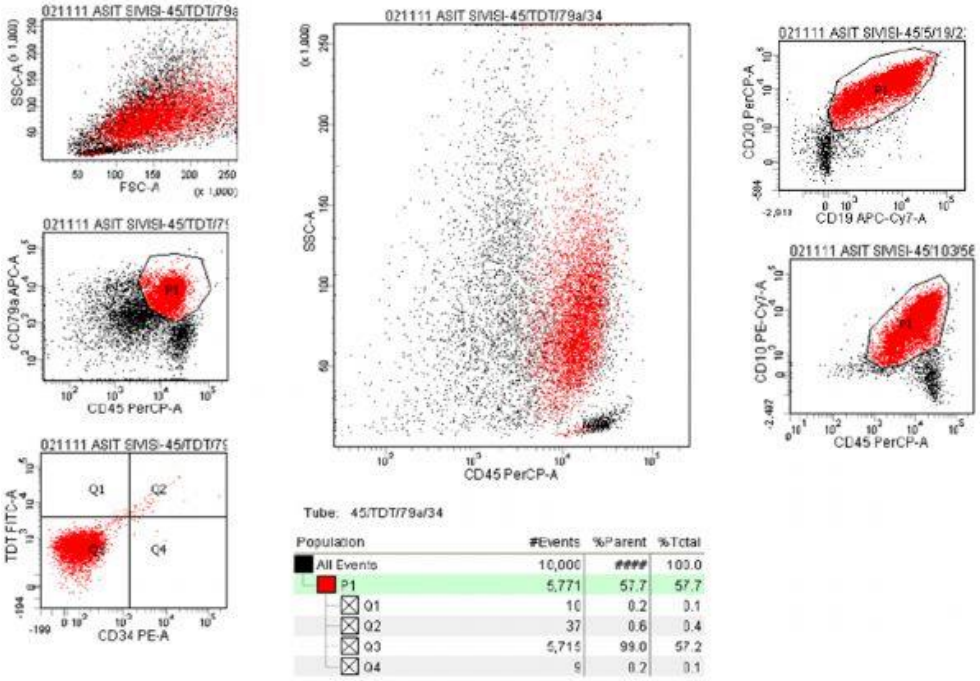
Introduction: In current clinical practice serous effusions are evaluated by cytopathologic, chemical and microbiologic examinations. As well as infections and inflammatory diseases, serous body fluids can also be observed in hematopoietic and solid neoplastic diseases. Flow cytometry(FC) is well established as a critical and quick diagnostik tool used routinely in the diagnosis of hematopoietic neoplasms by fine-needle aspiration and an alternative diagnostic method for the evaluation of serous body fluids.

Materials and Methods: During the time period of 2010-2014, a total of 79 consecutive serous effusion specimens (45 pleural, 33 peritoneal, 1 pericardial) of 76 cases (40 female, 36 male, 24-84 years of age) were investigated with the six-color FC (FACSCanto II, BD Biosystems, San Jose, USA) in the Division of Hematology Laboratory at Akdeniz University Hospital. We retrospectively analyzed these datas.
Results: FC was positive for definitive immunophenotypic evidence of a hematopoietic malignancy in 3 of 45 pleural fluid specimens (Diffuse Large B-cell lymphoma(1 case), Burkitt's lymphoma(1 case), T-cell Acute Lymphoblastic Leukemia / Lymphoma(1 case)) and 3 of 33 peritoneal fluid specimens (T-cell prolymphocytic leukemia(1 case), diffuse large B-cell lymphoma(1 case), Burkitt's lymphoma(1 case)(Figure 1)). Subsequent tissue studies confirmed the diagnosis of a hematopoietic neoplasm in these seperate six cases.
Discussion: Cytopathologic evaluation may lay long especially in the diagnosis of aggressive lymphomas which requires urgent evaluation and treatment. Immunophenotypic analysis of serous body fluids by FC can provide better access to early diagnosis and also accurate clinical staging.

Keywords: effusion, immunophenotyping, lymphoma

Figure 1



Burkitt Lymhoma (ascites specimen)

FLT3-ITD AND/OR FLT3-D835 AND/OR NPM1 POSITIVE ACUTE MYELOID LEUKEMIA CASES: SINGLE CENTER EXPERINCE

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Introduction: The treatment strategy in Acute Myeloid Leukemia (AML) is determined based on risk classification at diagnosis. Especially molecular genetic findings such as fms-like tyrosine kinase 3 (FLT3) gen mutation and nucleophosmin gene mutation are the potential prognostic markers. FLT3 gene encodes a transmembrane tyrosine kinase receptor that stimulates cell proliferation. There are two main types of FLT3 mutations leading to FLT3 tyrosine kinase activation. Internal tandem duplication (ITD) in the juxtamembrane domain of FLT3 gene is more common than point mutation within the activation loop of the tyrosine kinase domain, which mostly affects asparate 835 (D835). Nucleophosmin protein (NPM1) is a nucleocytoplasmic shuttling protein that has several functions between nucleus and cytoplasm.

Patients and Method: Between 2011 to 2014 15 of 54 patients (age≥18 years) who were FLT3-ITD, FLT3-D835 and NPM1 at least one positive by polymerase chain reaction (PCR) and quantitative real-time reverse transcriptase PCR method were retrospectively analysed.

Results: Demographic and clinical characteristics of the patients are presented in Table 1. While abnormal metaphases were observed in 7 patients, 6 patients had normal metaphase in karyotype analysis. The metaphase was not achieved in one patient and the results of one patient could not be reached. Three patients were only FLT3-ITD positive, 4 patients were only FLT3-D835 positive and 5 patients were only NPM1 positive. While two patients were FLT3-ITD and NPM1 positive, 1 patient was FLT-D835 and NPM1 positive. In bone marrow aspiration blast ratio was observed <%5 in 6 patients and >%5 in 6 patients on day 21 and/or 28 after the induction therapy. Two patients were lost to follow-up and 1 patient died before assessing the response of treatment. Consequently the response evalution could not be made in 3 patients.

Discussion: Currently, karyotype abnormalities remain the most important prognostic markers in AML. However, the most common cytogenetic group (comprising %40-50 of adult AML) is normal karyotype and associated with intermediate risk. In this group FLT3, NPM1, CEBPA like gene mutations are very important for risk classification and treatment strategy. There is not enough data about the clinical significance of the presence of concurrently FLT3 and NPM1 mutations. Here, we present data of patients who were carrying these markers in our clinic. Statistical analyses will be performed with new cases.

Key Words: FLT3, NPM1, AML

Table 1

Case no	Age	Sex	Diagnosis	Karyotype	FLT3ITD	FLT3D835	NPM1	Response to induction therapy	Last visit
1	57	F	AML	46,XX,-7,mar(7?)(9)	Negative	Negative	Positive	Could not be reached	Lost to follow-up
2	57	F	AML	46,XX,del(5)(q31)(3)/46,XX(3)	Negative	Negative	Positive	Could not be reached	Lost to follow-up
3	51	F	KML Blast phase	was not achieved metaphase	Negative	Negative	Positive	No	Dead
4	60	M	AML	46,XY(4)	Negative	Negative	Positive	No	Lost to follow-up
5	58	M	AML(relapse)	46,X,-Y,+21(7)/46,XY(7)	Negative	Negative	Positive	Yes	Alive
6	56	M	AML	46,XY,inv(16)(p13q22)(12)/46,XY(3)	Negative	Positive	Negative	Yes	Alive
7	46	F	AML(relapse)	46,XX(15)	Negative	Positive	Negative	Yes	Lost to follow-up
8	59	F	APL	46,XX,t(15;17)(q24q21) (14)/46,XX(2)	Positive	Negative	Negative	Yes	Alive
9	57	F	AML	46,XX(8)	Negative	Positive	Positive	No	Alive
10	60	M	AML	47,XY,+8(13)/46,XY(2)	Positive	Negative	Negative	Yes	Dead
11	62	M	AML	46,XY(15)	Positive	Negative	Positive	No	Alive
12	40	M	MDS/AML	could not be reached	Negative	Positive	Not done	Could not be reached	Dead
13	49	F	AML	46,XX,der(13)del(13)(q11q14)inv(13)(q21q34)(13)/46,XX(2)	Negative	Positive	Negative	No	Alive
14	38	M	AML	46,XY(10)	Positive	Negative	Positive	Yes	Alive
15	75	M	AML	46,XY(15)	Positive	Negative	Negative	No	Alive