UHOD

ULUSLARARASI HEMATOLOJİ-ONKOLOJİ DERGİSİ
International Journal of Hematology and Oncology

ISSN: 1306-133X

CONTENTS

Number: 2 [Supplement 1] Volume: 33 Year: 2023

8th National Blood and Bone Marrow Transplantation Congress

Congress Abstracts

May 18-20, 2023

Atasehir, ISTANBUL / TURKIYE

This Journal is indexed in

- Science Citation Index Expanded (SciSearch)
- TUBITAK Turk Tip Dizini
- Scopus
- Journal Citation Reports / Science Edition
- Chemical Abstracts (CAS)
- EMBASE / Excerpta Medica
- BIOBASE

UHOD

ULUSLARARASI HEMATOLOJİ - ONKOLOJİ DERGİSİ

International Journal of Hematology and Oncology

Number: 2 [Supplement 1] Volume: 33 Year: 2023

OWNER: AKADEMI DOKTORLAR YAYINEVI

ADDRESS FOR CORRESPONDENCE

AKADEMI DOKTORLAR YAYINEVI

316. Cadde 345. Sokak No: 2 / 11 06610 Kirkkonaklar, Cankaya, ANKARA / TURKEY

Tel - Fax : (+90-312) 495 89 83 - 0538-824 21 32 E-mail: uhod@uhod.org Website: www.uhod.org

WASP Venom has a Killing Effect on Leukemic Cells

Ali Zahit BOLAMAN[1], Rahmi CETINKAYA[2], Canan HAZIR[3], Selcuk HAZIR[3], Irfan YAVASOGLU[1]

[1] Aydin Adnan Menderes University, Faculty of Medicine, Hematology Department
[2] Aydin Adnan Menderes University, Stem cell Institute
[3] Aydin Adnan Menderes University, Faculty of Science, Biology Department

Introduction: Treatment of patients with drug-resistant acute leukemia can not be possible. New approaches are needed in the treatment of these patients. The efficacy of wasp venom in myeloid leukemia cell cultures was investigated in this study.

Patients and Methods: Vespula germanica genus wild bees were collected from Aydın- Kuşadası Dilek National Park. The venom sacs of the bees were removed by an expert biologist. Then, supernatant was obtained after washing with acetonitrile and trifluoroacetic acid and centrifugation, Cells in AML HL60 and K562 cell lines were passaged and multiplied when they reached 90% density. The cells were seeded at approximately 1×10^4 cells/well in a volume of 100 μl after cell viability was confirmed with trypan blue, Dose titration of wasp snake venom supernatant and doxorubicin, study groups were formed and their effects in cell cultures were examined and concentrations with IC-50 were examined., Absorbance was measured in a microplate reader after adding MTS/PMS to the wells. Apoptosis rates of cells were evaluated by flow cytometry using Annexin V.

Results: Both doxorubicin and wild bee venom showed lethal effect in AML HL60 and K562 lines depending on dose and time. Lethal effect on blast cells was evident in doxorubicin and bee venom at 48th hour. Apoptosis with annexin V was more prominent in wasp venom and doxorubicin groups than in the control group (p= 0.001).

Conclusion: Bee venom obtained from wild bee venoms of the genus Vespula Germanica has a lethal effect on leukemic cells in myeloid cell lines. This effect may be related to the lysis of blastic cell membranes.

8th National Blood and Bone Marrow Transplantation Congress
May 18-20, 2023, Atasehir, ISTANBUL / TURKIYE

ABSTRACT

A Rare Etiology of Hepatomegaly: Extramedullary Hematopoiesis after Allogeneic Stem Cell Transplantation

Bahar SEVGILI, Ajda GUNES, Tural PASHAYEV, Fatma KEKLIK KARADAG, Nur SOYER, Guray SAYDAM, Filiz VURAL

Ege University Faculty of Medicine, Department of Hematology

Introduction: Hepatomegaly is a challenging clinical finding with increased morbidity after allogeneic hematopoietic stem cell transplantation (Allo-HSCT). Extramedullary hematopoiesis is highly associated with bone marrow failure. We aimed to present a case report about hepatomegaly associated poor graft after allo-HSCT.

Case Report: Twenty-year-old male patient was admitted to Ege University HSCT Unit with B cell acute lymphoblastic leukemia in first remission. He was performed allo-HSCT with mismatched unrelated donor. His conditioning regimen included total body irradiation (TBI) +cyclophosphamide (Cy)+ anti-thymocyte globulin (ATG). On day 10, cytomegalovirus (CMV) DNA detected > 5000 IU/ml. Ganciclovir treatment was added by infectious disease specialist. Engraftments of three lines were completed on day 15. 1st month bone marrow (BM) biopsy control was normocellular and his chimerism was %100, CMV DNA was undetectable. He was discharged with valganciclovir maintenance for 2 weeks. On day 35, he was internalized with ascites, pancytopenia. He complained no weight change but loss of appetite. Liver/renal functions, bilirubin, C-reactive protein levels were normal. The BM aspiration and biopsy was performed as his pancytopenia were worsened. Biopsy was reported no increase of blasts but hypocellular bone marrow without any fibrotic changes. Cytogenetic analysis of BM showed no clinically significant mutations. Ascites sample was also analyzed. Serum- ascites albumin gradient was 1,1; cytologic analysis was reported neither infection nor malignancy. Abdomen ultrasound was reported with hepatomegaly (18 cm) and ascites. Liver biopsy was reported extramedullary hematopoiesis. There were neither inflammatory changes nor graft versus host disease. Filgrastim 5 μ/kg/day, eltrombopag 50-300 mg/day titrated by daily hemogram analysis, were given as supporting treatment. Valganciclovir was discontinued as CMV DNA clearance was detected. On day 90, his cytopenia tended to be improved also liver became nonpalpable. He is still under follow-up with full donor chimerism and no cytopenias recurred for 9 months.

Discussion: After allo-HSCT, several etiologies of hepatomegaly such as infections, venooclusice disease, malignant tumor infiltrations, GVHD should be evaluated carefully. Liver biopsy should be performed in case of unexplained hepatomegaly.

A Case of High-Grade B-Cell Lymphoma with Intravascular Involvement

Elmir ISRAFILOV, Sercan UNAL , Umit Yavuz MALKAN , Haluk DEMIROGLU, Hakan GOKER

Hacettepe University, Faculty of Medicine, Department of Hematology

Introduction: Intravascular large B-cell lymphoma (IVLBCL) is a rare disease that usually occurs between 34 and 90 years of age, is difficult to diagnose clinically and histologically, and most of the cases are diagnosed postmortem. In rare cases, atypical findings such as paraneoplastic syndromes (e.g. syndrome of inappropriate antidiuretic hormone secretion, ataxia, confusion) have also been described. There are two main histological variants of IVLBCL by geographic region: the classical or "Western" type and the hemophagocytic syndrome-associated or "Asian" type. Clinically, three different variant types (classical, cutaneous, and associated with hemophagocytic syndrome) have been described. IVLBCL associated with hemophagocytic syndrome or "Asian" type is usually worse.

Case Report: A 58-year-old female patient, born in Kyrgyzstan, applied to the emergency department of Hacettepe University Hospital due to fever, inability to walk, and a change in consciousness. It was learned that the patient's complaint occurred within 2-3 months. In the emergency department, the patient's neurological status was evaluated, brain CT and brain MRI were taken. In the blood picture of the patient who did not detect acute pathology in imaging studies, HB: 5.6 g/dL, leukocyte: 2.5 x $10^3/\mu$L, neutrophil: 1.8 x $10^3/\mu$L, platelet: 3x10^3 /μL, Ldh: 1143 U/L, Beta-2 microglobulin: 9502 ng/mL, ferritin: 1250 μg/L, he was consulted to the hematology department. Bone marrow aspiration and biopsy are performed by us, considering the blood picture of the patient who was found to have hepatosplenomegaly in the imaging examination. Bone marrow biopsy result: CD20, MUM1, Bcl-6, c-myc, CD5 and p53 resulted as diffuse positive high-grade intravascular B-cell lymphoma. The patient was Ann- Arbor Stage 4, his international prognostic index (IPI) score was 4, and R-CHOP (rituximab, doxorubicin, vincristine, cyclophosphamide) chemotherapy was started.The patient died in the first week of chemotherapy, as his general condition worsened and multiple organ failure developed.

Discussion and Conclusion: IVLBCL is a well-defined but rare disease in the literature. This disease can be masked and imitated. Collaboration of clinicians, radiologists and pathologists is important in such cases. Early diagnosis and early treatment can improve the outcome of IVLBCL.

.

ABSTRACT

Multiple Myeloma Secondary to HIV Infection: A Case Report

Gulay MART[1], Hakan GOKER[1], Çagkan INKAYA[2], Elifcan ALADAG KARAKULAK[1], Umit Yavuz MALKAN[1], Haluk DEMIROGLU[1]

[1] Hacettepe University Faculty of Medicine, Department of Hematology,
[2] Hacettepe University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology

Introduction: HIV-infected patients have increased risks for plasma cell disorders. MM is a plasma cell malignancy and is characterized by the presence of M-protein, the infiltration of clonal plasma cells in the bone marrow and the evidence of end-organ damage. Multiple myeloma (MM) is included in the list of neoplasia that may be associated with human immunodeficiency virus (HIV) infection. The exact mechanisms of plasma cell disorders in HIV patients are unclear. Two main mechanisms probably contribute to the development of plasma cell disorders in this population of patients: antigenic stimulation and immunodeficiency.

Case report: A 59-year-old male presented with a three-month history of fatigue, poor appetite, lack of energy, syncope and 20 kg weight loss. Anemia (hemoglobin 11.3 g/dL) and HIV positivity (HIV viral load - 162157 cp/mL) were found in the tests performed with these complaints. In the etiological examinations of the the anemia, a mass lesion of 27x15 mm size in the left third rib middle part of the expansil, lytic, soft tissue density causing destruction in the bony cortex was observed in the thorax tomography. In the tests performed for multiple myeloma, a peak in gamma in serum protein electrophoresis and monoclonal Igg-kappa in serum IFE were observed. IgG measured was 2930 mg/dL free kappa light chain, 92.32 mg/L monoclonal band 0.9 g/dL. Lenalidomide-dexamethasone chemotherapy was started to the patient with high viral activity of HIV, considering the possibility of negative effects of bortezomib treatment. Meanwhile, antiretroviral treatment was started by the infectious diseases department. After the HIV viral load decreased with antiretroviral treatment, bortezomib was added to the treatment from the second cycle.

Discussion: The incidence of monoclonal gammopathy in HIV-infected patients appears higher than that in the general population among persons 50 years of age or older. MM in HIV-infected patients shows atypical presentation. It tends to be associated with solitary bone plasmocytoma or extramedullary plasmacytoma. These patients also tend to have a low level of M protein despite the aggressiveness of the disease.

In some reported cases, MM was the first manifestation of HIV/AIDS infection. Bortezomib, which is approved for the clinical treatment of multiple myeloma, reactivates latent HIV by increasing cellular Positive transcription Elongation Factor b (P-TEFb) levels and activating Nuclear Factor kappa B (NF-κB).

Conclusion: Myeloma patients with HIV are harder to handle, and proteosome inhibitor and immunomodulatory drugs may be given for treatment.

Plerixafor for Stem Cell Mobilization: Case Report

Gulten KORKMAZ

Ankara Bilkent City Hospital Department of Hematology

Introduction: Stem cells are clonal cells with features such as self-renewal, differentiation, and engrafment. Hematopoietic stem cells (HSC) are recognized by certain surface markers such as CD34(+), Thy-1(+), CD38(-) and Lin (-). Peripheral, bone marrow and cord blood can be used as a source of hematopoietic stem cells. According to 2016 -2020 CIBMTR data, peripheral stem cells were used in 99.7% of patients who underwent autologous stem cell transplantation (ASCT).

Case Report: A 49-year-old man was admitted to thoracic surgery due to hemothorax after weightlifting. We were consulted because of the detection of PT and aPTT prolongation. HGB was 7.2 gr/dl, rouleaux formation in peripheral smear was detected. The laboratory tests detected total protein 7 g/dl, albumin 3.6 g/dl, calcium 8 mg/dl, creatinine 3,17 mg/dl.,PT 45 sec and aPTT 40 sec. Factor X activity was measured twice, and it was determined as 8% and 10%. Factor X deficiency is a rare bleeding disorder that can be associated with life-threatening bleeding events. It can be hereditary or acquired. Cases of acquired factor X deficiency can occur in patients with plasma cell dyscrasias as well as amyloidosis. Our case presented with bleeding and disturbances in hemostasis tests, and further tests were performed in terms of plasma cell dyscrasia. Serum free lambda was 1113 mg/L, and lambda light chain monoclonal protein was detected in serum and urine immunofixation electrophoresis. 90% atypical plasma cell infiltration and lambda positivity was detected in bone marrow biopsy, no presence of amyloidosis with congo red. Abdominal fat biopsy and echocardiography did not reveal any finding suggestive of amyloidosis. He had 30% del 17p mutation. The patient was diagnosed with ISS stage III, R-ISS stage III lambda light chain multiple myeloma.

After 4 cycles of VCD, 50% plasma cell infiltration in bone marrow was seen, after 2 cycles of VRD patient had a very good partial remission. Cyclophosphamide (2 gr/m^2/day) + filgrastim (5 μ/kg/day) regimen was started for stem cell mobilization. The first higher level of 1500/mm^3 peripheral stem cell was counted, upon detection of 5/microliter, plerixafor 0.24 μ/kg was applied.A total of 6.52x106/kg CD 34+ HSC were collected.

Discussion: Plerixafor for peripheral stem cell mobilization can be used in three ways: upfront, pre- emptive and remobilization. We planned mobilization with chemotherapy + G-CSF, however, patients' CD34 count was < 10/μl we used preemptive plerixafor and performed successful mobilization.

ABSTRACT

A Case of Chronic Myelomonocytic Leukemia Developing Intracranial Extramedullary Hematopoesis

Meral ILGAZ ERGIN, Umit Yavuz MALKAN, Haluk DEMIROGLU, Hakan GOKER, Osman Ilhami OZCEBE

Hacettepe University Faculty of Medicine, Department of Hematology

Introduction: Chronic myelomonociter leukemia (CMML) is a recently evolved entity that has been quite difficult to define since its discovery.CMML has overlapping features with other myeloid neoplasms such as MDS and MPN, which further complicates the task of their diagnosis. Extramedullary intracranial hematopoiesis (EMH) occurring in a patient followed up with CMML and non-immune hemolysis is presented.

Case Report: A 58-year-old male patient was diagnosed with MDS 3 years ago, when he applied with complaints of weakness and loss of 12 kilograms in 3 months.Hemolytic anemia and dysplasia in neutrophils were detected, and he was diagnosed with CMML by bone marrow biopsy. Jak2, Ph^+, CalRet, Mpl positivity was not detected in the genetic tests. Hemolysis tests resulted as follows: reticulocyte 24.6%, haptoglobulin < 5.83 mg/dl, LDH 856U/L, total bilirubin 3.5 mg/dl, indirect bilirubin 2.82 mg/dl, direct coombs negative. With the diagnosis of CMML, azacitidine treatment was started to the patient,but hemolysis worsened under this treatment; the hemoglobin decreased to 5.9 g/dl. In the imaging studies, the liver was 22 cm and the spleen was 25 cm. Splenectomy was performed due to non-immune severe hemolysis. The pathology of the splenectomy material was reported as extramedullary hematopoiesis. 4 months after splenectomy, the patient developed blurred vision and headache complaints for a week. He applied to the neurology outpatient clinic and papilledema was detected. Cranial MRI was performed in the patient and lobulated massive extraaxial masses involving all supratentorial dural surfaces (EMH) and orbital findings representing increased intracranial pressure were detected. The patient was admitted to the hospital due to increased intracranial pressure and intravenous steroid therapy was started. In order to clarify the diagnosis, a dural biopsy was performed with a burr hole. In the pathological material, cell population with various stages of myeloid, erythroid precursors and megakaryocytes was detected, and EMH was diagnosed. Allogeneic stem cell transplantation is planned after intracranial radiotherapy, but the patient died due to prolonged seizure.

Discussion: EMH is generally observed in the reticuloendothelial system outside the bone marrow in the presence of bone marrow failure and chronic anemias. Although liver, spleen, and lymph nodes are the tissues in which EMH is observed, intracranial EMH is a very rare condition. EMH is the clinical entity that should be considered in the differential diagnosis in cases with bone marrow failure or chronic hemolysis in the presence of newly developed neurological symptoms.

Bleeding Control with Probiotics in a Case of Glanzmann Thrombasthenia

Mine KARADENIZ, Olgu Erkin CINAR, Sercan UNAL, Umit Yavuz MALKAN, Hakan GOKER

Hacettepe University Faculty of Medicine, Department of Hematology

Introduction: Glanzmann thrombasthenia is an autosomal recessive hemostasis disorder characterized by a congenital defect of the fibrinogen receptor alpha IIb beta III integrin or the development of acquired antibodies against this receptor as a result of mutations in the ITGA2B or ITGB3 genes on chromosome 17. These patients also have deficiencies in the production of thrombin, the control step of hemostasis. In patients with lifelong mucocutaneous hemorrhages, the use of recombinant factor VIIa has come to the forefront in addition to local medical/surgical treatments and platelet support.

Case Report: A 25-year-old male patient with Glanzmann's thrombasthenia presented with gingival bleeding that did not stop despite the use of platelets and recombinant factor VIIa for dental procedures. In the initial evaluation of the patient, active bleeding in the oral mucosa and gingiva in multiple foci continued. Recombinant factor VIIa was infused at a dose of 90 μgr/kg every 2 hours. At the 24th hour follow-up, it was observed that the hemoglobin level decreased by one unit compared to the baseline value and bleeding decreased but could not be completely controlled. Factor support was continued with a dose increase (180-270 μg/kg) and the bleeding was minimized at the end of the 3rd day with HLA-matched platelet suspension, local treatments, transamine support, use of ankaferd and adrenaline. Upon the persistence of gingival bleeding despite adequate duration and dose of factor replacement, the patient was evaluated by the department of dental diseases and an immune-supportive probiotic containing Basillus clausii (*B. clausii*) spores was started. It is observed that the bleeding stops completely in the 48th hour of probiotic use.

Discussion: Glanzmann thrombasthenia is a hemostasis disorder with limited treatment options. In patients who do not respond to recombinant factor use, the path to be followed and supportive treatment is an unmet need. The use of probiotics, especially the spore-producing *B. clausii*-containing type, can be detected in the gastrointestinal tract for up to 16 days, its stimulatory effect on interferon production, T cell and lymphokine proliferation has been shown, its use in the fields of asthma, necrotizing enterocolitis, esophagitis, radiotherapy- chemotherapy-related mucositis is increasing with researches and its immunomodulatory benefits are being examined. The benefit of probiotic use in our patient is thought to have developed due to the fact that it supports vitamin K synthesis, contributes to cell proliferation with riboflavin release, and supports chronic inflammation control by increasing cellular activity.

ABSTRACT

Different Clinical Presentations in Monogenic Vexas Syndrome

Mine KARADENIZ, Olgu Erkin CINAR, Sercan UNAL, Umit Yavuz MALKAN, Yahya BUYUKASIK, Hakan GOKER

Hacettepe University Faculty of Medicine, Department of Hematology

Introduction: Vexas syndrome (vakoul, E1 enzyme, X-linked, autoinflammatory, somatic) is a monogenic disease with a clinical diversity characterized by inflammatory process and hematologic findings resulting from somatic mutation in the UBA1 gene. The disease may present with a faint picture or an aggressive process.

Case Presentations

Case 1: A 64-year-old male patient with a diagnosis of IgG4-related disease presented with complaints of acute phase elevation, fever, swelling in the right eye, and low blood counts, which did not respond to the use of immunosuppressive agents for 1 year. UBA1b (p.Met41Leu) gene defect was defined in the patient who had vacuolization in the myeloid series and dysplastic findings in two series in bone marrow examination. 5-azacytidine was initiated with the diagnoses of Vexas syndrome and Myelodysplastic syndrome (MDS). Improvement in cytopenias and acute phase response were obtained in the 2nd month.

Case 2: A 50-year-old male patient was diagnosed with high-risk MDS on hematologic examination due to episodic fever and neutropenia despite steroid use due to relapsing polychondritis and 5-Azacitidine treatment was initiated. The patient who was followed up in complete remission after 12 cycles of chemotherapy, presented with cytopenia and simultaneous polychondritis attacks 3 years later. After two cycles of decitabine chemotherapy, polychondritis regressed but hematologic improvement was not observed. In the control marrow evaluation, vacuoles in myeloid and erythroid cells and AML transformation observed. Vexas gene mutation test result sent before transplantation was positive.

Case 3: A 64-year-old male patient presented with malaise, fever and hard painful nodular lesions in the extremities. Pulse steroid treatment was started to the patient with a prediagnosis of vasculitis who had acute phase elevation and cytopenia. Bone marrow aspiration was positive for UBA1 (p.Met41Val) gene defect, in whom dysplastic findings and vacuoles observed in the myeloid series. 5-azacitidine was started but amputation was performed due to near-total occlusion of the right femoral artery in the imaging studies. The patient died with postoperative septic shock, recurrent thrombosis attacks and resistant infections.

Discussion: Vexas syndrome has different clinical courses and it is predicted that the change of amino acid sequences in the mutated gene is effective in prognosis. The response to hypomethylating agents is based on correction of the MDS-related clinic and partial suppression of the inflammatory process by these agents through cytokine pathways. Cases of remission by allogeneic stem cell transplantation have been reported.

Evaluations of Iron Overload Pattern and Frequency of Iron Chelator Use in Myelofibrosis: Single Center Experience

Muruvvet Seda AYDIN, Esra CENGIZ, Funda CERAN, Simten DAGDAS, Gulsum OZET

Ankara City Hospital, Department of Hematology

Introduction: Increased transfusion load due to anemia and ineffective erythropoiesis may cause iron overload in the management process of myelofibrosis. Iron toxicity may also aggravate bone marrow failure in this disease. In this study, we aimed to share our chelation experience and the presence of serum iron overload pattern findings in the diagnosis and course of the disease in patients followed up in our center with the diagnosis of myelofibrosis.

Patients and Methods: Serum iron tests of patients diagnosed with Primary Myelofibrosis or Post-Essential Thrombocytosis/Post-Polycythemia Vera Myelofibrosis between 01.01.1997 and 04.11.2021 at Ankara Numune Training and Research Hospital and Ankara City Hospital were investigated retrospectively. Patients with a transferrin saturation of > 45% and/or ferritin > 291 μg/L in women and > 322 μg/L in men were considered as patients with an iron overload pattern. Serum ferritin, transferrin saturation, and complete blood count parameters were evaluated before and after chelation in patients receiving iron chelation.

Results: Forty-three (21 male, 22 female) myelofibrosis patients were studied. The median age was 55 (19-77). Six of the patients had secondary myelofibrosis. There was an iron overload pattern in 5 patients at first admission and 6 patients at diagnosis. Iron overload was present in 13 patients during the follow-up. The pattern of iron deficiency was present in 14 patients at admission, 11 at diagnosis, and 6 patients at follow-up. Iron chelation was applied to four patients and deferasirox was the preferred agent in all of them. Chelator therapy was discontinued in patient 1 due to intolerance. In patient 2, although there was no significant decrease in ferritin, moderate improvement in thrombocytopenia was observed after initiation of chelation. In patient 3, the need for transfusion decreased with chelation. In the patient 4, pre- transplant chelation was applied but follow-up is not suitable for evaluation due to non-relapse mortality after hematopoietic stem cell transplantation.

Discussion: In this cohort, the iron overload at diagnosis may have occurred due to transfusions before the patients reached the diagnosis, and it is not very rare. Iron deficiency is also a common finding. It is the subject of current research to determine which myelofibrosis patients will benefit from chelation. Improvement in cytopenias with chelation has been reported. We suggest that it would be appropriate to evaluate the serum iron tests in myelofibrosis before any transfusion and during follow-up.

ABSTRACT

Rare Coexistence of Hodgkin Lymphoma Pulmonary Involvement and Pulmonary Tuberculosis:

Alper ATALAY[1], Nesibe TASER KANAT[2], Ali UNAL[2]

[1] Erciyes University Faculty of Medicine, Department of Internal Medicine
[2] Erciyes University Faculty of Medicine, Department of Hematology

Introduction: Tuberculosis and Hodgkin Disease (HD) are diseases that can mimic different pathologies. Co-existence of both disease is rare and is mostly seen in the adult patients especially in advanced Hodgkin's disease. Secondary lung involvement is seen in 15-40% of Hodgkin's disease. Immunosuppression may increase the risk of tuberculosis in malignancies. Here, we reported the coexistence of pulmonary tuberculosis in a patient with pulmonary involvement of Hodgkin's disease.

Case Report: A 20-year-old male patient with a known history of asthma was admitted to hospital with complaints of cough, night sweats, fever and weight loss for 2 months. Laboratory examinations of the patient; Hb: 15.3 g/dl, wbc: 9.300/μL, plt: 385000/ μL, sedim: 29 mm/s, kidney and liver function tests were in reference range. Imaging examinations of the patient, hilar lymphadenopathy was detected in thorax tomography. Bronchoscopy was performed and mycobacterium tuberculosis was observed in the Broncho Alveolar Lavage (BAL) culture. Excisional biopsy of right supraclavicular lymph node which showed intense FDG uptake on PET CT was performed. Histopathological examination revealed CD 15, CD 30 positive, classic hodgkin lymphoma, nodular sclerosing type. After the diagnosis of stage 4B Hodgkin lymphoma, ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) protocol with simultaneous anti-tuberculosis treatment was started.

Discussion: Tuberculosis and HD are diseases that can cause similar symptoms. In patients with malignancy, tuberculosis is more commonly presented in the form of extra-pulmonary tuberculosis. In our case, co-existence of pulmonary tuberculosis with HD is an example of a rare association. Obando et al. examined case series and concluded that; simultaneous initiation of chemotherapy and tuberculosis treatment did not cause worsening of tuberculosis infection in patients with coexistence of tuberculosis and HD. In countries where tuberculosis is endemic, tuberculosis should be considered in differential diagnosis, especially in immunosuppressed patients.

Nivolumab-Induced Autoimmune Hemolytic Anemia

Omer Faruk YURT, Sude Hatun AKTIMUR

Samsun University, Samsun Faculty of Medicine, Department of Internal Medicine

Introduction: Currently, immunotherapy has been used in the treatment of various solid and hematological malignancies. Nivolumab binds to the protein called the programmed death-1 receptor (PD-1), blocking its activity. There are few studies in the literature regarding nivolumab causing autoimmune hemolytic anemia (AIHA).

Case 1: A 53-year-old male patient treated with nivolumab for metastatic renal cell carcinoma (RCC) applied to the hematology clinic with complaint of fatigue for a week. The laboratory showed that the white blood cell count (WBC) was 5900/mm^3, hemoglobin 6.7 g/dL, haptoglobin 0.01 gr/L (0.3-2 gr/dl), reticulocyte 6.5%, lactate dehydrogenase (LDH) 1058 units/L (25-248 U/L), total bilirubin 2.19 mg/dL, direct coombs test was positive. Peripheral blood smear showed that multiple spherocytes and polychromasia, no schistocyte. The hemoglobin was 14.6 g/dL 45 days before. Nivolumab treatment was cut with a pre-diagnosis of AIHA secondary to immunotherapy because the patient did not use any drugs commonly involved in the etiology of AIHA and had anemia after starting nivolumab, the patient was started on 1mg/kg methylprednisolone. At the follow-up 2 weeks later, hemoglobin was 11.5 g/dL. At the follow- up three months later, hemoglobin increased to 12.7 g/dL. LDH decreased to 316 U/L, direct Coombs test turned negative.The patient's treatment continue with the reduced dose of methylprednisolone.

Case 2: A 70-year-old male patient who was diagnosed with RAI stage 1 Chronic Lymphocytic Leukemia (CLL) and followed in hematology clinic, was diagnosed with metastatic squamous cell lung cancer. The patient was treated with nivolumab. The patient applied to the hematology clinic with the complaint of fatigue. The laboratory showed that the WBC was 6050/mm^3, hemoglobin 5.9 g/dL, direct coombs test was positive, reticulocyte 8.53%, haptoglobin 0.41 gr/L, LDH 356 U/L. Before nivolumab treatment, the hemoglobin was 10g/dL. Nivolumab was cut and 1 mg/kg methylprednisolone was started. At the follow-up 2 weeks later, hemoglobin was 10.2 g/dL. The patient, who was called for check-up one month later, died while under treatment in the ICU due to respiratory failure.

Discussion: Approximately 50% of AIHA cases are idiopathic.Other etiologies are malignancies, autoimmune disorders, drugs, infections. A few AIHA cases secondary to nivolumab have been reported in the literature due to increasing use of immunotherapy, primarily PD-1 inhibitors.No cases of AIHA secondary to nivolumab have been reported in patients with metastatic RCC and CLL with metastatic lung cancer.

ABSTRACT

Unfavorable Prognosis in Relapsed INV(16) AML: A Case Report of Treatment Resistance And Infectious Complications

Sercan UNAL, Gulay MART, Umit Yavuz MALKAN, Haluk DEMIROGLU, Hakan GOKER

Hacettepe University, Faculty of Medicine, Department of Hematology

Introduction: Acute myeloid leukemia (AML) with inv(16) /t(16;16) is one of the most common subtypes. It is recognized by the detection of CBFB-MYH11 fusion and has a good prognosis regardless of the presence of secondary cytogenetic abnormalities. However, the impact of additional genetic abnormalities in inv(16) AML patients on their outcomes is controversial. Some recent case reports have shown an unfavorable prognosis, such as early relapse and death, associated with the presence of high-risk rearrangements. In this case presentation, we would like to present a case of relapsed inv(16) AML patient who was resistant to multiple salvage therapies and eventually died.

Case Report: A 62-year-old male patient presented to the emergency department with complaints of confusion. Imaging revealed a subdural hematoma and pancytopenia. Peripheral blood smear showed blast cells, and a bone marrow biopsy confirmed a diagnosis of acute myeloid leukemia (AML). Cytogenetic analysis revealed a 46, XY karyotype with inv(16) positivity. The patient was started on the 2+5 protocol (mitoxantrone+cytarabine) due to his overall condition. After induction, bone marrow remission was achieved. As he belonged to the good prognosis class, the patient was planned to undergo 4 cycles of consolidation with HD-ARAC (high-dose cytarabine). The patient remained in remission for approximately one year.However, the patient presented again with complaints of pancytopenia, and a bone marrow biopsy confirmed a diagnosis of relapsed AML with inv(16) positivity. Consequently, the patient was started on the venetoclax + cytarabine protocol, but no bone marrow remission was achieved after induction. The patient was then given the 3+7 protocol (idarubicin+cytarabine) as a rescue therapy, but remission was still not achieved. Following that, the patient received the FLAG-IDA protocol (fludarabine+cytarabine+idarubicin), but once again, no remission was achieved.As a last resort, the patient was treated with the EMA protocol (etoposide+mitoxantrone+cytarabine) to reduce the blast count as much as possible, and allogeneic transplantation was planned. However, the patient was diagnosed with an Aspergillus flavus infection after treatment. Unfortunately, the patient passed away during this process due to infectious complications. At the time of the patient's passing, bone marrow remission was not achieved, and inv(16) positivity was still present.

Discussion: Inv(16) positive AML is generally considered a subtype with a good prognosis. However, some factors may negatively affect the prognosis of inv(16) positive AML patients. For example, it has been shown that inv(16) positive patients may be resistant to salvage treatments and may experience relapse. In addition, some subtypes of inv(16) positive AML may be more aggressive. In one study, it was shown that only about 50% of inv(16) positive AML patients achieved complete remission and long-term survival. Furthermore, it has been reported that some inv(16) positive patients were lost due to severe infections or other complications. Therefore, evaluating a single factor is not sufficient to determine the prognosis of inv(16) positive AML patients, and their response to treatment and clinical characteristics should also be taken into account.

Can SARS CoV-2 Infection Cause Pseudothrombocytopenia? Case Report

Mustafa SINANOGLU[1], Unal ATAS[2], Volkan KARAKUS[2]

[1] Alanya Alaaddin Keykubat University, Alanya Training and Research Hospital, Department of Internal Medicine

[2] Health Sciences University, Antalya Training and Research Hospital, Department of Hematology

Introduction: In December 2019, SARS-CoV-2 emerged in Wuhan, China, causing a pandemic that has led to 660 million cases and 6-7 million deaths worldwide, with continued spread. While SARS-CoV-2 infection is typically associated with mild upper respiratory symptoms and myalgia, it can also lead to severe conditions such as pneumonia, Acute Respiratory Distress Syndrome (ARDS), and various hematologic pathologies, including rare conditions like coagulopathy, immune thrombocytopenia, and thrombotic thrombocytopenic purpura (TTP). In cases of thrombocytopenia following SARS-CoV-2 infection or vaccination should be excluded, as with all cases of thrombocytopenia. We present a case of pseudo-thrombocytopenia in a 35-year-old woman who was referred to us for thrombocytopenia caused by SARS-CoV-2 infection.

Case Report: A 35-year-old woman was referred to us due to thrombocytopenia detected during routine check-ups. The patient had a known history of gastroesophageal reflux disease and was using proton pump inhibitors and anti acids. She had no SARS-CoV-2 vaccination but had SARS-CoV-2 pneumonia with lung involvement 8 months before. Prior to SARS-CoV-2 pneumonia, her platelet counts ranged from 150-200x10^9/L in different years. However, 16 days after SARS-CoV-2 pneumonia, her platelet count was 181x10^9/L, 35 days later it was 89x10^9/L, and 2 months later it was 19x10^9/L. Other hemogram parameters and biochemical tests were normal, and a peripheral blood smear showed numerous platelet clumps and platelet satellitism around neutrophils. A citrate tube blood count showed a platelet count of 196x10^9/L. We concluded that our clinically asymptomatic patient had EDTA-dependent pseudothrombocytopenia following the SARS-CoV-2 infection.

Discussion: Pseudothrombocytopenia, estimated to have a prevalence of 0.1%, is most commonly associated with EDTA use. Although its pathophysiology is not fully understood, it is suggested that EDTA interacts with the glycoprotein-IIb/IIIa molecule on the platelet membrane by binding calcium ions, thereby exposing the glycoprotein-IIb epitope and causing platelet clustering in individuals with autoantibodies against this epitope. Pseudothrombocytopenia associated with EDTA can occur in individuals without any underlying medical conditions as well as in the course of various diseases. Immunoglobulins resulting from immunactivation caused by SARS-CoV-2 infection can lead to some immune system-related diseases such as immune thrombocytopenia, or TTP. Similarly, autoantibodies against the glycoprotein IIb epitope may have developed in the pathophysiology of pseudothrombocytopenia in our patient due to immunactivation. In cases of newly developed EDTA phenomena without prior history, questioning the patient's SARS-CoV-2 infection and vaccination process may be helpful in explaining the patient's clinical condition and may aid in further focusing on the pathophysiology in the future.

ABSTRACT

Could the 3 Prime UTR+101G>C Mutation Detected in Two Sibling Cases be a Mutation Affecting the Clinic in Thalassemia Patients?

Unal ATAS[1], Volkan KARAKUS[1], Erdal KURTOGLU[2]

[1] Health Sciences University, Antalya Training and Research Hospital, Department of Hematology
[2] Sisli Kolan International Hospital, Department of Hematology

Introduction: Beta-thalassemia is a molecularly heterogeneous disease with different mutations emerging in different ethnic backgrounds. Homozygous and compound heterozygous forms of these mutations can result in transfusion-dependent β-thalassemia. Here, we report two siblings with a diagnosis of thalassemia intermedia, despite compound heterozygosity for previously identified mutations, due to an unreported mutation.

Case Report: The 68-year-old male patient diagnosed with thalassemia intermedia has been under our follow-up for the last 12 years due to transfusion requirements, chelation and heart failure. The patient, who did not have any clinical pathology in his parents was first diagnosed with splenomegaly at the age of 7. However, the patient, who did not have a clear diagnosis and follow-up, was investigated for weakness and abdominal distension at the age of 35. At that time, microcytic anemia that did not require transfusion, along with hepatosplenomegaly, gallstones, and elevated HbF levels in hemoglobin electrophoresis, were detected, and the patient was put on follow-up as having thalassemia intermedia. Starting at the age of 54, the patient began to receive regular transfusions for an unknown reason at an outside center and received iron chelation due to transfusional iron accumulation. Despite chelation, the patient developed heart failure 4 years later. Upon joining our follow-up, the patient's DNA sequence analysis showed heterozygous mutations in c.92+6T>C (rs35724775) (IVS-I-6) and c.93- 21G>A (rs35004220) (IVS-I-110) genes, which can cause β-thalassemia disease, as well as 3 prime UTR+101G>C (+233 relative to termination codon) (rs12788013) gene, which is suspected to cause β-thalassemia disease. The patient's younger sister, who is one year younger than him and is being followed up for thalassemia intermediate without transfusion dependence, was also found to have the same mutations.

Discussion: In the Turkish population, more than 40 mutations have been identified so far. Guzelgul et al. detected 22 different β-thalassemia mutations in 52 pediatric patients in their study conducted in the Cukurova region. Homozygous mutations were identified in 36 of these patients (IVS-I-110 (58.0%), IVS-I-6 (5.6%)), while compound heterozygous mutations were found in 13 patients. Two of these patients were reported to have compound heterozygous mutations of IVS-I-110 and IVS-I-6, similar to our two sibling cases. Despite the compound heterozygosity of these two mutations in our cases, both patients clinically exhibit thalassemia intermedia. The presence of a previously unreported but detected 3 prime UTR+101G>C mutation in both patients raises the question of whether this mutation could be "a mutation that mitigates the clinical presentation."

Retrospective Analysis of Tyrosine Kinase Inhibitor Molecules Used in The Second and Third Line Treatment of Chronic Myeloid Leukemia Patients in Terms of Efficacy, Side Effect, and Survival

Yasemin EVLENDI[1], Umit Yavuz MALKAN[2], Ibrahim C. HAZNEDAROGLU[2], Hakan GOKER[2]

[1] Hacettepe University, Faculty of Medicine, Departman of Internal Medicine

[2] Hacettepe University Faculty of Medicine, Department of Hematology

Introduction: To investigate the response rates in the first-line Tyrosine Kinase Inhibitor (TKI) treatment of patients with Chronic Myeloid Leukemia (CML), the rate of transition to second and third-line TKI treatment. We aimed to analyze the efficacy, survival, depth and duration of molecular response of nilotinib and dasatinib treatments in second-line therapy.

Patients and Methods: This study, which was designed as an observational retrospective cohort study, included 105 patients over the age of 18 who were followed up in our clinic with the diagnosis of CML. Groups were compared for categorical variables using Pearson's chi-square. Kaplan-Meier method was used for survival analysis. SPSS software was used for statistical analysis tests.

Results: The 5-year survival rate in the study was calculated as 96.8% ± 0.019. A statistically significant correlation was found between ELTS risk groups and overall survival (p= 0.003). 43 (40.9%) patients switched to second-line TKI therapy, and 14 (13.3%) patients switched to third-line TKI therapy. It was observed that 26 (60.5%) patients received dasatinib and 17 (39.5%) nilotinib treatment in the second-line treatment. A statistically significant difference in favor of dasatinib was found between dasatinib and nilotinib treatments in terms of early molecular response in second-line TKI treatment. No significant difference was observed between dasatinib and nilotinib treatments in terms of the duration of molecular remission in second-line therapy, the rate of reaching MR 4.0 and MR 4.5 response targets, and the time to reach MR 4.0 and MR 4.5 responses.

Discussion: The ELTS risk score is the newest scoring system recommended by the European Leukemia Network (ELN) for predicting survival in patients treated with TKI. In our study, ELTS risk scoring was found to be more significant than Sokal, Hasford, and EUTOS scoring in predicting overall survival in patients with CML, so we recommend using ELTS risk scoring. Prospective randomized studies are needed to determine whether there is a difference between dasatinib and nilotinib treatments in terms of achieving early molecular response, molecular remission time, molecular response depth, and achieving MR 4.0 and MR 4.5 responses in second-line TKI therapy.

ABSTRACT

Malignities Accompanying Chronic Myeloid Leukemia: Experience of Two Centers

Yildiz IPEK[1], Hakan KESKI[2], Esra TURAN ERKEK[1]

[1] Kartal Dr. Lutfi Kirdar City Hospital, Department of Hematology

[2] Umraniye Training and Research Hospital, Department of Hematology

Introduction: With the use of tyrosine kinase inhibitors (TKIs) in the treatment, the overall survival of patients with chronic phase chronic myeloid leukemia (CML) has approached the normal population. Due to the prolonged life expectancy, the incidence of secondary malignancy has increased in CML patients. CML progression, secondary malignancy and death due to comorbidities (cardiovascular diseases) are common in these patients.

Patients and Method: A total of 213 patients with CML who were followed up in Lütfi Kırdar City Hospital and Umraniye Training and Research Hospital between 2012 and 2023 were retrospectively scanned, and data on 12 patients were obtained. Blastic or accelerated phase patients were not included in the study. Data were evaluated with descriptive data and within-group distribution parameters using GraphPad Prism 8.

Results: Secondary primary malignancy was observed in 12 patients out of 213 CML patients. The mean follow-up period of the cases was 70.83±42.36 months. 58.33% of the patients were female and 41.67% male. The most common comorbidities were diabetes mellitus (DM, 41.6%) and hypertension (HT, 41.6%). The median age at diagnosis of CML was 64.5 years (48.0-79.0). According to the EUTOS risk score, 66.67% were in the low risk group and 33.33% were in the high risk group. All patients (n= 12) received imatinib in primary care. 25% (n= 3) patients were switched to 2nd line TKI therapy (dasatinib n= 2, nilotinib n= 1) due to loss of response/intolerance. No use of 3rd and 4th-line TKI was detected in these patients. In our retrospective study in which 213 CML patients were screened, the rate of accompanying malignancy was found to be 5.63% with 12 cases. Secondary primary malignancy was diagnosed before CML in 2.8% of cases, while it was diagnosed after CML in 2.8%. In terms of timing, the ratio among patients with CML and secondary primary cancer was 50/50. In order of frequency malignencies are, colorectal adenocarcinoma (25%), thyroid papillary carcinoma (16%), renal cell carcinoma (16%), pancreatic ca (8%), breast ca (8%), bladder ca (8%), basal cell (8%) and squamous cell skin cancer (8%).

Death was observed in 25% of patients during a median follow-up of 70 months (n= 3). Death due to solid organ malignancy progression (colorectal and pancreatic adenocarcinoma) were 66.6% (n= 2), AML transformation was 33% (n= 1). In patients with mortality, the rate of use of 2nd line treatment was observed in 66.67%.

Discussion: In our study, the frequency of secondary primary, before or after the diagnosis of CML, did not differ with 2.8%. In a multicenter study evaluating 14.897 patients between 2001-2014, the rate of other malignancies before CML was found to be 8%, and after CML diagnosis to be 4.5%. The lower rate in our study may be related to the small number of patients. According to a study of 861 patients in which the current Turkish CML demographic data were evaluated, the median age of diagnosis was 48 in the study, while the median age of diagnosis of CML patients with concomitant malignancy was 64.5, and it was remarkable that our patients were older. The rate of concomitant comorbid diseases, especially DM and HT rate, was found to be considerably higher than the rate of cardiovascular disease and DM in the same study.

Conclusion; The presence and follow-up of other accompanying malignancies in CML patients should be considered as an important part of CML management. There is a need for multicenter studies on the effect of additional malignancy on survival and disease management, especially in elderly CML patients in our country.

8th National Blood and Bone Marrow Transplantation Congress
May 18-20, 2023, Atasehir, ISTANBUL / TURKIYE

Retrospective Prognosis Evaluation of 18FDG PET/CT Results of Patients with Hodgkin's Lymphoma According to Delta SUVmax and Deauville Score

Onur SAHIN, Derya Deniz KUREKCI, Engin KELKITLI, Memis Hilmi ATAY, Mehmet TURGUT

Ondokuz Mayıs University Faculty of Medicine, Department of Hematoloji

Introduction: Positron Emission Tomography (PET) is used in the diagnosis, treatment selection and treatment response evaluation of Hodgkin Lymphoma (HL) patients. In this study, deauville criteria and suvmax changes (SUVmax) of PET in Hodgkin Lymphoma were examined and the contribution of PET to the long-term clinical outcomes of the disease was investigated.

Patients and Methods: Patients diagnosed with Hodgkin Lymphoma (HL) between 2012 and 2019 were included. Demographic data of patients, risk factors, pre-treatment staging (PET0), post-chemotherapy interim (PETint) and end-of-treatment (PETend) PET results; Deauville scores at baseline, intermediate and end of treatment, and Standardized maximum uptake (SUVmax) values, treatment responses and long-term results were evaluated.

Results: A total of 74 patients diagnosed with HL were included in our study. According to PET images, patients were divided into two groups as responding to treatment (Deuville negative) and partial response or treatment failure (Deauville positive). When the PFSs of these two groups were compared according to the intermediate PET imaging; it was found that PFS was 91.75±5.37 months in Deauville-negative patients and 50.57±15.59 months in Deauville- positive patients. This difference was found to be statistically significant (p= 0.008). The cut- off value for ΔSUVmax (Int) was 66% and 77%, as determined in previous studies, and 73% for DeltaSUVmax (End). If the cut-off value is taken as 66% for ΔSUVmax (Int), a statistically significant relationship was found between ΔSUVmax (Int) and PFS (p= 0.016).

Conclusion: Based on current data, ΔSUVmax appears to be a robust and independent prognostic factor for HL.

ABSTRACT

Developing Renal Failure Diagnosed Multiple Myelom Kidney with Treatment in Patients Effective on Correction of Failure Examination of Factors

Ahmet Faruk SOYLU, Derya Deniz KUREKCI, Engin KELKITLI, Memis Hilmi ATAY, Mehmet TURGUT

Ondokuz Mayıs University Faculty of Medicine, Department of Hematoloji

Introduction: In our study, it was aimed to evaluate the overall survival of patients diagnosed with Multiple Myeloma (MM) and admitted with acute renal failure (ARF) by examining the relationship between renal failure and prognosis, the factors affecting the reversibility of renal failure, and the response of patients to treatment.

Patients and Methods: In our study, the files of 520 patients, diagnosed between January 2010 and December 2021 in Ondokuz Mayıs University Medical Faculty Hospital Hematology Department, were scanned. The study included 97 patients, who were treated and followed-up in this department, who were diagnosed with MM according to the IMWG criteria and applied with ARF according to the RIFLE criteria, who were older than 18 years old, who received at least 4 cycles of induction chemotherapy, and whose response was evaluated after KT. The files of the patients were reviewed retrospectively.

Results: ARF was seen in 97 (18,6%) of 520 patients diagnosed with MM. 69.07% (n= 67) of the patients were male, 30.93% (n= 30) were female, and the male/female ratio was found to be 2.23%. The median age of the patients was 63. The median estimated glomerular filtration rate (GFR) was 21 ml/min (4.6-49 ml/min), and 73.2% of patients had ISS stage 3. Twenty-four (24.74%) patients were taken to hemodialysis at the time of admission. It was observed that renal failure improved in 49.5% (n= 48) of the patients, and it did not improve in 50.5% (n= 49). The median survival time of the patients was found to be 54.3±7.3 months. It was observed that creatinine, calcium, phosphorus, total protein and beta 2 microglobulin levels at the time of admission were effective in the improvement of renal failure. At the same time, it was determined that plasmapheresis at the time of admission, no need for hemodialysis, and early treatment (≤ 5 days) were effective in the improvement of renal failure. It was observed that the improvement of renal failure did not change the myeloma response to treatment, but OS decreased in patients who developed end-stage renal disease (ESRD).

Discussion: Recovery of kidney damage appears to have a positive effect on long-term survival. For this reason, it is important to determine the factors affecting the recovery of kidney functions and to start treatment early.

A case of Gastrointestinal Bleeding due to Duodenal Ulcer Perforation in a Patient with İnhibitory Hemophilia A

Elmir ISRAFILOV, Gulay MART, Elifcan ALADAG, Umit Yavuz MALKAN, Haluk DEMIROGLU, Hakan GOKER

Hacettepe University, Faculty of Medicine, Department of Hematology

Introduction: Hemophilia A (HA) is an X-linked recessive genetic bleeding disorder caused by a deficiency of the clotting protein factor VIII (FVIII). If patients with severe HA do not receive appropriate prophylaxis, spontaneous bleeding episodes may ocur. Up to 30% of patients with hemophilia A develop inhibitors, which renders treatment with regular factor concentrates ineffective, increasing morbidity and mortality rates. Several genetic and non- genetic factors may be involved in the formation of inhibitors, and at this time there was no clear biomarker to predict whether a patient would produce FVIII inhibitors.

Case Report: A 41-year-old patient with hereditary inhibitory hemophilia A applied to the emergency department with the complaint of hematemesis and hematochezia while taking 3500 IU prophylactic prothrombin complex concentrate (FEIBA) every 12 hours, 3 days a week. The patient is hypotensive and anemic, and is taken to the intensive care unit because of blurred consciousness. The patient is consulted to the hematology department and the gastroenterology department. The patient's mouth was closed by the gastroenterology department and pantoprazole infusion was started. Upon consultation by our hematology team, 4 units of plasma and 2 units of erythrocyte replacement were performed upon the patient's HBV level of 5.6 g/dl, and FEIBA was adjusted as an infusion of 100 IU/KG with 8-hour intervals. Active bleeding in the form of leakage on the anterior bulb wall is detected by the gastroenterology team, and 2 hemoclips are applied to the patient, and the procedure is terminated by applying sclerotherapy with adrenaline. In the follow-up of the patient, as the hemodynamics was unstable and the hematochezia continued, abdominal CT angiography was performed. Venous bleeding due to duodenal ulcer perforation was observed in CT angio. The patient was urgently operated on. The patient, whose FEIBA infusion continued in the preoperative and postoperative periods, was discharged by switching to a prophylactic dose due to the stable course of his hemodynamics.

Discussion: Peptic ulcers are most commonly seen in the duodenal region in the gastrointestinal tract. All these lesions can lead to gastrointestinal bleeding and cause very difficult decision- making problems in terms of diagnosis and treatment. A multidisciplinary approach that includes a hematologist, surgeon, anesthetist, endoscopist and interventional radiologist is mandatory to ensure appropriate diagnosis and management of these patients.

ABSTRACT

In a Steroid-Resistant Graft-Versus-Host Patient with Allogenic Hematopoetic Stem Cell Transplantation α1–Antipripsin Experience: A Case Report

Elmir ISRAFILOV, Meral ILGAZ ERGIN, Umit Yavuz MALKAN, Haluk DEMIROGLU, Hakan GOKER

Hacettepe University, Faculty of Medicine, Department of Hematology

Introduction: Allogeneic stem cell transplantation is a curative treatment option for AML patients in complete remission. Acute graft-versus-host disease that develops after allogeneic hematopoietic stem cell transplantation progresses with high morbidity and mortality in patients. α1-antitrypsin, a serine protease inhibitor with anti-inflammatory, anti-apoptotic and immunomodulatory effects, plays an important role in this process.

Case Report: A 65-year-old male patient applied to family medicine with complaints of fever, fatigue, and weakness. Upon detection of pancytopenia on admission, he was consulted to the hematology department. After the necessary examinations were made, the patient was diagnosed with AML on the basis of MDS with 25% blastic cells in the bone marrow. The patient was given 2 courses of azacitidine treatment. An increase in the rate of blastic cells was observed in the bone marrow examined after the treatment. The patient received 3 cycles of venetoclax and ARA-C chemotherapy regimen. In the control bone marrow examination, the blast rate was reported as 3-4% normocellular bone marrow. Afterwards, the patient underwent Allogeneic stem cell transplantation. Skin rashes developed during the follow-up of the patient. A skin biopsy was performed after consultation with the dermatology department. The pathology result was compatible with graft versus host disease. The patient had grade 3 skin GVHD. The patient was started on steroid and tacrolimus treatment. During the follow-up of the patient, myopathy and neuropathy developed. When the patient's skin lesions did not regress, mycophenolate mofetil and ruxolitinib were given. When thrombocytopenia developed as a side effect of medical treatment in the patient, the drug was discontinued and a1 antitrypsin in the form of intravenous infusion of 60 mg/kg twice a week was started. Due to the decrease in the skin lesions of the patient, his medical treatment was completed in 28 days. During this period, no hematological or non-hematological side effects were observed in the patient. Currently, the patient is being followed hematologically.

Discussion: Although monoclonal antibodies, antithymocyte globulin, extracorporeal photopheresis, various agents and other strategies have been tried in patients with steroid- resistant GVHD, partial success has been achieved. Treatment with α1-antitrypsin has a role in preventing GVHD through mechanisms such as increase in Tregs and decrease in Teffs, expression of proinflammatory cytokines such as IL-1, tumor necrosis factor and IL-32, which are involved in the pathophysiology and clinical manifestations of GVHD. α1- antitrypsin is a suitable candidate for controlled trials in preventing GVHD.

Hydroxyurea-Associated Cutaneous Squamous Cell Carcinoma in a Patient with Polycythemia Vera: A Case Report

Gulay MART[1], Elmir ISRAFILOV[1], Sercan UNAL[1], Irmak GUNESLI[2], Umit Yavuz MALKAN[1], Yahya BUYUKASIK[1]

[1] Hacettepe University Faculty of Medicine, Department of Hematology

[2] Hacettepe University Faculty of Medicine, Department of Internal Medicine

Introduction: Hydroxyurea (HU) is a is a non-alkylating antineoplastic agent that is ribonucleotide diphosphate reductase inhibitor that interferes with the S phase of cell replication and inhibits DNA synthesis and frequently used to treat myeloproliferative disorders, including polycythaemia vera. Although HU is easy to use and effective and has high tolerance, the cutaneous side effects of hydroxyurea treatment are diverse and frequent during long-term therapy with HU. Squamous cell carcinoma (SCC) is one of the most challenging side-effect. Herein, we describe an additional case of cutaneous squamous cell carcinoma (cSCC) associated with long-term HU therapy.

Case Report: Our case is a 71-year-old male patient diagnosed with polycythemia vera and using hydroxyurea since 2014. It was observed that a lesion developed on the scalp at him outpatient clinic admission, and squamous cell carcinoma was detected in the biopsy taken by the dermatologist. He was taking 500 mg of hydroxyurea twice a day since eight years. The hematocrit value seen in the last clinical control of the patient was 46.5 %, the last need for phlebotomy was 2 years ago. Due to the development of cSCC, hydroxyurea was discontinued and Peginterferon Alfa-2a was started once weekly.

Discussion: The association of HU treatment with secondary skin tumors has been widely documented in the literatüre. A regular dermatological examination and UV protection are essential for patients on long–term hydroxyurea treatment. Lesions are usually localized on sun-exposed areas such as the scalp, face, and extremities. Patients should be informed about the possible cutaneous toxicities of HU treatment in advance, and regular protection against UV rays should be recommended. When cSCC is identified, HU treatment withdrawal is necessary. Since the skin toxicity of HU is late toxicity, patients should be followed for years after HU is discontinued.

Conclusion: The observation of the clinical course of our patient disclosed that cutaneous squamous cell carcinoma is a possible complication of hydroxyurea treatment.

ABSTRACT

A Rare Case of Chronic Lymphocytic Leukemia and Renal Amyloidosis

Gulay MART, Meral ILGAZ ERGIN, Sercan UNAL, Nilgun SAYINALP, Osman Ilhami OZCEBE

Hacettepe University Faculty of Medicine, Department of Hematology

Introduction: Immunoglobulin light chain (AL) amyloidosis is a monoclonal plasma cell disorder characterized by tissue deposits of fibrils composed of monoclonal light chain fragments. Rarely, AL amyloidosis can be due to abnormal light chains produced by lymphomas such as chronic lymphocytic leukemia (CLL). Treatments of AL amyloidosis are similer to plasma cell disorders, and range from low-dose chemotherapy to high-dose chemotherapy with autologous stem cell transplantation. We presented a case with CLL and renal AL amyloidosis who is treated with combination chemotherapy.

Case Report: A 70-years-old male patient was diagnosed with CLL one year ago. He was on watch and wait protocol, he applied our outpatient clinic with edema and fatigue. Lymphocyt count was 9500/microlitre and progressive creatinine increase from 1.7 to 4 mg/dl were observed. Serum free kappa light chain level was 241 mg/dl (baseline 3.3-19 mg/dl) and 24 hr urine free kappa light chain level was 828 mg/day (baseline 0.39-15 mg/day). No monoclonal band was observed in serum and urine immunofixation electrophoresis. Renal biopsy was compatible with AL amyloidosis. Kappa monotypic plasma cell increase with CD138 staining 10% of cells, amyloid deposition, and low-grade B-cell lymphoma infiltration were shown in bone marrow biopcy. Melphalan and dexamethasone (MD) were given. After one cycle, progressif renal disfonction was seen and, we switched the treatment to combination of daratumumab, bortezomib, cyclophosphamide, dexamethasone. Although there was a decrease in serum free kappa levels and lymphocyte count after six cycle of chemotherapy, renal function did not improve and routine dialysis program was required due to the development of electrolyte imbalance, hypervolemia and metabolic acidosis.

Discussion: Although AL amyloidosis typically results from an underlying plasma cell clone disorder, it has rarely been reported in association with chronic lymphocytic leukemia (CLL). In this patient with CLL, AL amyloidosis was caused by a coexisting plasma cell clone. Ourpatient had both a plasma cell clone and a CLL clone that shared the same light chain. Although AL amyloidosis is the result of clonal proliferation of plasma cells, most patients don't meet criteria for multiple myeloma. Systemic AL amyloidosis is not cured with conventional treatment. Treatment directed at the plasma cells aims to decrease amyloid production, restrict further organ damage, this approach, may provide regression of tissue amyloid deposits but it is uncommon; as such, symptoms due to these deposits are likely not reversible.

Conclusion: Based on our clinical information CLL and renal AL amyloidosis may present together and treated with combination chemotherapy.

A Case of JAK2 V617F Positive Familial Polycycemia Vera (PV)

Meral ILGAZ ERGIN, Elmir ISRAFILOV, Gulay MART, Sercan UNAL, Ibrahim Celaleddin HAZNEDAROGLU

Hacettepe University Faculty of Medicine, Department of Hematology

Introduction: Myeloproliferative neoplasms(MPN) are hematological diseases characterized by clonal proliferation of one or more myeloid series. JAK2 V617F mutation is observed in non-chrnic myeloid leukemia (CML) MPNs. While it is detected in 90-98% of policytemia vera (PV) patients, it is seen in approximately 50% of patients with essential throbocytosis (ET) and primary myelofibrosis (PMF). MPN mostly develops sporadically, but; familial clustering of MPN has also been reported. A case of familial JAK2 V617F positive PV followed in our clinic is presented.

Case Report: A 52-year-old female patient was diagnosed with Jak2 V617F (+) PV 12 years ago. She was followed up with acetylsalicylic acid and hydroxyurea The patient continued to follow up every 6 months. After the patient developed fever and weight loss complaints, the blood count was found to be leukocyte: 4300/mcl neutrophil: 1000/mcl monocytes: 1000/mcl, and 19% blasts were found in the blood smear. Bone marrow biopsy was performed, it was reported as AML transformation in the background of chronic myeloproliferative disease (CMPD). Induction therapy was started in the patient diagnosed with high-risk AML and family screening was initiated for allogeneic transplantation.Since a full match donor could not be found, it was planned to transplant the patient from his 7/10 matched son. The examination results of his 21-year-old son, who was selected as the donor candidate, were found to be hemoglobin 17.3 g/dl hct: 50.3 platelets 590000/mcl. The physical examination and history of the donor candidate had no findings suggestive of secondary polycythemia, and the spleen size was 115 mm. When the erythropoietin level was 2.55 miu/ml, the Jak2 V617F mutation test performed on the donor candidate was positive. The bone marrow biopsy performed was reported as polycythemia vera. Unrelated donor screening was initiated for the patient who had no other suitable family donor candidates.

Discussion: In a large population-based study, it was found that the risk of developing MPH in the first degree relatives of people with MPH is 5 to 7 times higher than the control group. Studies on PV cohorts show that the prevalence of familial cases is between 0.9% and 2.4%. Patients with familial PV and ET have a similar prognosis to patients with non-familial MPN, but the presence of the JAK2V617F mutation has been associated with transformation to myelofibrosis in patients with familial PV and possibly ET. However, its effect on the progression to AML has not been associated.

ABSTRACT

Atypical Hemolytic Uremic Syndrome Presented with Gastrointestinal Findings

Meral ILGAZ ERGIN[1], Mehmet ERGIN[2], Umit Yavuz MALKAN[1], Yahya BUYUKASIK[1], Hakan GOKER[1]

[1] Hacettepe University Faculty of Medicine, Department of Hematology
[2] Etlik City Hospital, Department of Nephrology

Introduction: Atypical Hemolytic Uremic Syndrome (AHUS) is a rare, complement-mediated disease characterized by microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury with an annual incidence of 1-2 per million. A case of AHUS developing in a patient followed up with acalculous cholecystitis is presented.

Case Report: A 48-year-old female patient applied to the emergency department with sudden onset, severe abdominal pain in the back, nausea and vomiting 3-4 times in a row. The patient had watery diarrhea 5-6 times on the same day. She hasn't had a fever. She had no history of drug use. In abdominal ultrasonography, the gallbladder wall thickness increased and pericholecystic edema was observed. No stones were found in the gallbladder. The patient was admitted to the general surgery service with a preliminary diagnosis of acalculous cholecystitis. Laboratory tests resulted as follows: ALT: 219U/L AST: 409U/L ALP: 57U/L GGT: 56U/L total bilirubin: 3.2 mg/dl direct bilirubin: 0.8 mg/dl BUN: 32 mg/dl creatinine: 3.5 mg/dl Hb: 9.9 g/dl Leukocyte: 19000/mcL Platelet: 72000/mcL. The patient, who developed anuria in the follow-up, was started on hemodialysis due to acute kidney injury. The patient with thrombocytopenia, anemia and AKI was evaluated for thrombotic microangiopathy (TMA) , and a large number of schistocytes were observed in his peripheral smear. The patient's prothrombin and partial thromboplastin time were within normal limits, and LDH: 4527 U/L, D-dimer: 25 mg/ml fibrinogen: 354 mg/dl haptoglobulin: < 5.8 mg/dl direct coombs: negative. Plasmapheresis was started in the patient who was thought to have TMA. *E. Coli* O157-H7 and shiga-toxin test, which were evaluated in terms of differential diagnosis were negative. ADAMTS-13 activity required for TTP exclusion was within normal limits. The patient had no known chronic disease no use of drugs or herbal products. The frequency of plasmapheresis gradually decreased and eculizumab treatment was started with the diagnosis of atypical HUS after the necessary vaccinations. With eculizumab treatment, the patient's follow-up continues without the need for hemodialysis.

Discussion: AHUS is a serious clinical picture that starts suddenly and leads to organ failure and death if not treated. Plasmapheresis should be started immediately in patients with TMA detected by clinical and laboratory findings. In patients diagnosed with AHUS, C5 monoclonal antibody eculizumab treatment has been shown to inhibit the hemolytic process and recover native kidney function, thus significantly altering the prognosis of this potentially fatal syndrome.

Familial CEBPA Mutation-Associated Acute Myeloid Leukemia: A Case Report

Sercan UNAL, Elmir ISRAFILOV, Gulay MART, Meral ILGAZ ERGIN, Yahya BUYUKASIK

Hacettepe University, Faculty of Medicine, Department of Hematology

Introduction: CCAAT/enhancer binding protein-alpha (CEBPA) plays an important role in the maturation of the granulocyte series. Since 2016, germline predisposition to myeloid neoplasms has been recognized as part of the World Health Organization's (WHO) classification of hematological malignancies. Germline CEBPA mutation provides susceptibility to acute myeloid leukemia (AML) through autosomal inheritance. In this case report, we present a 39-year-old male patient with AML who previously had a family history of CEBPA mutant AML in 2 siblings and a daughter.

Case Report: The 39-year-old male patient presented with weakness, palpitations, decreased exercise capacity, and shortness of breath, and was diagnosed with known type 2 diabetes mellitus. Blood tests showed pancytopenia and peripheral smear revealed blast cells. The patient underwent a bone marrow biopsy, which showed infiltration with 80% blasts and was consistent with MPO(+) acute myeloid leukemia. Molecular tests showed CEBPA positivity. The patient received 3(+)7 (daunorubicin+ARA-C) induction chemotherapy. After achieving remission, the patient received high dose ARA-C consolidation chemotherapy. 6 thioguanine, cytarabine, daunorubicin (TAD) maintenance therapy is currently being administered to the patient who remains in remission. The search for an unrelated donor for bone marrow transplantation is ongoing for the patient. The patient has five siblings, and germline CEBPA mutation was detected in 4 of them. The patient's brother was diagnosed with AML in 2003 and his sister was diagnosed in 2004. Both siblings have been in remission since induction and consolidation therapy. The patient is married and has a daughter who was diagnosed with AML in 2009 and also has germline CEBPA mutation. After induction and consolidation therapies, the daughter underwent an allogeneic bone marrow transplant from an unrelated donor and has remained in remission without any complications.

Discussion: The incidence of relapse is higher in familial CEBPA-positive AML cases. Although there is no consensus on the necessity of allogeneic stem cell transplantation in these patients, donor selection is controversial. We suspect that similar problems may arise after transplantation if similar mutations are detected in the family. Therefore, we believe that unrelated donor searches play an important role in these cases.

ABSTRACT

Diffuse Large B-Cell Lymphoma Presenting with Orbital Involvement: A Case Report

Sercan UNAL, Elmir ISRAFILOV, Meral ILGAZ ERGIN, Gulay MART, Yahya BUYUKASIK

Hacettepe University, Faculty of Medicine, Department of Hematology

Introduction: Diffuse large B-cell lymphoma is the most common subtype of non-Hodgkin lymphomas. Involvement of the ocular region, including the eyelids, conjunctiva, lacrimal gland, and lacrimal sac, with diffuse large B-cell lymphoma is relatively rare and accounts for 8-13% of ocular adnexal lymphomas. In this paper, we aim to present a case of diffuse large B-cell lymphoma that presented with swelling of the lip and eye.

Case Report: A 62-year-old male with an unremarkable medical and ocular history presented to the ear, nose, and throat department with a one-month history of painless, swollen left eye and swelling lip. He also complained of fatigue, headache, and vomiting. The patient did not have night sweats, fever, or weight loss. MRI of the patient's right orbital inferior showed a homogeneous mass with significant diffusion restriction in the extraconal space, filling the orbital apex-superior and inferior orbital fissures, infiltrating the right cavernous sinus-pterygopalatine fossa-foramen rotunda, entering the right nasolacrimal duct, spreading to the right masticator-infratemporal space, maxillary sinus roof, and lateral region. A biopsy was taken from the best location detected in the patient's imaging. The pathology result showed diffuse and strong positivity with CD20, MUM-1, Bcl-6, and Bcl-2 consistent with lymphoid neoplasm containing areas of necrosis that diffusely infiltrate the mucosal and bone tissues, and an index of Kİ-67 was 80-90% compatible with high-grade B-cell lymphoma. In the patient's PET-CT, increased FDG uptake in the soft tissue mass covering the right orbita-maxillary sinus and destroying the bone structures, increased FDG uptake in a few right cervical lymph nodes, findings consistent with metabolic active disease were observed. No lymphoma involvement was detected in the bone marrow biopsy. Acellular cells were detected in the patient's cerebrospinal fluid sampling. The IPI score was evaluated as high-intermediate. Systemic treatment was planned primarily for the patient, considering the stage of the disease and the pathology result. The patient was started on the R-CHOEP (rituximab-cyclophosphamide-vincristine-etoposide-doxorubicin-prednisolon) chemotherapy protocol together with intrathecal prophylaxis.

Discussion: In conclusion, lymphoma should be considered in the differential diagnosis of orbital masses, although it is rare. Ocular adnexal diffuse large B-cell lymphoma predominantly affects the elderly, and most patients present with unilateral orbital involvement. Bone marrow involvement and high IPI score are independent poor prognostic factors. Therefore, in our patient with a high IPI score, we are planning upfront autologous bone marrow transplantation after systemic treatment.

8th National Blood and Bone Marrow Transplantation Congress
May 18-20, 2023, Atasehir, ISTANBUL / TURKIYE