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# 7th National Blood and Bone Marrow Transplantation Congress

## *Congress Abstracts*

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# Myeloid Clonal Disorders Following the Administration of the BNT62b6 Covid mRNA Vaccine

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**Introduction:** The BNT62b6 covid mRNA vaccine has played a very important role in reducing covid related deaths by creating a strong immune response with full-length spike protein synthesis. Acute myeloid leukemia (AML), the most common leukemia in the adult population and accounts for about 80% of all cases. We wanted to present cases that developed acute myeloid leukemia after administration of covid mRNA vaccines.

**The first case** is a 61-year-old man without any additional disease, applied with a cough complaint on the 30th day after the 3rd dose BNT62b6 covid mRNA vaccine. Covid 19 pcr was seen as positive. Pancytopenia was found in the examinations. Diffuse blasts were seen in the peripheral smear of the patient. The patient's bone marrow aspiration biopsy was evaluated as 80% blastic cell infiltration, diffuse positive mpo with tdt negative and he was diagnosed as AML. The npm1 mutation was positive. The patient was given a 3+7 protocol.

**The second case** is a 28-year-old female patient with no covid history and no additional disease. she applied with the complaints of weakness, bleeding in the mouth, petechiae in the extremities that started 30 days after receiving the 2nd dose of BNT62b6 Covid mRNA vaccine. Bone marrow aspiration biopsy was performed in the patient who had leukocytosis, thrombocytopenia and anemia. AML M5 was diagnosed in the patient with blastic infiltration and 3+7 protocol was given. Control bone marrow was in remission. Allogeneic stem cell transplantation was performed from his fully compatible sibling. Followed as in remission in the 3rd month control after transplantation.

**The third case** is a 72-year-old man with a history of diabetes, hypertension, and coronary artery disease, was evaluated with the complaint of melena that started on the 40th day after the 5th dose BNT62b6 covid mRNA vaccine. Pancytopenic was detected in the examinations. Bone marrow aspiration and biopsy of the patient were performed. It was seen as infiltrated with 70% blast.Venetoclax (100 mg 1 day 200 mg 2nd day 400 mg 3-28 days azacitidine 130 mg 7 days) was started.

**Discussion:** mRNA-based covid vaccines create an immune response by supporting viral spike protein synthesis. Spike protein has been shown to affect hematopoiesis and myeloid differentiation in vitro. It also disrupts DNA repair mechanisms. Suppression of type 1 interferon response may also lead to deterioration of innate immunity. This may potentially lead to an increased risk of neoplasia after vaccination.

***7th National Blood and Bone Marrow Transplantation Congress***
*May 19-21, 2022, Atakoy, ISTANBUL / TURKIYE*

ABSTRACT

# Rare Complication of Chronic Graft Versus Host Disease: Large Pericardial Effusion

**Batuhan ERDOGDU, Sercan UNAL, Olgu Erkin CINAR, Mine KARADENIZ, Umit Yavuz MALKAN, Hakan GOKER, Haluk DEMIROGLU, Ibrahim Celalettin HAZNEDAROULU**

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**Introduction:** Acute and chronic graft-versus-host disease (GVHD) is a major cause of morbidity and mortality in patients who undergo allogeneic haematopoietic cell transplantation (HCT) and affects approximately 30-40% of recipients. Graft versus host disease (GVHD) typically manifests as injury to the skin, gastrointestinal mucosa, and liver. Serositis is a recognized but rare manifestation of chronic GVHD (cGVHD). It is defined as inflammation of any of the serosal linings of the body, including the pleura, peritoneum and pericardium.

**Case Report:** A 39-year old male with T cell acute lymphoblastic leukemia (ALL) received BFM 95 regimen, intrathecal methotrexate protocol and cranial radiotherapy (10 days). In complete remission he underwent myeloablative allogenic stem cell transplantation from his HLA identical brother. A pretransplant echocardiogram revealed normal heart structure. GVHD prophylaxis consist of cyclosporin a 200 mg/day from day 1. Two months after transplant he had diarrhea and macular skin lesions as acute GVHD which was confirmed by biopsy. In the follow up, CMV colitis and pulmonary aspergilloma were detected. Patient was treated with ganciclovir and variconazole. Nine months later, patient reported erythematous and squamatous skin lesions on bilateral arms compatible with chronic GVHD. On the twentieth months of transplantation the patient presented with dyspnea and cough. Blood pressure, pulse respiratory rate, temperature and oxygen saturation was 145/65 mmHg, 112 /min, 40/min, 37.1$^0$C, %88. On physical examination pretibial edema was noted. Thorax CT revealed massive pericardial effusion. Up to 2000 cc serous liquid was drained by pericardiocentesis. According to pathology report the pericardial fluid had mesothelial cells, lymphocytes, macrophages, pericardial fluid and cell block. The fluid was sterile and contained no malignant cells. Colchine treatment started.

**Discussion:** Pericardial effusion end pericarditis are rare but life threatining complication in GVHD. Incidence and pathology are not defined. Serositis is a recognized but rare manifestation of chronic GVHD (cGVHD). In the literature, a few case has been reported and most largest data has 20 patients. This complication is mostly seen in male allogeneic HSCT and has been received TBI regimen. This presentation is usually seen concomidant with eyes, liver and skin lesions. Large pericardial effusion and cardiac tamponade are more rarely than pericarditis, an overall incidence of 0.998% and an incidence of 0.67% for the four late-onset cases. Similar to previous studies, our case presented with large pericardial effusion after underwent myeloablative allogenic stem cell transplantation.

# Succesfull Regresion of Granulocytic Sarcoma Associated with BNT162b2 mRNA COVID-19 Vaccine after Venetoclax / Azacitidine Treatment

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**Introduction:** Granulocytic sarcoma (GS) is a very rare condition characterized by the proliferation of immature myeloid cells in the extramedullary regions. Although it most commonly develops in patients with acute myeloid leukemia (AML), it can also be seen as an isolated mass. The treatment paradigm is generally the same as the standard treatment of AML. the combination of venetoclax and hypomethylating agents provide high response rates in elderly and unfit patients, as well as in relapsed/refractory (r/r) patients, although data on use in granulocytic sarcoma are scarce. We want to present a case of granulocytic sarcoma that emerged after mrna vaccine and with venetoclax azacitidine treatment.

**Case Report:** A 60-year-old male patient with no comorbidities applied to an external center months ago due to widespread swelling in the parietooccipital region, neck and groin that started after the 4th dose of the BNT162b2 mRNA Covid-19 vaccine. Fever, night sweats, and weight loss were absent. he was referred to us for typing after inguinal and cervical lap biopsy results showed non-hodgkin lymphoma. PET CT: Increased FDG uptake and diffuse lymph nodes were seen in the parietooccipital region, bilateral neck, mediastinum, and abdomen. Hemoglobin - 15.2 g/dl, leukocytes - 11.8 x $10^3/\mu$l, monocyte- 1.6 x $10^3/\mu$l, platelets - 362 x $10^3/\mu$l ldh (lactate dehydrogenase) - 386 $\mu$/l. biopsy was performed from the bone marrow and parieto occipital region. As a result of lap biopsy, it was evaluated as g.s cd43 and mpo and diffuse positive cd123 and focal positive cd56, tdt, cd34, cd3 and cd19 negative. 5% blastic cells were seen in the bone marrow. Blasts were seen in the peripheral smear of the patient who had leukocytosis on the third day after biopsy. Venetoclax (20 mg on day 1, 50 mg on day 2, 100 mg on day 3, 200 mg for 4-28 days) and azacitidine (130 mg day 7 days) chemotherapy was started. Complete regression was observed in peripheral laps at the end of the first cycle.

**Discussıon:** The effect of the covid mRNA vaccine on the bone marrow ras system and T and B cell response dysregulation may lead to neoplasms. In a study of 18 GS patients response rate was 45% with the treatment of venetoclax azacitidine, clinically good response was obtained with this treatment in our patient. Further studies are needed for the diagnosis and treatment approach in patients.

ABSTRACT

# Distinct Clinical Presentation of the BNT162b2 Covid Vaccine Induced Thrombotic Thrombocytopenia

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**Introduction:** An increasing number of vaccine induced thrombotic thrombocytopenia (VITT) has been noted after Covid-19 vaccination. Here, with this case series, we would like to report vaccine-induced thrombosis and thrombocytopenia due to administration of BNT162b2 mRNA Covid-19 vaccine with different clinical presentations.

**The first case** is 40 year old male patient applied for bleeding occurred in the gingiva and nose, petechial rashes on the legs which started 24-hours after the second dose of BNT162b2 vaccine. The thrombocyte count was 10.000/$mm^3$ with normal aPTT and INR. Considering ITP, 1 mg/kg methylprednisolone, and IVIG were started. No response was seen and bone marrow biopsy was performed. An increased number of dysplastic megakaryocytes was observed, myeloid and erythroid series were normal. Pulse steroid, eltrombopag, rituximab, and vincristine, splenectomy, and romiplostim were also ineffective. The daily plasma exchange (PEX) was performed with platelet count 3000/$mm^3$. After PEX, the platelet count increased to 150 x $10^3$/$mm^3$, but his platelet count decreased again. The patient doesn't have active bleeding and is followed-up with < 10.000 platelet count.

**The second case** is a 32 year old female patient who underwent splenectomy due to IVIG and steroid-resistant ITP 20 years ago. She was followed up without medication. She applied for diffuse petechiae in the lower extremities that started on the 7th day after the BNT162b2 Covid- 19 vaccine , The thrombocyte count was 8000/$mm^3$ with normal aPTT and INR . The treatment was started as IVIG and methylprednisolone 48 mg daily. In the follow-up of the patient, rituximab was given due to the continuation of thrombocytopenia and eltrombopag was added. The patient's last use of eltrombopag 75mg day was found to be platelet 60.000/$mm^3$.

The third case is a 51-year-old female patient with no history of disease. Left retinal venous obstruction was detected in her application with the complaint of blurred vision in the left eye that started at the 48th hour after the second dose of BNT162b2 mRNA Covid-19 vaccine. Blood parameters were normal. Medical treatment for thrombosis was started in the patient.

**The fourth case is**, a 51-year-old male was operated 3 times for congenital tricuspid atresia and great vessel malposition. The patient with a fontan shunt and followed under 100 mg of acetylsalicylic acid was evaluated because of thrombus in the control cardiac MRI on the tenth day after the Second dose of BNT162b2 mRNA Covid-19 vaccine, while there was no finding on the cardiac MRI before the vaccine.

**Discussion:** VITT was especially defined with viral vector vaccines and was seen as rare after mrna vaccines. Diagnosis criteria can be defined as thrombocytopenia starting 4-42 days after vaccination, venous or arterial thrombosis, elevation in d-dimer, and showing antibodies against pf4. IVIG, steroid, anticoagulants, platelet infusion, plasma exchange, aspirin and rituximab and other supportive treatments can be used in the treatment.

# A Neurolymphomatosis Case Diagnosed with Polyneuropathy and Relapsed with Facial Paralysis and Paraplegia

**Batuhan ERDOGDU[1], Alihan ALTUNAY[2], Sercan UNAL[1], Olgu Erkin CINAR[1], Mine KARADENIZ[1], Umit Yavuz MALKAN[1], Hakan GOKER[1], Haluk DEMIROGLU[1]**

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**Introduction:** Diffuse Large B-cell Lymphoma (DLBCL) constitutes 25% of all non-Hodgkin lymphomas. Extramedullary Involvement is found in 40% of the cases, extramedullary involvement occurs most frequently in the gastrointestinal system. It can also occur in the testis, skin, bone, liver, kidney, breast or nervous system. We wanted to present a DLBCL patient who was diagnosed while investigating his neurological symptoms and relapsed with involvement of the central nervous system after treatment.

**Case Report:** A 70-year-old male patient applied with the complaint of numbness and touch pain in the right upper and lower extremities for 20 days. There was no loss of motor strength. There were stories of recurrent swelling on one side of the face and accompanying double vision and headache in the 9 month period before admission. His complaints had regressed spontaneously. Pathological contrast in bilateral C7 C8 and right T1 posterior nerve roots and diffuse soft tissue thickenings were seen on magnetic resonance imaging. Excisional biopsy revealed as MYC positive DLBCL. The patient was evaluated as stage III DLBCL. He was seen as in remission after 6 cycles R-CHOP. Spinal MRI lymphoma involvement was observed in the patient who applied with right facial paralysis and weakness in the right lower extremity at the 3rd month after the treatment. The motor in the right lower extremity lost and progressed and it started on the left. Nearly complete regression was observed in the control imaging given 3 cures of R-MPV chemotherapy.

**Discussion:** Neurolymphomatosis expresses lymphomatous involvement of nerve roots. Symptoms are asymmetrical motor and sensory loss according to nerve roots. In the literature, patients presented with the most common painful peripheral neuropathy as in this case. In this case, the involvement of which disappeared in the radiological imaging observed after the 4th course of R-CHOP treatment. Relapse was observed with cranial and peripheral nerve involvements and additional medulla spinalis involvement after the treatment.

ABSTRACT

# Experience with Ruxolitinib for Central Nervous System Chronic Graft-Versus-Host Disease

**Beyza OLUK[1], Tarik Onur TIRYAKI[1], Dilek Ozden OZLUK[1], Farah Jamal TAHA[2], Meliha NALCACI[1], Ipek Yonal HINDILERDEN[1]**

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**Introduction:** Central nervous system graft-versus-host disease (CNS-GVHD) is a rare neurological complication after allogeneic haematopoietic stem cell transplantation (allo-HSCT), whose clinical presentation is pleomorphic and whose diagnosis remains challenging.

**Case Report:** A 54-year-old male diagnosed with IgA kappa myeloma with agressive relapse including CNS involvement after autologous HSCT underwent myeloablative peripheral allo-HSCT from his HLA-matched male sibling donor. Cyclosporine and post-transplant cyclophosphamide were administered for GVHD prophylaxis. In the early post-transplant period, he developed stage IV acute gastrointestinal system GVHD and stage 2 acute liver GVHD. At follow up, severe chronic GVHD involving skin, gastrointestinal system and liver developed which responded to cyclosporine and corticosteroids. At 9th month of allogeneic HSCT under cyclosporine, he presented with weakness, pain and maculopapular rash over the trunk and bilateral upper and lower extremities. Methylprednisolone 1 mg/kg/day was initiated to treat flare of chronic skin GVHD. On physical examination, weakness in dorsiflexion of the right foot was noted. IV contrast enhanced MRI showed no abnormality. Electromyography demonstrated severe sensorimotor neuropathy. Cytopathological examination and oligoclonal band analysis of the cerebrospinal fluid (CSF) were negative. CSF biochemistry was normal except for elevated CSF protein level (108 mg/dl). Serologic tests for CSF HSV, EBV and CMV were negative and no micoorganism was isolated on CSF culture. Muscle nerve biopsy could not be performed due to technical difficulties. During his folllow up, he developed moderate Broca's aphasia. Considering the history of chronic GVHD and the increase in elevated CSF protein, the neurological findings were attributed to CNS-GVHD. Taking into consideration the progressive symptoms under methylprednisolone, ruxolitinib 10 mg bid was added. On the 3rd day of concomitant steroid and ruxolitinib treatment, skin lesions completely regressed. On the 10th day, symptoms of Broca's aphasia disappeared. Ruxolitinib was planned to be administerd as single agent after gradual taper of methylprednisolone.

**Discussion:** CNS GVHD is a rare and severe complication after allo-HSCT that can be difficult to diagnose. In 2010, neurological manifestations of chronic GVHD were described as a distinct entity in the Consensus Conference on Clinical Practice in chronic GVHD. MRI and CSF analysis are vital to rule out other CNS disorders including infections, drug toxicity, or relapses of underlying malignancies. No established treatment protocole for CNS GVHD is present and the treatment is mainly based on immunosuppressive drugs, especially high-dose corticosteroids. The dramatic response in our patient to ruxolitinib needs to be confirmed by furher observations.

# Neurological Symptoms and GVHD after Allogenic Stem Cell Transplant

**Beyza OLUK[1], Tarik Onur TIRYAKI[1], Dilek Ozden OZLUK[1], Farah Jamal TAHA[2], Ipek Yonal HINDILERDEN[1]**

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**Introduction:** Allogeneic hematopoietic stem cell transplantation is the only curative treatment for many malignancies. However, serious treatment-related complications such as GVHD and infections can occur. Although the skin, gastrointestinal tract and liver are the most frequently affected organs. It can be seen in all tissues and clinical findings are therefore very diverse. Central nervous system GVHD (CNS-GVHD) is a serious complication that adversely affects the prognosis of which the diagnostic criteria and treatment cannot be determined with accurate criteria.

**Case Report:** A 54-year-old male patient was diagnosed with IgA kappa myeloma as a result of examinations for lower back pain. The patient, who was evaluated as stage ISS 2, was applied autologous stem cell transplantation with partial response after first line treatment. In the second year after transplantation he was admitted with fever and headache, no pathology was detected in MRI scans. In the CSF sample, plasmacytic and plasmoblastic cells were observed. IgA kappa in the CSF immunfixation test was also observed. The patient was evaluated as a central nervous system recurrence, and intrathecal and systemic chemotherapy were started. His neurological complaints did not recur. Allogeneic stem cell transplantation was performed from his HLA-matched male donor to the patient who needed treatment due to resistant disease and frequent recurrences. Cyclosporine and post-transplant cyclophosphamide were administered for GVHD prophylaxis. In the post-transplant period, he developed stage 4 hyperacute hemorrhagic gastrointestinal system GVHD and stage 2 acute liver GVHD. It was controlled with methylprednisolone and cyclosporine treatments. At the 9th month of transplantation, he presented with weakness, pain, redness in the right leg. Physical examination revealed cellulitis on the right tibia and weakness in flexion of the right foot. There was no finding to explain drop foot in MRI. No cells were detected in CSF examination, and no monoclonal band was observed in immunofixation electrophoresis. On CSF biochemistry test glucose 104 mg/dl, protein 108 mg/dl, albumin 61 mg/dl, LDH 75 U/l were detected . No malignancy was detected in the cytological examination. EMG examination revealed a polyneuropathy in which sensory and motor fibers were affected and signs of diffuse neurogenic involvement. Considering the likely diagnosis of chronic inflammatory demyelinating polyneuropathy, IVIG was administered at a dose of 0.4 g/kg for 5 days. GVHD was considered in the differential diagnosis but muscle nerve biopsy could not be performed due to technical difficulties. During this period the liver and skin GVHD findings of the patient regressed and steroid therapy was tapered and discontinued. The patient presented with abscess in the same region 2 months later. In his neurological examination, weakness in flexion continued. Additionally, he complained of stuttering while speaking. The abscess was drained and meropenem was started. His skin GVHD flared up in the first week of antibiotic therapy. Methylprednisolone was started at a dose of 1mg/kg/day. CSF examination did not reveal any finding in favor of myeloma recurrence, but CSF protein was found to be high. Neurological complaints and skin lesions regressed after steroid initiation. No pathological feature was detected in cranial MRI. The patient is being followed up with steroid and ruxolitinib treatment.

**Discussion:** The diagnosis of CNS-GVHD in a transplant patient can be made by excluding other possible causes such as recurrence of the primary disease, autoimmune diseases, vascular diseases, by careful examination and investigations. A number of criteria were determined by Openshaw in 2009; occurence concomitant with chronic GVHD affecting other organs, neurological signs of CNS involvement without other explanation, consistent brain MR abnormalities, abnormal CSF studies (pleocytosis, elevated protein or IgG oligoclonal bands), pathological brain biopsy and response to immunosuppressive therapy.

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ABSTRACT

# A Case of CML Entering Blastic Phase under Imatinib Treatment (CML-BP) with Multiple Tyrosine Kinase Inhibitory Resistance

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**Introduction**: Chronic Myeloid Leukemia (CML) is a stem cell disease characterized by abnormal clonal proliferation of myeloid precursor cells and accounts for 15-20% of adult leukemias. In the pathogenesis of CML, the BCR-ABL1 fusion gene is formed. That causes abnormal proliferation of myeloid cells with uncontrolled tyrosine kinase stimulation. The discovery of imatinib, a tyrosine kinase inhibitor, significantly contributed to the prognosis of CML. However, resistance to tyrosine kinase inhibitors that occurred in recent years urged us to make changes in the treatment of the disease. Point mutations observed in BCR-ABL1 are crucial due to the effect of tyrosine kinase inhibitors. G250E, M244V, E255K/V, F359V, Y253F/H, M351T and T315I account for 85% of these mutations.

**Case Report:** A 30-year-old male patient was admitted to our hematology outpatient clinic due to complaints of fatigue and early satiety. Based on the examinations, the patient with elevated white blood cell count was diagnosed with chronic myeloid leukemia (Sokal Score: 0.82 intermediate risk group). Imatinib treatment was started. During the routine outpatient follow-ups of the patient entered blastic phase CML. Induction treatment was started and imatinib gene resistance was sent to the patient diagnosed with CML-BP. Based on the imatinib gene resistance, G250E and M244V mutations were detected. As a result of these mutations, due to strong resistance to imatinib and moderate resistance to bosutinib, imatinib treatment was discontinued and the patient was started with dasatinib treatment. The patient underwent allogeneic stem cell transplantation.

**Discussion:** Point mutations observed in BCR-ABL1 gene are highly risky in terms of imatinib, dasatinib, bosutinib and nilotinib resistance, reduced efficacy, poor prognosis, and progression of the disease. Therefore, mutation analysis is the most important point to keep in mind before changing tyrosine kinase inhibitors.

# Ocular Extranodal Marginal Zone Lymphoma Presenting with Visual Impairment: A Rare Case

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**Introduction**: Non-Hodgkin lymphomas constitute 90% of all lymphomas. Orbital lymphomas are a rare subgroup of non-Hodgkin lymphomas and constitute approximately 1% of them. However, orbital lymphomas form approximately 55% of primary orbital cancers in adults. Orbital lymphomas are ocular-orbital adnexal masses and they can be anatomically located in the conjunctiva, lacrimal gland and eyelid. While a painless, red, salmon- colored lesion is observed in ocular extranodal marginal zone lymphomas with conjunctival involvement, visual impairment and ptosis may be observed in those with orbital involvement. It can sometimes be diagnosed during imaging methods performed for other reasons.

**Case Report**: A 66-year-old female patient with the diagnosis of diabetes mellitus, hypertension and hyperlipidemia applied to the ophthalmology outpatient clinic with complaints of decreased visual acuity, blurred vision, and fatigue lasting for about one month. A nodular lesion adhered to the orbital floor was detected in the physical examination of the patient, and a mass was found adjacent to the orbit in the orbital MRI performed. The pathology result was reported as extra nodal marginal zone lymphoma staining diffusely with CD20, positive IgM and negative cyclin D1 and SOX11. The patient was referred to the hematology department since having complaint of fatigue. R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine, methylprednisolone) protocol was started for the patient whose PET-CT result was evaluated as stage IV-E. The patient's symptoms decreased after two cycles of chemotherapy.

**Discussion**: In the literature, although rare, orbital adnexal extranodal lymphoma cases have been reported in middle-aged patients with visual impairment complaints who were diagnosed with anemia. Although it is a disease with a slow course and a good prognosis in the long term. It should be kept in mind since it is a rarely encountered entity.

ABSTRACT

# An Unexpected Coincidence: Small Lymphocytic Lymphoma and Bcr-Abl Positive Acute Myeloid Leukemia

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**Introduction:** In this study, we present a case with BCR-ABL (+) acute myeloid leukemia (AML) and small lymphocytic lymphoma (SLL), which was treated by a joint protocol. This is the first case with BCR-ABL positive AML and SLL in the literature.

**Case Report:** A 69-year-old male patient was consulted for lymphocytic infiltration in the prostate biopsy in 2012, and SLL diagnosis was made. The Ann-Arbor stage was IV-E with bone marrow involvement and no lymphocytosis. He has remained in complete remission for four years after "R-CVP" chemoimmunotherapy. In 2017, he had night sweats, thrombocytopenia, and diffuse conglomerate in abdomen. After relapse was proven, the CR2 was achieved with 6 cycles of 'FCR' chemoimmunotherapy. In 2021, therapy-related MDS has emerged. He was admitted to the ICU due to gastrointestinal bleeding. In the bone marrow biopsy, blastic infiltration was seen, and AML diagnosis was made. After etoposide-cytarabine non-intensive induction, t(9;22) p210 RT-PCR resulted positive, and imatinib has started. In the control biopsy, leukemia-free status and residual SLL involvement were seen. Then, MRI showed CNS relapse after vision loss. CSF cytology was positive for myeloblasts. His symptoms improved after methotrexate, cytarabine and dasatinib treatment. For co-effectivity for SLL and AML, the systemic therapy changed to venetoclax-dasatinib.

**Discussion:** When BCR-ABL is detected in AML, it is important to distinguish whether there is a CML blastic crisis or not. The basophilia, organomegaly, non- blastic myeloid findings are important. A basophil ratio above 2% is in favor of CML. In our case, basophils were 0.12% without organomegaly which was considered against CML. The BCR-ABL protein other than p210 may favor de novo AML. Additional cytogenetic anomalies are more frequent in CML. The coexistence of CML and CLL/SLL is very rare, and only seven cases have been reported in the literature. As far as we know, our case is the first case in which SLL was seen together with BCR-ABL+ AML. It is unknown what the ideal treatment is in such coexistence. Venetoclax is increasingly used in CLL/SLL, also gives promising results in patient with AML who can't tolerate intensive treatment.

# Blasturia, an Atypical Presentation of Acute Myeloid Leukemia

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**Introduction:** Extramedullary (EM) involvement of acute myeloid leukemia (AML) is a rare condition. In this report, we offer the details of a patient with AML who relapsed after hematopoietic stem-cell transplantation with infiltration of cerebrospinal fluid (CSF) and showed progression with infiltration of the urine.

**Case Report:** The patient was a 48-year-old man who had FLT3-ITD positive AML. The patient was treated with a 7+3 induction regimen and consolidated with two cycles of high-dose cytarabine (HDC). Then, a myeloablative allo-HCT performed from a full-match sibling donor. In the third month after HCT, the patient was admitted with severe back pain and meningeal irritation findings. Flow cytometric analysis (FCA) of the CSF revealed a blast population. Simultaneous blast rate in the bone marrow was about 10%. His relapse initially was treated with HDC, etoposide and intrathecal chemotherapy. During the next follow-up, no blasts in the CSF were observed but the neurologic findings appeared to be worsening. In the following days, the patient complained of abdominal discomfort. Abdominal examination revealed distension of the abdomen, with pain and tenderness in the right lower and upper quadrants radiating to the left flank. Urinalysis showed a high number of WBCs. The urine and blood cultures were sterile. Computed tomography imaging revealed cortically located patchy hypodense lesions in both renal parenchyma, suggesting possible AML involvement or renal infarction. FMA was conducted using the sample of the urine and revealed the infiltration of myeloblasts. Due to the poor performance status of the patient, azacitidine was initiated and sorafenib was added. After two cycles of chemotherapy, the patient died because of sepsis.

**Discussion**: EM disease in patients with AML is a rare manifestation. However, central nervous system involvement is more common in patients with AML including a monocytic component, hyperleukocytosis, elevated lactate dehydrogenase level, expression of CD56, and some molecular/cytogenetic findings. In our case, the WBC count at diagnosis was quite high, paired with a monocytic component and an FLT3 ITD mutation. The infiltration of blasts into the urine is quite rare. Even if the patient is diagnosed with leukemia and shows pyuria in the urine, blasturia is an unexpected finding and can easily be overlooked if careful attention is not paid. Although pyuria is frequently encountered due to the increased tendency of leukemia patients to develop infections, it should be kept in mind that blasts in the urine can also be a cause of pyuria.

ABSTRACT

# Correlation Between Baseline PET/CT Findings and Clinical Parameters in Multiple Myeloma Patients

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**Introduction**: FDG PET/CT is considered a valuable tool to demonstrate disease activity and predict prognosis in multipl myeloma (MM) patients. The aim is to compare the initial clinical characteristics of MM patients with baseline PET/CT parameters.

**Method**: 105 newly diagnosed MM patients were enrolled in this study, who were diagnosed between February 2015 and May 2020. Patients' clinical parameters at diagnosis (albumin, β2-microglobulin, creatinine, calcium, lactate dehydrogenase (LDH), hemoglobin, International Staging System (ISS), immunohistochemical markers, Ig subtypes and age) and baseline PET parameters (presence of positive PET findings, number of focal hypermetabolic bone lesions (FLs), SUVmax of the lesion showing highest FDG uptake, presence of extramedullary disease (EMD) and/or plasmacytoma) were retrospectively analyzed.

**Results**: 105 patients consisted of 38 women and 67 men patients with a median age of 64 (42-84) years were reviewed. At diagnosis, the distribution of the ISS was I (n= 20, 19.4%); II (n= 37, 35.9%); III (n= 46, 44.7%), respectively. Based on PET/CT findings at diagnosis; 43 (41%) patients had no FLs. There were 15(14.3%) patients with ≤ 3 FLs, 19(18.1%) patients with 4-9 FLs and 28 (26.7%) patients with ≥ 10 FLs. The mean SUVmax value of the lesion that had the highest FDG uptake was 9.56 ± 7.64 (2.9-47). Plasmacytomas were detected in 25 patients and 7 patients had EMD which including soft tissue, lymph nodes, muscles, lung, pleural tissue and pancreas. SUVmax values had no significant difference between these groups (Mann-Whitney U, p> 0.05). When comparing clinical characteristics based on the number of FLs, Ig subtypes revealed significant differences (Pearson's chi-squared, p= 0.002). The patients that has more than 10 focal lesions, 46.2% of them has IgA subtype, besides 26.9% of them has IgG subtype. Comparison of the clinical characteristics based on the number of FLs also revealed significant difference between the patients according to β2-microglobulin (Pearson's chi-squared, p= 0.009). In the patients with ≥ 10 FLs, patients with high β2-microglobulin levels were significantly more than those with normal β2-microglobulin levels. When comparing clinical characteristics based on the the plasmacytoma; anemia, azotemia and CD19 immunohistochemical marker groups showed significant differences (Pearson's chi-squared, p= 0.019; 0,012; 0.004, respectively). In the patients without plasmacytoma; anemia, azotemia and CD19 absence percentages were significantly higher than the group with plasmacytoma.

**Conclusion**: Regarding PET parameters, FLs are more likely to be related to the prognostic clinical parameters compared to the SUVmax values. The different Ig subtypes can predict prognostic significance and these subtypes were associated with the number of FLs. Besides, the results revealed that CD19 could be related to the plasmacytoma presence.

# A Rare Transplantation Complication: Passenger Lymphocyte Syndrome

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**Introduction**: Passenger lymphocyte syndrome (PLS) refers to immune hemolytic anemia (IHA) after a hematopoietic stem cell or solid organ transplantation. PLS is caused by the donor's B lymphocytes transmitted to the recipient. We report a patient with type B, Rh-positive blood developed IHA following orthotopic liver transplantation (OLT) from a donor with type O, Rh-positive blood.

**Case Report:** The patient was a 57-year-old male with cryptogenic, decompensated liver cirrhosis (DLC), no comorbid diseases, type B, Rh-positive blood and he underwent OLT from a live donor. There were no complications during the operation. Tacrolimus was used as an immunosuppressive agent.

The patient's complete blood count test (CBCT) showed that hemoglobin (Hb), leukocyte, and platelet count were 6 g/dl, $0.9 \times 10^9$/L, and $18 \times 10^9$/L, respectively on the post-op second day. After two bags of type B, Rh-positive packed red blood cells (PRBC) transfusion, the Hb level increased to 7.7 g/dl. Severe anemia (HGB 3.4 g/dl) developed on the 8th-day post-operation; bleeding was excluded as a cause. In the peripheral smear, clustered hemoglobin, erythroid precursors, and polychromasia were evident, but fragmented erythrocytes were not seen.

Crossmatch (CM) between the patient's blood and a type B, Rh-positive blood sample identified a "+3" reaction with anti-human globulin. The patient then received two units of PRBC replacement of type B, Rh-positive group administered with 500 mg methylprednisolone; subsequent hemoglobin value was 4.9 g/dl. However, a CM between the patient's blood and the donor's type O, Rh-positive blood showed that they were compatible, while the patient's anti-A titers were 1/16 (+3), 1/32 (+1), and 1/64 (negative), and his anti B titers were 1/8 (+3), 1/16 (+1), and 1/32 (negative). After three additional PRBC transfusions of type O, Rh-positive blood, the hemoglobin increased to 7.8 g/dl. Now the patient has been followed up at the end of the six months with normal hemoglobin values.

**Discussion:** PLS is an important entity for post-transplant anemia. PLS is more commonly seen in ABO minor blood group incompatibility, Tacrolimus associated IHA and thrombotic microangiopathies (TMA) may develop after transplantation. In this case, findings were not consistent with TMA's. Among 333 pediatric OLT patients, PLS was diagnosed at a median of 10 days after transplantation. Hemolysis is typically self-limiting within weeks, given the lifespan of existing lymphocytes; however, one 6-month-long case has been previously reported. In our case hemolysis appeared on the 8th day and was limited within days.

ABSTRACT

# A Case of Allogeneic Hematopoietic Stem Cell Transplant Patient with Mild COVID-19

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**Introduction:** Precursor B-cell acute lymphoblastic leukemia (B-ALL) is the most common immunological subtype of ALL with an incidence of 1-2/100,000. The main compused of treatment in B-ALL is induction chemotherapy, followed by consolidation chemotherapy. Allogeneic hematopoietic stem cell transplantation (AHSCT) is recommended after consolidation in selected high risk groups. Emergence of the current COVID-19 pandemic has created a great hassle for the medical community. Initial reports from China, patients with cancer higher than non-cancer patients (39% vs. 8%) demonstrated a risk of serious events (need for intensive care, death). We wanted to present our patient who was diagnosed with COVID-19 pneumonia under AHSCT preparation regimen.

**Case Report:** A 31-year-old male patient without chronic disease, diagnosed with philedelphia chromosome positive B-ALL as a result of his bone marrow aspiration biopsy performed in July 2021, after cytopenia was observed in his examinations with complaints of weakness and widespread pain in his body. Cyclophos phamide,doxorubicin,vincristine, asparaginase, prednisone induction chemotherapy and dasatinib treatment were given according to the CALBG protocol.He was given consolidation treatment in December 2021 and maintenance therapy in January 2022. AHSCT was planned from a donor (sister) of the patient. The Covid PCR tests taken and, the patient was admitted to our transplant service. For the patient whose transplantation preparations were completed; busulfan and cyclophosphamide was started. Covid PCR test taken on March 21 was positive. It was decided to administer molnupiravir, whose side effects on bone marrow suppression are unknown, not to be applied 24 hours before the transplant day, but to be started again 24 hours after the transplant. After completing molnupiravir treatment, Covid PCR tests taken on two different days were negative. The patient was accepted for engraftment on April 8th, 2022.

**Conclusion:** COVID-19 has a wide spectrum of clinical presentation and severity. The inflammatory state with cytokine storm and hypercoagulation, there is increasing evidence that it contributes the pathophysiology of a systemic disease other than lung infection alone. It has been reported in some studies that the later the patient becomes infected with the COVID virus after AHSCT, the lower the mortality. We think that AHSCT under COVID pneumonia will take its place as a very rare condition in the literature.

# Successful Treatment of Relaps IgD Kappa Multiple Myeloma with Daratumumab Based Therapy

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**Introduction:** IgD Multiple Myeloma (MM) accounts for < 2% of all MMs, while IgD- Kappa-MM accounts for 3-4% of IgD-MMs. It's more aggressive, associated with less treatment response and poor prognosis, with a median survival of 13-21 months. We present; an IgD-Kappa-MM patient, who had a response to autologous stem cell transplantation (auto-SCT) following VCD and had a good response after 2 courses of daratumumab treatment because of relapse presenting autoimmune hemolytic anemia (AIHA) and thrombocytopenia.

**Case Report:** 54 years old male patient presented with lumbar pain in 2017 Lab findings were; Hgb: 11.2 g/dl, ESR: 32 mm/h, beta2 microglobuline: 2640 mg/L, P.IgA: 66.6mg/dl, P.IgG: 1570 mg/dl, P.IgM: 7.7 mg/dl, plasma free lambda light chain (PFLLC): 4.82 mg/L, plasma free kappa light chain (PFKLC): 591 mg/L, kappa/lambda: 122.61. Plasma protein electrophoresis (PPE) showed a peak on gamma, plasma immunofixation electrophoresis (PIFE) monoclonal IgD kappa. There was no monoclonal band on Urine IFE. Lytic bone lesions were found on the cranium, left iliac wing, bilateral trochanter majus, bilateral humerus. Bone marrow had diffuse atypical plasma cell infiltration, diffuse stain with CD138, positive with kappa and cyclin D1.

The patient had auto-SCT after 5 courses of VCD and 2 courses of VD treatments. On the second month's follow-up bone marrow, he had rare cell positive with CD138, kappa, and lambda. 1,5 years follow-up bone marrow control had 70-80% atypical plasma cell, positive stain with CD138. VRD treatment was started. He had DVT under lenalidomid. AIHA occurred under warfarin treatment with anemia (Hgb; 5 g/dl) and thrombocytopenia (plt: 19000/mm$^3$). There was no response to steroid treatment, while had PFKLC: 282.35 mg/L, PFLLC: 6 mg/L, kappa/lambda: 47.06, PIFE; monoclonal IgD-kappa, bone marrow had atypical plasma cell infiltration, diffuse CD138 positive stain.

Admitted as relapse, and Daratumumab-VD-PACE treatment was started. Thrombocytopenia and AIHA were regressed on follow-up. After the second course of treatment, rare atypical plasma cells, 30-40% CD138 and kappa monotypic stain, PPE minimal peak on Gamma, PIFE monoclonal IgD-kappa were shown PFKLC decreased to 11.58 mg/L. The current treatment plan is a second auto-SCT after the third course.

**Discussion:** Monoclonal antiCD138 antibody Daratumumab can be used alone or combined with other anti-MM agents. We chose Daratumumab- VD-PACE combination due to relapse IgD- Kappa-MM. After second course, there was a regression in AIHA, PFKLC, and bone marrow plasma cells. IgD-MM had a median survival of 13-21 months before specific drugs and auto-SCT. Although the survival is longer with auto-SCT after treatments. It's still shorter than other myeloma types. This shows the importance of innovative treatments for IgD-MM.

ABSTRACT

# Nodal EBV+ Cytotoxic T-Cell Lymphoma Presented with Hemophagocytic Syndrome: A Rare Case

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**Introduction:** Peripheral T-cell lymphomas (PTCL) are covered under 2016 Classification of Mature T-cell and NK-cell neoplasms of the World Health Organization. Peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS) sub-group; is the most common subtype. Cytotoxic molecule (CM) - PTCL, NOS [also known as Cytotoxic T-cell lymphoma (CTL)] are classified as a distinct variant of PTCL, NOS. Lymphadenopathy (LAP), at least one T-cell antigen (CD3, CD 4, CD5, CD8), CM or related antigens (Granzyme B, granzyme M, perforin, TIA-1) must be present for the diagnosis of nodal EBV+ CTL. Nodal EBV+ CTL can presented in a wide spectrum, from an indolent course to an aggressive course. Here, we will present a Nodal EBV+ CTL case presented with hemophagocytic syndrome, which is rarely found in the literature.

**Case Report:** A 31-year-old male patient with no history of chronic disease admitted to our clinic with the complaints of fever, fatigue and jaundice which had been present for 3-4 weeks. Pancytopenia, hyperbilirubinemia, hyperferritinemia and hypofibrinogenemia were present ın addition to LAP and hepatosplenomegaly. Submandibular LAP and bone marrow biopsy were performed on the patient. Ferritin: 99499 $\mu$g/L, fibrinogen: 0.62 g/L, and histiocyte increase consistent with hemophagocytosis were observed in the preliminary pathological assessment. Hemophagocytic syndrome diagnosis was made according to HLH diagnosis criteria, and the treatment protocol for HLH 2004 (Etoposide, dexamethasone, cyclosporine, I.V. immunoglobin) was initiated. Partial improvement was achieved in the ferritin (9383), fibrinogen (1.84) values and the clinic manifestation. It was reported as EBV associated T-cell lymphoma with EBV VCA Ig G positive, pathology positive for cytotoxic molecules, and clonal peak identified at TCR β and TCR γ. CHOEP (cyclophosphamide, mesna, vincristine, adriamycin, prednisolone, etoposide) protocol was initiated on the patient. The patient, whose overall condition continued to worsen in the follow-ups was exitus on the 8th day of CHOEP chemotherapy.

**Discussion:** Many factors that would cause an aggressive course such as EBV positivity, presence of cytotoxicity, detection of distinct clonal peaks in both TCR β and TCR γ in TCR gene rearrangement, detection of clonality especially in the rare TCR γ, presentation with HLH were present in the current case. In such cases which have a clinically aggressive course, the disease gives a partial response to chemotherapy despite the rapid onset of treatment. There is a need for novelty treatments that will contribute to the diagnosis and treatment phase of Peripheral T-cell lymphomas, particularly in nodal EBV+ CTL.

# Recurrent Renal Cell Carsinom Diagnosed by Parotis Biopsy in a Patient with Chronic Lymphocytic Leukemia

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**Introduction:** Renal cell carcinoma (RCC) is the most common subtype accounting for approximately 90% of kidney tumors. The incidence of RCC is 100.000/12.5 in the general population while 100.000/31.8 in the population with hematological malignancies. In light of this data, the risk of RCC occurring in hematological malignancies is high compared to normal population. However, the co-occurrence of RCC and hematological malignancies in the same case is typically rare. We present here a case with the co-occurrence of RCC+ Chronic lymphocytic leukemia (CLL).

**Case Report:** Three years ago elevated white blood cells were detected during the pre-operative evaluation of a 70-year-old female patient who was diagnosed with renal cell carcinoma and planned for left nephrectomy.The patient was diagnosed with Chronic Lymphocyte Leukemia (CLL) as a result of advanced tests for the etiology of elevated white blood cells. The patient who has been followed untreated for 3 years post-nephrectomy had a submandibular swelling. In the superficial ultrasonography of the patient, who had no 17p deletion detected but whose heavy chain mutation was positive, a 62 x 53 mm, central necrotic hyperdense mass with irregular margin was detected at right parotid gland. A tru-cut biopsy of the mass was performed with the preliminary diagnosis of CLL, Richter's transformation and another malignancy. The pathology result of the patient was reported as RCC metastasis. The patient who had no treatment indicated for CLL was referred to the medical oncology department for the planning of RCC treatment.

**Discussion:** The occurrence of malignancies secondary to various diseases and treatments has been known for a long time. In the case series reporting the co-occurrence of RCC and lymphoma, the number of cases with co-occurrence of RCC and CLL was 2 out of 8 patients in one study and 1 out of 9 patients in the other study. Co-occurrence of RCC and hematological malignancies in the same case is very rare. In the light of these data, there may be an underlying genetic etiology or dysregulation of the immune system in the co-occurrence of RCC and lymphoma.

ABSTRACT

# PDGFR-Negative Hypereosinophilic Syndrome Responsive to Imatinib Treatment: A Rare Case Report

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**Introduction:** Hypereosinophilic syndrome (HES), which is a rare entity is diagnosed by an eosinophil count of > 1500/$\mu$L in the peripheral blood for more than 1 month along with an organ dysfunction attributed to eosinophilia. HES is classified into 3 subgroups as primary (clonal), secondary (reactive) and idiopathic (cause unknown). The idiopathic subgroup is defined by exclusion of primary and secondary causes. We hereby report a case of hypereosinophilic syndrome with gastrointestinal symptoms.

**Case Report:** A 25-year-old female patient who has no known chronic disease, has admitted to an external center with nausea, vomiting, abdominal pain, diarrhea, weakness and pain in lower extremity that started about 10 days ago. Test results have indicated eosinophilia and the patient was referred to our clinic. The patient's laboratory values were WBC: 32.8 x $10^3/\mu$L, eosinophils: 15.9 x $10^3/\mu$L, Hgb: 15.1 g/dL, platelet: 464 $10^3/\mu$L. Stool testing, echocardiography, c omputed tomography of the neck-thorax and abdomen, bone marrow biopsy, Ig E level, endoscopy and colonoscopy were performed for etiology. The patient had a diffuse edematous intestinal wall. Prednisolone treatment at a dose of 1 gr/kg was started in the patient with no additional pathology detected. Follow-up tests showed negative mutations of BCR-ABL, JAK-2 V617F, PDGRF-A, PDGFR-B, JAK-2 exon 12, FLT-3 ITD, FLT-3 D835. Eosinophil values were normal following treatment with prednol however the patient was re-admitted to our clinic about a month later with nausea, vomiting, abdominal pain, diarrhea and muscle weakness. Tests showed an eosinophil count of 34.8 x $10^3/\mu$L with no additional pathology detected in the repeated etiological investigation. The patient was started on pegylated-interferon at 135 $\mu$cg/week, but due to the lack of response to this treatment, the patient was started on imatinib at 100 mg/day as off-label approval. The patient is 5 months into imatinib treatment and is followed by normal eosinophilic values.

**Discussion:** The most common presentation of HES with systemic involvement is dermatological (69%), pulmonary (44%), gastrointestinal (38%). As with current case, the most common gastrointestinal symptoms are abdominal pain, nausea, vomiting and diarrhea. Gastrointestinal involvement may be diffuse or patchy, as with current case. The main treatment for HES is Prednol. Interferon, cyclosporine, cladribine, mepolizumab, alemtuzumab and imatinib treatment options are available in refractory or relapsed cases. Imatinib at 100 mg/day is the effective and first preferred drug in positive PDGFR mutation. As in current case, imatinib is an effective treatment option that should be kept in mind for disease control and maintenance in patients with negative PDGFR mutations.

# A Case of Prolonged QTC with Midostaurin Therapy in a FLT3 Positive Acute Myeloid Leukemia Patient, New Agents, Attention to Side Effects

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**Introduction:** Acute myeloid leukemia (AML) treatments recently have been focusing on important cytogenetic and molecular genetic alterations. Presence of Fms related receptor tyrosine kinase 3 (FLT3) mutation affects recurrence and long-term survival. Midostaurin is a multikinase inhibitor that targets FLT3. Side effects of new targeted agents are reported in case reports or case series. We presented a patient that QT prolongation was observed during midostaurin therapy.

**Case Presentation:** 40 year-old female patient was referred to our clinic for leukocytosis. Leucocyte number was 98.5 x $10^9$/L, platelet was 65 x $10^9$/L, hemoglobin level was 7.5 g/dl. Bone marrow aspiration/biopsy was compatible with AML. Genetic tests showed that she had FLT3 ITD mutation positivity. 7+3 remission induction chemotherapy was started. On the 14th day, 50% blast was detected in the control bone marrow aspiration, and the patient was given 7+3 reinduction chemotherapy. Bone marrow aspirasyon showed complete remission with a 1.72/10 000 minimal reziduel disease according to flow cytometry on day 28. First consolidation intermediate dosage cytarabin treatment was given to the patient with midostaurin treatment was added on the 8th day. Daily electrolyte monitoring was performed, and replacement treatments were made so that potassium and magnessium levels could be in the normal range. The patients electrocardiogram (ECG) was totally normal before midostaurin therapy. On the 6th day of the midostaurin treatment bradycardia with prolonged QT interval in ECG. All the drugs the patient using was evaulated. She wasn't receiving a QT prolonging drug except midostaurin. Midostaurin was stopped on the 7th day of midostaurin treatment. After stopping midostaurin, ECG was totally normal.

**Discussion:** Cardiovascular side effects of midostaurin include edema, prolonged QT interval on ECG, acute myocardial infarction, heart failure, hypotension, ischemia, pericardial effusion. The absolute and comparative risk of many drugs associated with QT prolongation is difficult to determine because most of the available data are from case reports or small case series. In our patient, the corrected QT length after the drug exposure was > 500 msn. After the drug cessation QT interval had come to normal. The frequency of QT prolongation was determined as 11% for midostaurin. We recommend to perform ECG before midostaurin treatment and regularly follow-ups during treatment.

ABSTRACT

# Treatment Responses in Advanced Age Refractory/Relapsed Diffuse Large B-Cell Lymphoma Patients

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**Introduction:** The optimal treatment regimen has not been determined in diffuse large B-cell lymphoma (DLBCL) patients who are 70 years of age and older and who are not candidates for transplant. This study performed second-line treatment responses and survival analyses in refractory/relapsed DLBCL patients aged 70 years and older.

**Methods:** The study included 14 refractory/relapsed patients aged 70 years and older who were treated in the hematology clinic of Ondokuz Mayıs University between January 2010 and April 2022. The mean age was 75 (70-83) and 10 (71.4) of the patients were male. The subtype of DLBCL was a germinal center in 57% of patients. Distribution of the disease according to the stage; 5 (35.7%) patients were stage 2, 5 (35.7%) patients were stage 3 and 4 (28.6%) patients were stage 4. In terms of the initial treatment, regimens patients received; 9 (64.3%) of the patients were R-CHOP (Rituximab-cyclophosphamide, adriamycin, vincristine, prednol), 3 (21.4%) R-B (Rituximab-bendamustine), 1 (7.1%) R-CVP (Rituximab-cyclophosphamide, vincristine, prednol) and 1 (7.1%) received R-EPOCH (Etoposide, prednol, vincristine, cylophosfomid, adriamycin).

**Results:** The response rate for the first-line therapy was 85.7% (CR+PR). In patients with refractory /relapsed disease; 5 (36%) patients were treated with R-B,4 (29%) R-CE (ifosfamide, cisplatin, etoposide), 3 (21%) R-GDP (gemcitabine, cisplatin, prednol) and 2 (14%) were treated with R-GEMOX (Gemzar oxaliplatin) . Response rates for second-line treatments with refractory / relapsed disease were 28.5% (CR+PR). The mean overall survival (OS) from the first diagnosis was determined as 25 months. OS was statistically significant in patients who responded to first-line therapy (p= 0.001). Progression-free survival (PFS) was statistically significant in patients who responded after second-line therapy (p= 0.002) There was no difference in PFS between the second-line treatment regimens (p= 0.3).

**Conclusions:** There is a need for new studies to increase response rates and survival in refractory/relapsed patients aged 70 years and older who are not transplant candidates

# Effect of COVID-19 Infection on Patients with Acute Myeloid Leukemia Receiving Treatment

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**Introduction:** Large cohorts of patients with active malignancies and Covid-19 infection are needed to provide evidence for the association of treatment and type of hematologic malignancies with Covid-19 mortality. In this study, we analyzed the clinical course of patients who were treated for acute myeloid leukemia (AML) during the Covid-19 pandemic.

**Methods:** Between 19 March 2020 and 19 February 2022, 65 AML patients who were treated at Ondokuz Mayıs University Faculty of Medicine Hematology clinic were included in the study. Data for demographic characteristics, diagnoses, clinical course, and cancer treatment details of the patients were created from the hospital registry system and patient files.

**Results:** Thirty-seven (56.9%) of the patients were female. The median age was 54 (22-82). 11 (16.9%) of AML patients were AML-M3. Active Covid-19 infection was diagnosed in 16 (28%) of the patients. Two (11.1%) of these patients were diagnosed with active Covid-19 infection at the time of diagnosis, while 6 (33.3%) were receiving induction chemotherapy, 6 (33.3%) were receiving consolidation chemotherapy, and 4 (22.2%) were receiving relapse treatment. In 16 (89%) of the patients, Covid-19 contagion occurred while receiving active chemotherapy in the hospital. In our study, 14 (21.5%) of 65 patients who received active AML treatment died. Eight (17%) of 47 AML patients who were not infected with Covid-19 died. Six (33%) of 18 AML patients with Covid-19 who received active treatment, died due to active Covid-19 infection. Statistically, mortality rates were found to be markedly significant in the Covid-19 positive AML group compared to the group with negative Covid-19 (p= 0.001). interestingly, in 2021; when the Covid-19 Omicron variant was dominant,exitus was observed in only one of the positive cases.

**Conclusions:** In the Covid-19 pandemic, the majority of our AML patients were infected while receiving treatment in the hospital. Each clinic should determine the treatment strategy for patients who are treated for AML and also have Covid-19 infection, according to their circumstances. As a result, in our study, we showed that although the death rate in AML patients infected with Covid-19 was lower in the last year compared to the first year of the pandemic, it was higher when infected during the pandemic.

ABSTRACT

# Primary Cutaneous Follicle Center Lymphoma on Scalp: A Rare Case

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**Introduction:** Primary cutaneous follicle center lymphoma (PCFCL) is the most-common primary cutaneous B-cell lymphoma. PCFCL may show a diffuse and/or a follicular growth pattern. It is most often seen in white men aged 50-60 years. PCFCL commonly present with erythematous papules or plaques on the scalp,forehead or trunk.

**Case Report:** Skin biopsy was performed at another hospital in 2018 to a 70-years-old male patient who has red-colored, raised skin lesions on scalp. Skin biopsy reported as "large cell atypical lymphoid proliferation in nodular diffuse pattern". No systemic involvement detected in PET- CT which performed after skin biopsy. Follow-up was recommended to the patient. The patient admitted to our outpatient clinic in November 2021 with an increase in the number and size of the lesions on the scalp (Figure 1). Skin biopsy was performed and reported as "High grade B-cell lymphoma; EBV (-), primary cutaneous follicular lymphoma, with diffuse growth pattern". The SUV max value of the lesions on the scalp was 4.34 and no systemic involvement was detected in PET-CT performed for disease staging. Dermatology opinion was obtained for treatment planning. Disease staging was T2 N0 M0 and 4 cycles of intralesional steroid was given. No treatment response to intralesional steroid. Another treatment opinion was radiotherapy to involved area. This treatment opion was not planned due to possible side effects on the area to be delivered. Rituximab was started for treatment at 375 mg/m$^2$ dosing The patient's treatment is still ongoing.

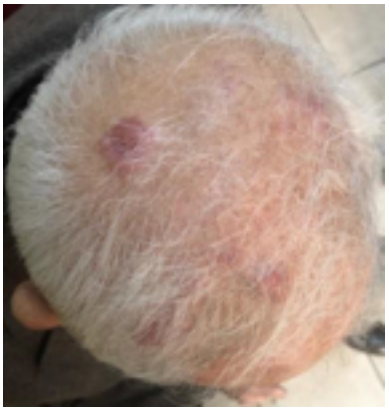

**Figure 1.** Lesions on scalp

**Discussion:** Primary cutaneous B-cell lymphomas are approximately 25% causes of all cutaneous lymphomas. It is divided into three subgroups as primary cutaneous marginal zone lymphoma, primary cutaneous follicle center lymphoma and diffuse large B-cell lymphoma leg type. Primary cutaneous follicle center lymphoma has indolent course and the disease- specific 5-year survival is 95%. In the differential diagnosis, acne, cyst, arthropod bite, basal cell carcinoma and other cutaneous lymphomas should be considered. Surgical excision or radiotherapy can be used to solitary lesions for curative treatment. Intralesional (corticosteroid, rituximab) or topical (corticosteroid, nitrogen mustard, imiquimod, cryotherapy) treatment options are available. Systemic use of rituximab is an effective treatment option in cases with extensive skin lesions. In rare cases with extracutaneous involvement, systemic multiagent chemotherapy (R-CHOP) can be given.

We present this case, although it is limited to the skin it does not respond to local treatment and requires systemic treatment.

# Ankle Fracture Management in a Hemophilia B Case

**Merih Reis ARAS[1], Suleyman OZEN[2], Fatma YILMAZ[1], Caner CANDAR[1], Abdulkerim YILDIZ[3], Hacer Berna Afacan OZTURK[1], Bugra SAGLAM[4], Murat ALBAYRAK[1]**

[1] University of Health Sciences, Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara

[2] University of Health Sciences, Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Department of Orthopedics and Traumatology, Ankara

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[4] Ministry of Health, Sanliurfa Mehmet Akif Inan Training and Research Hospital, Department of Hematology, Sanliurfa

**Introduction:** Hemophilia B is a recessive X-linked bleeding disorder characterized by deficiency of factor IX. The severity of bleeding correlates with the level of factor deficiency. Hemophilia B classified depends on the levels of factor IX as mild (5% - 40%), moderate (1% - 5%), or severe (< 1%). The mainstay of treatment is replacing of the missing factor IX. Treatment options include replacing FIX when bleeding episodes occur (on-demand treatment) or by scheduled infusions several times per a week to prevent bleeding (prophylactic treatment).

**Case Report:** Ankle fracture (Figure 1) detected in a 45-year-old man who has factor IX deficiency. At admission to the hospital, the activated partial thromboplastin time (aPTT) was 61 seconds. Factor IX level was 3.4% and factor IX inhibitor was negative. His body weight was 75 kg. The target factor level was calculated as 100% and treatment was planned. Preopeative loading dose infused and patient operated (Figure 2). Desired factor levels gradually decreased and factor IX replacement given ten days. No bleeding findings were observed in the postoperative follow-ups. After discharge, the patient came for control. The patient's follow-up and treatment continues without complications.

**Discussion:** Patients with Haemophilia B are at an increased risk of bleeding due to the underlying factor IX (FIX) deficiency during operation period. Therefore, factor IX replacement is required to minimize bleeding and maintain hemostasis. High levels of factor IX should be targeted ve replaced in major surgery. In the postoperative period, treatment should be planned to reduce the target factor level every three days. We present this case because hemophilia B is relatively rare, perioperative follow-up and treatment is difficult, and an uncomplicated postoperative period is observed.

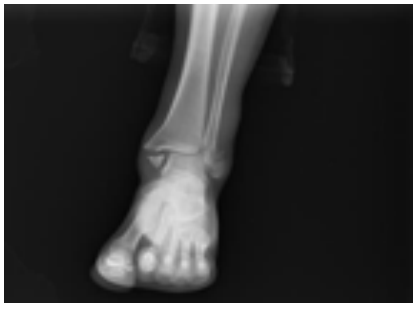

**Figure 1**. Preoperative X-ray image of the ankle

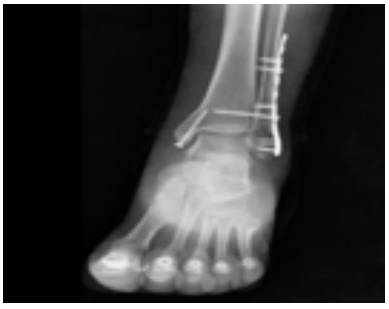

**Figure 2.** Postoperative X-ray image of the ankle

ABSTRACT

# Nilotinib-Associated Multiple Silent Arterial Stenosis in Patient with Chronic Myeloid Leukemia

**Mert TOKATLI[1], Rashad ISMAYILOV[1], Olgu Erkin CINAR[2], Ibrahim Celalettin HAZNEDAROGLU[2]**

[1] Hacettepe University Faculty of Medicine, Department of Internal Medicine
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Nilotinib is a second-generation tyrosine kinase inhibitor (TKI) used for chronic myeloid leukemia (CML). Studies show that nilotinib is associate with peripheric arterial or cerebrovascular diseases in CML patients. We report a case of 70-year-old nonsmoking, nondiabetic Caucasian female with no history of vascular disease who diagnosed with CML in 2004. The patient initially treated with imatinib 400 mg/day, but due to secondary loss of cytogenetic response it was switched to dasatinib at 6th year. Then the patient complicated with recurrent pleural effusion and therapy replaced with nilotinib 2 x 300 mg/day in 2016. There was a cytogenetic remission with nilotinib therapy, and it was well tolerated by patient. Serum hemoglobin A1c and low-density lipoprotein cholesterol were within normal range during this period. At the 3rd year of the nilotinib therapy significant inter-arm blood pressure difference was detected in routine visit. Computed tomography angiogram (CTA) showed severe stenosis of the left subclavian and right internal carotid arteries (ICA) and total occlusion of the celiac artery in February 2019. Endovascular stents placed into celiac and left subclavian arteries and dual antiplatelet therapy was started. The use of nilotinib was continued to control of the CML. A year later, control follow up CTA showed increased stenosis of the right ICA and severe stenosis of left proximal ICA within fibrofatty plaque (Figure 1). Although she still had no neurologic symptom, nilotinib was replaced with bosutinib to prevent possible cerebrovascular events.

According to long term results, arterial occlusive diseases are more reported with nilotinib compared with other TKIs. Most of the reported cases of nilotinib associated arterial disease, the patients have vascular risk factors before the treatment such as arterial hypertension, coronary artery disease, smoking, diabetes mellitus and hyperlipidemia. They also dramatically presented with stroke, transient ischemic attack, or myocardial infarction. In our report significant bilateral internal carotid arterial stenosis developed without preexisting vascular risk factors. This report also indicates multiple arterial stenosis may be seen asymptomatically. Therefore, physical examination and close clinical follow-up have vital importance in nilotinib using CML patients.

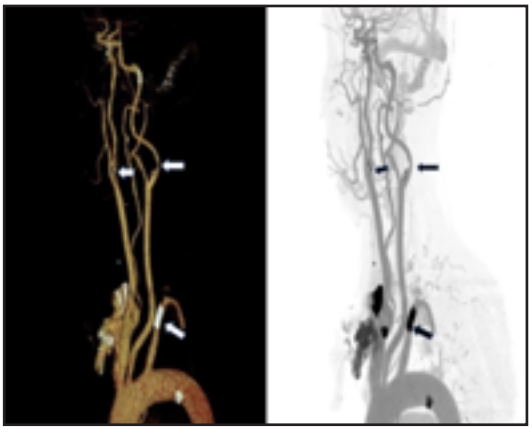

**Figure 1.** Computed tomography angiography shows right and left internal carotid artery stenosis (> %50) and endovascular stent in the left subclavian artery

***7th National Blood and Bone Marrow Transplantation Congress***
*May 19-21, 2022, Atakoy, ISTANBUL / TURKIYE*

# Diffuse Large B-Cell Lymphoma Protruding into the Mouth

**Merve Ecem ERDOGAN YON, Ahmet Kursad GUNES, Mehmet Sezgin PEPELER, Funda CERAN, Simten DAGDAS, Gulsum OZET**

Ankara City Hospital, Department of Hematology, Ankara

**Introduction:** Lymphomas are a heterogeneous group of malignancies arising from lymphocytes. The average age at diagnosis is about the sixth decade of life, although certain subtypes of NHL, such as Burkitt lymphoma and lymphoblastic lymphoma, have been diagnosed at the younger age. While HL usually starts from the supradiaphragmatic lymph nodes and involves the adjacent lymph nodes, NHL progresses by skipping nodal or extranodal involvement. In this case , we wanted to present a HL-like presentation young adult patient diagnosed with NHL.

**Case Report:** A 23-year-old male patient presented with a complaint of swelling in the neck that started 2 months ago. Physical examination revealed a left cervical lymph node extending from the left submandibular area to the anterior cervical, and a mass lesion in the mouth protruding into the left tonsil (Figure 1) .

Radiological and hematological investigations were performed. Pet-CT revealed multiple conglomerated lymph nodes with SUV: > 20 in the left palatine tonsil and left neck level 2, 3, 4 and 5. Excisional biopsy was done for the left level 2-3 lymph node and ımmunohistochemistry (IHC) was performed which markers used were PAX5, CD10, Bcl6 and CD20 was diffuse positive in neoplastic cells. These findings the case was diagnosed high grade B-cell lymphoma in the pathology. Bone marrow biopsy was reported as normocellular. The patient who was staged as Ann Arbor Stage 2, IPI: 2 , CNS-IPI : 2 (extranodal involvement and LDH elevation ), was started on R-CHOP chemotherapy. It was observed that the intraoral mass regressed almost completely after the first cure.

**Discussion:** Lymphomas initially arise within the lymphatic tissues and may progress to an extranodular mass (NHL) or to a non-tender mass or masses in a lymph node region (HL) that later may spread to other lymph node groups and involve the bone marrow. In the head and neck, Waldeyer's ring is the most common site of origin and may be accompanied by cervical node involvement. Nose, paranasal sinus, orbits, and salivary glands are other possible organs affected in decreasing order of frequency, with rare spread to the regional lymph nodes. While HL more frequently presents as the involvement of adjacent lymph nodes, head and neck involvement is frequently encountered in NHL, and it usually involves the lymph nodes in a skipped manner. We wanted to emphasize once again the importance of physical examination in lymphomas with our case who presented with a protruded mass in the mouth.

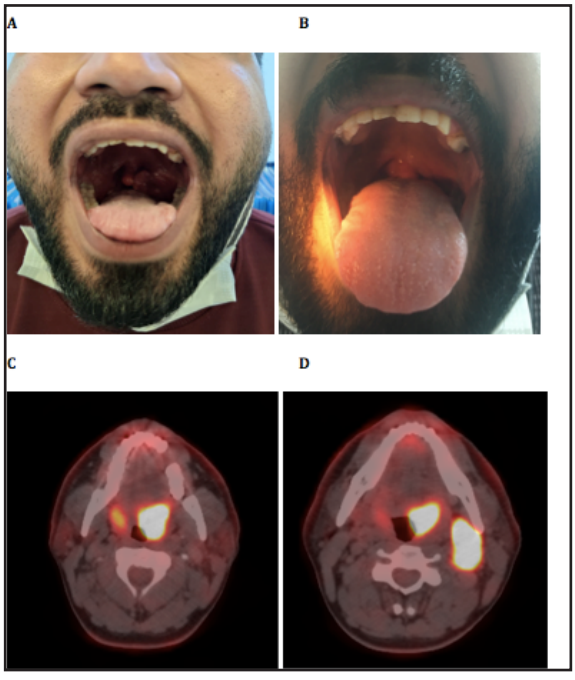


**Figure 1. (A)** Mass in the mouth at the time of diagnosis **(B)** Intraoral mass after 1 cycle of chemotherapy **(C-D)** PET-CT image at the time of diagnosis

ABSTRACT

# COVID-19 Related Fatality and Risk Factors in Multiple Myeloma: A Multicenter Cohort Study

**Mine KARADENIZ[1], Hakan GOKER[1], Oznur AYDIN[2], Mehmet TURGUT[2], Umit Yavuz MALKAN[1], Elif SENER[2], Batuhan ERDOGDU[1], Olgu Erkin CINAR[1], Ibrahim Celalettin HAZNEDAROGLU[1], Nilgun SAYINALP[1], Osman OZCEBE[1], Yahya BUYUKASIK[1], Haluk DEMIROGLU[1]**

[1] Hacettepe University, Faculty of Medicine, Department of Hematology, Ankara
[2] Ondokuz Mayıs University, Faculty of Medicine, Department of Hematology, Samsun

**Introduction:** The Novel Coronavirus Disease 2019 (Covid-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has become a pandemic that was first started in Dec, 2019. The clinical course and outcomes of Covid-19 infection in a distinct subgroup of hematological malignancies are still not exactly known. In this study, we have investigated the clinical outcomes of Covid-19 in patients with multiple myeloma (MM).

**Materials and Methods:** In this study, the clinical outcomes of multiple myeloma patients who developed Covid-19 are analyzed.

**Results:** A cohort of thirty patients data was analyzed, retrospectively, in this study. Autologous hematopoietic stem cell transplantation (AHSCT) was performed in 63.3% of the patients and 36.7% of the transplanted patients were in complete remission when the infection was detected. The total fatality rate (FR) was 36%, Covid-19 related fatality rate (CFR) was 9/30, 30% in MM patients in our study. There was two non-Covid related mortality. The CFR was associated with intensive care unit (ICU) admission (26.7%) ($p< 0.001$), mechanical ventilation (26.6%) ($p< 0.001$), increased lactate dehydrogenase (LDH) ($p= 0.008$) and lymphopenia ($p= 0.042$). Older age (> 65 years), stem cell transplantation, having co-morbidities was not effective in the fatality rate.

**Conclusion:** In this study, we have showed that the CRF rate was high in MM patients in both groups who underwent AHSCT or not. We suggest strict monitoring and adequate vaccination in this group. Further studies including vaccination data with the larger group of patients are needed to clarify this issue.

# A Case of Drug-Induced Hypersensitivity Syndrome

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**Introduction:** Lenalidomide is an immunomodulatory agent approved for use in the treatment of multiple myeloma (MM) and myelodysplastic syndrome (MDS). Thromboembolic events and cytopenias are the leading side effects associated with lenalidomide. Skin rash is seen in a high proportion of patients, however; regresses with medical support. In this article, we wanted to share a case of DIHS (drug-induced hypersensitivity syndrome) developed with the use of lenalidomide.

**Case Report:** A 73-year-old female patient was diagnosed with a mass in the cervical vertebrae in the magnetic resonance examination performed in 2010 due to neck swelling and pain. As the excisional pathology of the mass was compatible with plasmacytoma, the patient was diagnosed with immunoglobulin (Ig) A lambda type MM by performing bone marrow aspiration and biopsy. She received radiotherapy (RT) to the mass site, was followed up in remission until 2020 after systemic chemotherapy. When a lytic lesion was detected due to left shoulder pain in 2020, palliative RT was applied to the patient. She was evaluated as a recurrence due to multiple bone involvement and marrow involvement in June 2021 and carfilzomib, lenalidomide, and dexamethasone chemotherapy was started. She had widespread skin eruptions during the 4th cycle treatment (Figure 1). Drug-induce d hypersensitivity syndrome (DIHS) was considered due to fever, eosinophilia and increased liver tests. Lenalidomide treatment was interrupted, systemic steroid therapy was started and she was followed up in terms of organ functions. The patient, whose rashes and eosinophilia regressed with steroid support and no signs of organ tumor were detected, was discharged with the plan to continue treatment with a different immunomodulatory agent.

**Conclusion:** Skin rash is a common side effect of lenalidomide and may cause systemic complications that may lead to discontinuation of treatment. In a study including patients with MDS; it has been shown that the leading cause of permanent early discontinuation of lenalidomide is non-serious skin rashes. Similarly in the literature, Stevens-Johnson syndrome induced by lenalidomide use was reported in a 73-year-old female patient who received MM induction therapy, and the patient's skin biopsy was reported as a hypersensitivity reaction to the drug. In a series in which lenalidomide-containing regimens were applied, 44.4% of skin eruptions of various morphology and severity were observed. It has been shown that the incidence of drug-related skin rash increases with advanced age, myeloma subtype, lenalidomide dose and patients who have not received chemotherapy before.

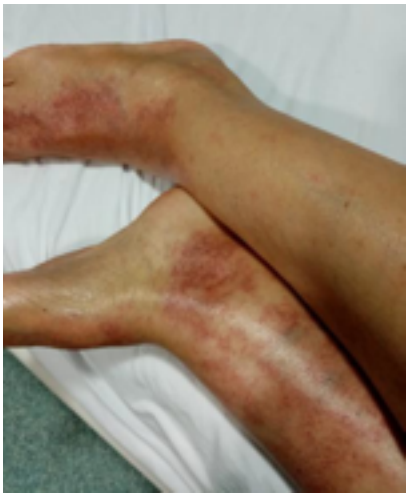

**Figure 1.** Erythematous, exanthematous, itchy widespread skin rashes

ABSTRACT

# Prognostic Factors in Myelofibrosis

**Mine KARADENIZ, Umit Yavuz MALKAN, Hakan GOKER**

Hacettepe University Faculty of Medicine, Department of Hematology, Ankara

**Introduction:** Myelofibrosis (MF), primary (PMF) or secondary due to polycythemia vera (PV) or essential thromboctythemia (ET) is BCR-ABL1 negative chronic myeloproliferative disease with reticulin, colagen fibrosis and osteonecrosis of the bone marrow, marrow failure and cytopenies and has no specific or curative treatment. Allogeneic hematopoietic stem cell transplantation (AHSCT) may supply potential cure for high risk group patients but high mortality rates due to transplantation is the major problem in this option. In this study, we shared our single center experience about clinical challenges and prognostication in myelofibrosis.

**Materials and Methods:** Fourty five patients following up with primary or secondary myelofibrosis between 2008 and 2021 were included. The patients data was analyzed retrospectively.

**Results:** 21 patients (46.6%) was over 65 years and 22 (48.9%) of them were female. The frequency of PMF, PV and ET were 48.9%, 31.1% and 20%, retrospectively. Mortality rate was 33.3% in 1 year and 46.6% in 3 years. In Kaplan- Meier univariate survival analyses; age> 65 and liver size were statistically significant (p= 0.041 vs 0.408). Leukemic transformation had the worst outcomes (p= 0.002). All risk stratification scores; International Prognostic Scoring system (IPSS), dynamic IPSS (DIPSS) and DIPSS- plus determined mortality. Multivariate analyses showed that transformation, JAK mutation positivity, the liver size and splenectomy were statistically significant in mortality. Pairwise comparison of ROC curve analysis revealed that all these four parameters were non-inferior to each other (mutation & liver (mm), difference between areas (dAUC):0.0415, Standard Error (SE): 0.127, Z statistics (Z): 0.326 and p= 0.744; mutation & splenectomy, dAUC: 0.0263, SE: 0.0942, Z:0.279 and p= 0.7800; mutation & transformaion, dAUC: 0.0030, SE: 0.0849, Z: 0.0358 and p= 0.9715; liver (mm) & splenectomy, dAUC: 0.0152, SE: 0.111, Z: 0.137 and p= 0.890; liver (mm) & transformation, dAUC: 0.385, SE:0.0943, Z:0.408 and P=0.6832; splenectomy & tranformation, dAUC: 0.0233, SE: 0.0757, Z:0.307 and p= 0.7586).

**Discussion:** Myelofibrosis pathophysiology is well known but treatment is still the main cornerstone of the disease. Almost all patients are fragile and balancing the benefits and risks is so difficult with limited options. In this study, like many other studies, we have shown that mortality rate is very high with novel therapies and supportive treatments. Liver not spleen size was significant in our study and so that maybe improving liver funtions and size can help clinicians about management. Further studies are needed for new prognostication strategies on MF.

# Pulmonary Graft Versus Host Disease after Haploidentical Stem Cell Transplantation

**Mine KARADENIZ[1], Rashad ISMAYILOV[2], Umit Yavuz MALKAN[1], Haluk DEMIROGLU[1], Hakan GOKER[1]**

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

**Introduction:** Chronic graft versus host disease (cGVHD) that develops after allogeneic/haploidentical stem cell transplantation (SCT) is one of the important causes of morbidity and mortality in stem cell recipients. Although there are publications showing that late-onset non-infectious pulmonary complications such as restrictive lung injury, cryptogenic organizing pneumonia and bronchiolitis obliterans are associated with cGVHD, their pathophysiology is not clearly known. The characteristic T-cell mediated epithelial destruction seen in skin, liver and intestinal GVHD could not be demonstrated in pulmonary GVHD. In this article, we presented a case of pulmonary GVHD who had a complete response with corticosteroid therapy.

**Case report:** A 46-year-old male patient with the diagnosis of acute myeloblastic leukemia (AML) underwent haploidentical stem cell transplantation with complete hematological remission after induction therapy including idarubicin 12mg/m2 on days 1 to 3, cytarabine 100 mg/m2 continuous infusion for 7 days and 3 cures of high dose cytarabine consolidation chemotherapy. The patient who had no history of smoking, occupational or environmental aerosol exposure was admitted to our clinic with the complaint of dyspnea in the 9th month after haploidentical SCT. In the physical examination, bilateral rhonchi in the lung bases and decreased arterial oxygen saturation to 86% with effort were detected. The Covid-19 PCR test of the patient was negative. In thorax computed tomography (CT), peribronchovascular fibrotic changes consistent with organizing pneumonia, traction bronchiectasis and ground-glass opacities in the form of confluent were observed. In the histopathological examination of the bronchoalveolar lavage (BAL) fluid, mixed type inflammatory cells (45% macrophage, 40% PMNL, 15% lymphocyte) were seen, no malignant cells were found. The sputum sample and BAL cultures were negative for infections. Methylprednisolone tretment was started to the patient at a dose of 48 mg daily with a prediagnosis of subacute-chronic stage pulmonary GVHD based on radiological findings. In the clinical follow-up, the patient's symptoms regressed significantly with steroid support and the treatment was discontinued after completing 12 months. A significant regression was detected in the findings observed at the time of diagnosis in the control thorax CT (Figure 1).

**Conclusion:** Currently, the most characteristic lesion for pulmonary GVHD is considered to be bronchiolitis obliterans. Patients present with signs of obstructive pulmonary disease and benefit significantly from corticosteroid therapy. However, data on duration of treatment and management of steroid-refractory cases are limited. Multicenter studies with large patient groups are needed in this regard.

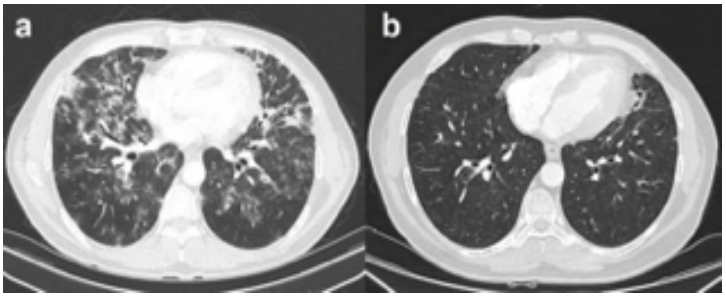


**Figure 1.** Thorax computed tomography. a) Peribronchovascular fibrotic changes consistent with organizing pneumonia in both lungs, traction bronchiectasis and ground-glass opacities in the form of confluent in places. b) Significant regression in symptoms after one year of corticosteroid therapy.

International Journal of Hematology and Oncology

ABSTRACT

# A Case of Lenalidomide-Associated Eosinophilic Pneumonitis

**Mine KARADENIZ, Batuhan ERDOGDU, Olgu Erkin CINAR, Sercan UNAL, Fatma Tugba CATAN, Hakan GOKER, Yahya BUYUKASIK**

Hacettepe University Faculty of Medicine, Department of Hematology, Ankara

**Introduction:** Lenalidomide is an immune-modulatory agent approved for the treatment of relaps/ refractory multiple myeloma and myelodysplastic syndrome. Comman side effects include cytopenia and thromboembolic events. Pulmonary toxicity and eosinophilic pneumonitis is less notified. We wanted to share a case of hypereosinophilic peumonitis due to lenalidomide use.

**Case Report:** 70-year-old woman was referred to our clinic with complaints of increasing weakness, weight loss, bone pains and night sweats for 5 months. The patient's laboratuary results as hemoglobin: 10.8 g/ dl, MCV: 96.5 fL, leukocytes: 16.2 x $10^3$ / $\mu$L, sedimentation rate: 82 mm/ hr, total protein: 11.7 g/ dL, globulin: 8.6 g/ dL, anemia parameters at normal range, Immunoglobulin G (Ig G): 8230 mg/ dL, beta-2 microglobulin: 13045 ng/ mL. She was evaluated with a preliminary diagnosis of multiple myeloma; gamma peak in protein electrophoresis detected and monoclonal Ig G kappa with band level 4.58 g/ dL was monitored in serum immunofixation electrophoresis. Bone marrow aspiration and biopsy had confirmed the diagnosis of plasma cell leukemia and autologous stem cell transplantation (ASCT) was performed with marrow remission after chemoteraphy courses including lenalidomide and daratumumab. Lenalidomide as maintenance treatment was started in the 6th month after transplantation. In the second week, she admitted with complaints of shortness of breath, cough and fever. Blood eosinophilia and bilateral mosaic attenuation, linear atelectasis, focal ground glass areas were observed on thorax computed tomography (CT) (Figure 1). Upon the development of oxygen demand of 3 lt/min, she was hospitalized with a pre-diagnosis of treatment related pneumonitis. Lenalidomide treatment was stopped. It was decided to perform bronchoalveolar lavage and culture for the patient after exclusion of infectious causes and immunologic etiology. Steroid was added to the treatment due to eosinophilia (20%) in the lavage sampling. The patient was followed up 6 weeks after steroid discontinuation, then lenalidomide treatment was restarted at a lower dose. After a week, blood eosinophil level started to increase with mild cough complaint, so that the drug was again stopped immediately. Alternative therapy plan was concidered for the patient.

**Conclusion:** Pulmonary toxicity due to lenalidomide use is reported as a reversible drug-induced adverse event in the literature. This toxicity progresses in a wide range of clinics from simple eosinophilia to acute respiratory distress syndrome. Interstingly; our case had used lenalidomide before ASCT and neither clinical nor laboratuary side effects were noticed before.

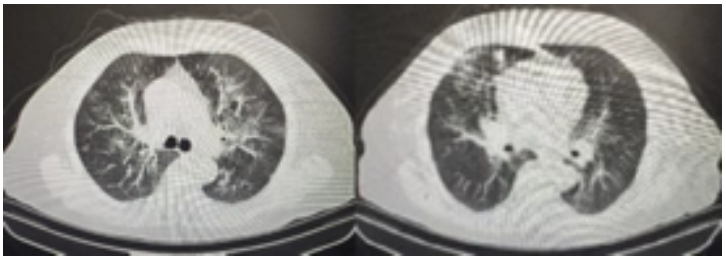

**Figure 1.** Thorax CT images of the patient; mosaic attenuation, linear atelectasis, focal ground glass areas

# A Case of Plasma Cell Leukemia Presenting with Pleural Effusion and Pleural Involvement

**Mine KARADENIZ[1], Ahmet KOCAGER[2], Olgu Erkin CINAR[1], Batuhan ERDOGDU[1], Sercan UNAL[1], Umit Yavuz MALKAN[1], Hakan GOKER[1]**

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

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

**Introduction:** Multiple myeloma (MM) is a malignant disorder characterized by proliferation of malignant plasma cells from a single clone. These plasma cells mainly accumulate in bone marrow although extramedullary tissues may be infiltrated as well. Pleural effusion in the course of MM is rare, only seen in 6% of patients. Furthermore myelomatous pleural effusion is particularly rare, seen in < 1% of the patients and especially in advanced stage or refractory disease. In this report, we present a case MM whom the myelomatous pleural effusion is the initial sign.

**Case Report:** A 74 year old male patient with severe chronic obstructive pulmonary disease (COPD) was admitted to hospital because of shortness of breath and malaise for one month. The computed tomography scan of chest revealed emphysema and right pleural effusion. Thoracentesis was done due to not improvement of the symptoms. In the cytological analysis of the pleural fluid sampling, plasmacytoid cells with eosinophilic cytoplasm was notified. Immunohistochemical staining of the sample demonstrated CD138 positivity and kappa monoclonality and pleural involvement was confirmed with pleural biopsy. In serum protein electrophoresis, spike in the gamma region and 6.3 gr paraprotein was noted. Serum immunofixation examination detected monoclonal IgG kappa. In pathological analysis of bone marrow sample; diffuse infiltration of marrow with plasma cells stained positive for CD138, CD56 and monotypic kappa light-chain expression were detected. The patient had the diagnosis of plasma cell leukemia with bone marrow sample pathological examination and evaluation of peripheral smear including 50% atypical plasma cells in the structure of blastic chromatin. PET- CT revealed increased FDP uptake in bilateral pleural effusion and pleural thickening and lytic lesions in the right iliac crest and sacrum. The patient had pandemic SARS-CoV-2 infection so that; we had decided to give a lighter initial induction regimen in order to decrease tumor burden promptly.

**Discussion:** Common causes of pleural effusions in MM patients include congestive heart failure, renal failure, pulmonary embolism, infections due to immunosuppresion and chylothorax or bleeding. In the case reports effusion directly due to myeloma occurs in less than 1% of cases with approximately 80% of these being in IgA type disease. Interestingly; our patient had Ig G type myeloma and there is not enough information about the disease course with such pleural effusion and pleural involvement. On case by case basis; myelomatous pleural effusion carries a poorer prognosis.

International Journal of Hematology and Oncology

ABSTRACT

# A Case of Primary Pulmonary Hodgkin Lymphoma

**Mine KARADENIZ, Olgu Erkin CINAR, Batuhan ERDOGDU, Umit Yavuz MALKAN, Salih AKSU, Hakan GOKER**

Hacettepe University, Faculty of Medicine, Department of Hematology, Ankara

**Introduction:** Hodgkin lymphoma (HL) is one of the rare (10-15%) malignancies of the lymphatic system originating from B lymphocytes with an incidence of 2-3/100.000. Pulmonary involvement is observed at a rate of 10-40% in advanced stages and usually in refractory disease. Cases of primary pulmonary Hodgkin lymphoma (PPHL) have been described in small numbers in the literature; in this case, we wanted to present our patient who was diagnosed with PPHL and started treatment.

**Case Report:** A 23-year-old female patient with complaints of dyspnea, pleuritic chest pain and night sweats for the past month applied to our clinic. Contrast-enhanced thorax computed tomography (CT) was performed because of suspicious findings in terms of pneumonic infiltration in the posterior-anterior chest X-ray. In the thorax CT report, bilateral ventilation loss, a heterogeneous wide pneumonic infiltration in the left lung upper lobe apicoposterior segment, adjacent to the mediastinum and a heterogeneous heterogeneous pneumonic infiltrate in the right lung lower lobe superior and posterior segments were observed. In addition, minimal pleural fluid was also detected in the images (Figure 1). A CT-guided tru-cut biopsy from the lesion in the upper lobe of the right lung was performed to the patient because of the inconsistent radiological findings and the clinical course. The histopathological examination of the sample was demonstrating classic type Hogdkin lymphoma (cHL). FDG-PET CT imaging for disease staging preferred for the patient and pathological FDG consistent detected localized to the pulmoner area only (Figure 2). We had chosen brentuximab-adriamycin-vincristine-dacarbazine (B-AVD) chemotherapy. Interim evaluation with FDG-PET CT after two cycles of B-AVD treatment was reported as significant regression of the mass size. We decided completing treatment to 6 cources with B-AVD.

**Conclusion:** Primary pulmonary Hodgkin lymphoma (PPHL) is a concept that usually presents with non-specific infection-like findings, therefore difficulties in diagnosis and evaluation of this group of patients still remains unclear in the literature. PPHL is characterized by clonal proliferation of lymphoid cells and mass lesion of these cells only in the pulmonary area. HL-targeted agents are used in the treatment and there is no data on the use of bleomycin in terms of pulmonary toxicity yet. For this reason, we preferred the combination of brentuximab to the classical treatment component bleomycin in our patient and we had a good response in the first evaluation.

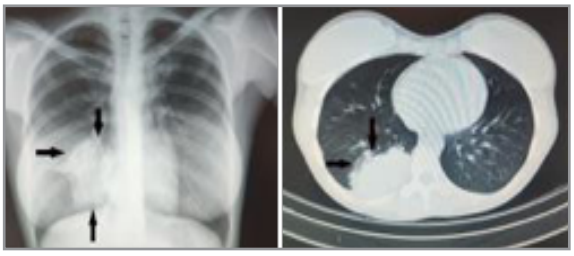

**Figure 1.** Pulmonary lesions in the patient's chest X-ray and Thorax CT imaging

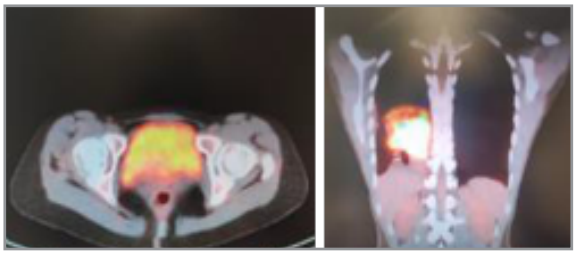

**Figure 2.** Images of pulmonary lesion in FDG-PET CT

# Experience of Glasdegib in Patients with Elderly Acute Myeloid Leukemia

**Nanise Gizem FENER, Oktay BILGIR**

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**Introduction:** Acute myeloid leukemia (AML) is a disease mostly seen in older adults. Many older adults with AML are unable to receive intensive chemotherapy because of its toxicity. In this study, we aimed to evaluate AML patients treated with Glasdegib-based regimens retrospectively at our center.

**Case Reports:**

**Case 1:** A 75-year-old male patient with congestive heart failure was diagnosed with AML and was treated with idarubicin and cytarabine chemotherapy protocol. He received LDAC+glasdegib as a second course after first protocol. It was observed that the patient was in remission after the 5th cycle.

**Case 2:** An 82-year-old male patient with chronic renal failure was diagnosed with AML intermediate risk. LDAC+glasdegib treatment was given to the patient who did not go into remission after 4 cycles of decitabine treatment. The patient, who was followed in remission after 4 cycles, died due to pneumonia.

**Case 3:** A 76-year-old male patient with cerebrovascular disease was diagnosed with moderate risk AML. We started with azacitidine treatment. After 2 courses of azacitidine, remission was achieved and LDAC+glasdegib treatment was started as a the third course of treatment.

**Discussion:** The data of the patients with AML who were treated with Glasdegib-based regimens were evaluated retrospectively from their files in Bozyaka Training and Research Hospital Department of Hematology. One of our patients, who was followed up in remission, died due to pneumonia. 2 patients are still being followed up with LDAC + glasdegib treatments. In 2018, the FDA approved glasdegib, a Hedgehog signaling pathway inhibitor, in adults 75 years of age or older with a diagnosis of AML or those with comorbidities that preclude the use of low-dose cytarabine plus intensive induction chemotherapy. Approval is based on interim results from the phase 2 BRIGHT 1003 study evaluating glasdegib in combination with LDAC or LDAC alone. The median OS was 4.9 months for LDAC versus 8.8 months in patients treated with glasdegib+LDAC. This differencere presented an approximately 50% reduction in mortality in patients treated with glasdegib+LDAC. The BRIGHT 1003 study confirmed that LDAC significantly improved the operating system compared to LDAC alone. Also, adding glasdegib to LDAC did not cause a significant increase in adverse events.

ABSTRACT

# Pathologic Bone Fracture Due to Granulocytic Sarcoma in Acute Myeloid Leukemia: A Case Report

**Olgu Erkin CINAR[1], Fatıma Gul GULBAHCE INCESU[2], Haluk DEMIROGLU[1], Hakan GOKER[1]**

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**Introduction:** Myeloid sarcomas may occur in less than 5% of AML, usually with skin/gingival infiltration, and are often associated with monocytic subtypes and therapeutic challenges. In this report, we will present a extremely rare case of pathological fracture of bone due to myeloid sarcoma.

**Case Report:** A 55-year-old female was admitted with complaints of weakness, shortness of breath, and widespread ecchymotic lesions on the legs. Upon bicytopenia and 50% blasts in the peripheral blood smear were found, bone marrow aspiration and biopsy (BMB) were performed. Hypercellular bone marrow showing diffuse blastic cell infiltration was consistent with AML. Cytogenetic and molecular analyzes at diagnosis revealed trisomy 8 without CBF or FLT3 mutations. Idarubicin-cytarabine combination was given for induction. In control BMB, blast percentage was 5-6% with residual disease. High-dose cytarabine treatment was given. The CRi was achieved, and the allogeneic HSCT was planned. The patient applied two months later with the complaint of blurred vision, a mass in the right eyeball, which was evaluated in favor of the involvement of the primary disease, was seen in cranial MRI. The CNS relapse was proven by CSF cytology, and orbital RT was started. Since concurrent BMB showed relapse, the need for systemic and intrathecal therapies arose. After orbital RT, MEC (mitoxantrone, etoposide, cytarabine) protocol was started. After four intrathecal methotrexate-cytarabine combinations were given, CSF cytology turned negative. A right shoulder MRI was performed for severe pain, and findings were compatible with diffuse leukemic involvement in the bones, especially in the humerus. The pain worsened in the forearm region, and right proximal radius fracture was seen in the X-ray. There was no history of trauma or intervention. Latter MRI was reported as "diffuse leukemic infiltration and pathological fracture in the proximal humerus, with a lesion compatible with granulocytic sarcoma. Since pathological fracture due to myeloid sarcoma was extremely rare, diseases involving bone primarily were ruled out.

**Discussion:** Bone involvement and pathological fractures are unexpected complications in AML. The case we present is one of the few cases in the literature in which granulocytic sarcoma and pathological fracture were found. Sarcomas are more common in monocytic subtypes, but there was a distinct morphology in this case. Such rare complications gain importance in understanding the unique phenotypes, genotypes, and courses of the AML. The role of trisomy 8 in this rare manifestation will be revealed, if any, as reports in the literature increase.

# Start for the Hematopoetic Stem Cell Transplantation and First Experiences from the Tertiary Bone Marrow Transplantation Center

**Pelin AYTAN, Anıl TOMBAK, Aydan AKDENIZ, Ipek AZIZOGLU, Fatma AKBAS, Eyup Naci Tiftik**

Mersin University, Faculty of Medicine Department of Hematology, Mersin

Haematopoetic stem cell transplantation (HSCT) evolved with the successful transplant of E. Donnall Thomas in the late 1950s, which earned him the Nobel Prize in 1990. This transplant was performed in the twin of the patient with leukemia. In 1968, the first non-twin donor (allogeneic) transplant was successfully performed in Minnesota, the donor was a sibling (sister). Multiple HSCT was performed successfully from a Danish unrelated donor in New York in 1973. The first allogeneic bone marrow transplantation in Turkey was performed by Prof. Dr. Korkut Özerkan in 1978, the first autologous HSCT was performed in 1984 by Prof. Dr. Onder Berk and his team. Our transplant center, which may be small for the world, but a great development for our country and our beautiful Mersin, has six positive pressure rooms with hepa filter and is arranged in a building isolated from the main building and in a way that a limited number of defined health personnel can enter.

Mersin University Bone Marrow Transplant Center started with autologous HSCT on September 10, 2021. Mobilization success has been achieved in 20 patients so far, mobilization failure after KT-GCSF in 1 multiple myeloma patient, and insufficient stem cells for autologous transplantation with CD 34 count less than 2x10E6/kg after GCSF-plerixafor have been collected. Stem cells were collected in 2 days in three of our myeloma patients who were planned to collect for two transplants, and in one of our patients with diffuse large B-cell lymphoma and primary amyloidosis. In our myeloma patient whose stem cells were collected, 43.75% IgG Kappa, 18.7% IgG lambda, 12.5% lambda light chain, 12.5% kappa light chain, 6.25% IgA lambda and 6.25% IgA kappa was of the subtype. 56% of myelomas were ISS stage2, 25% were ISS stage1, 12.5% were ISS stage 3. We performed 15 autologous HSCTs (11 multiple myeloma, 1 primary amyloidosis, 2 diffuse large B-cell non-Hodgkin lymphoma, 1 mantle cell lymphoma) consisting of 8 female 7 male patients and allogeneic HSCT from 6 fully matched sibling donors (3 flt 3 positive, 1 TP 53 mutation positive, 1 standard risk acute myeloid leukemia and 1 Burkitt lymphoma). The mean age of all our autologous and allogeneic transplant patients was 56.96 ± 8.39 years, mean neutrophil engraftment and platelet engraftment time were 11.16 ± 0.76 and 13.53 ± 2.74 days.

As a clinical program director, it must be always remembered that to perform successful hematopoetic transplantations we shall be responsible for all elements of the design of the clinical program including quality management, the selection and care of recipients and donors, and cell collection and processing.

International Journal of Hematology and Oncology

ABSTRACT

# Exploring the Distribution and Prognostic Effect of the ABO Blood Types of COVID-19 Patients During Delta and Omicron Waves

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**Introduction:** We aimed to delineate the effects of the ABO groups and the main clinical outcomes with the current SARS-CoV-2 variants, i.e., delta and omicron.

**Patients and Methods:** In this retrospective case-control study, the total 360 adult COVID-19 patients who were followed in the pandemic waves of delta and omicron variants and had ABO blood group analysis were included and divided into two groups according to the waves of variant. Demographic characteristics, comorbidities, length of hospitalization and intensive care needs, survival and ABO groups of cases were recorded. These groups were then compared with the ABO group distribution of population-reflecting 1881 healthy individuals and 186 historical alpha variant cases. Approvals for this study were obtained from the local ethics committee and the Ministry of Health of the Republic of Turkey.

**Results:** The demographic characteristics of the case groups and control group were similar. ABO distributions of the delta and omicron wave groups compared to the control group did not show a statistically significant difference. While advanced age ($p< 0.001$) and presence of comorbidity ($p= 0.006$) showed statistically significant differences in terms of overall survival, ABO blood group was not found to be a risk factor for mortality ($p= 0.114$ in delta, and $p= 0.526$ in omicron), hospitalization time ($p= 0.148$ in delta, $p= 0.224$ in omicron), and intensive care unit admission ($p= 0.096$ in delta, $p= 0.229$ in omicron).

**Conclusion:** The risk of infection among ABO blood groups, which has been shown in previous studies for the alpha variant against group A and in favor of group O, does not appear to be valid for delta and omicron period patients. Therefore, the anti-infective measures, especially vaccination, should not differ for individuals according to ABO blood group.

# The Effect of Changing Paradigms in Multiple Myeloma on Survival in the Last Two Decades

**Sema Nur OZSAN[1], Hakan GOKER[2], Olgu Erkin CINAR[2], Umit Yavuz MALKAN[2], Haluk DEMIROGLU[2], Yahya BUYUKASIK[2]**

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

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

**Introductin and Aim:** Dramatic changes have occurred in the treatment of multiple myeloma (MM) in the last two decades. The treatment paradigm changed as cytotoxic agents were replaced by proteasome inhibitors and IMiDs in induction. We planned this study to reveal how this translates into disease outcomes.

**Patients and Methods:** This study is a retrospective comparative cohort study includes 495 myeloma patients who were admitted our university hospital between 2003 and 2020. ISS stages, induction regimens, AHSCT status and overall survival of the patients were recorded. As a result of the changing reimbursement conditions by periods, cytotoxic (mostly VAD) versus bortezomib-based treatment groups were formed and compared for OS.

**Results:** The median follow-up duration was 53.15 months (1.7 - 233.43). In the younger than 65 year-old patients(n= 352), the median OS of first-line VAD or other cytotoxic combination patients (n= 252) was significantly higher than bortezomib-based subgroup (n= 86, p= 0.027). The median age, and AHSCT rate were similar between subgroups. The OS in the VAD (n= 59) and bortezomib-based regimen(n= 83) subgroups was similar for over-65 age patients (n= 142, p= 0.82). The median age, AHSCT rate, and ISS stages were similar.

**Discussion and Conclusion:** While the abandonment of cytotoxic agents in MM initially appeared to be an attractive and promising development, the evidence of AHSCT providing a survival benefit in many current trials seems to rule out this possibility for now. The MM literature is one of the richest fields of hematological oncology with its high number of randomized clinical studies. However, crossover studies and studies in which different treatments are used sequentially are scarce, and the fact that sometimes clinical trial results may not fully deliver the benefits envisaged in clinical practice underlines the importance of clinicians monitoring outcomes in their myeloma practice. In our cohort, starting treatment with VAD seems to provide a survival advantage in a significant, if not all, patient group aged younger than 65. There are limitations due to the design of the study and uncontrolled factors, and further studies are planned that will enable more detailed and well-directed analyses.

ABSTRACT

# Stem-Cell Transplantation as Dual Therapy for HIV and AML

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**Introduction:** Clinical outcomes have changed among people living with HIV through highly active antiretroviral therapy (HAART). Although different by gender,race,risk group and CD4 count,the life expectancy of HIV-infected individuals receiving HAART is similar to that of the general population. However,thereis a decrease in viral replication and opportunistic infections after HAART use,but malignancy rates still remain high. Recently, remission has been reported in HIV- infected cases after Stem-Cell Transplantation (SCT) from HIV innately resistant donors. In this case report,our experience with a HIV-infected AML patient,who was followed up after two HLA- haploidentical peripheral blood (PB) SCTs,will be discussed.

**Case Report:** A 62-year-old man had a 20 year history of HIV withno AIDS-defining illness.In April 2021,2 weeks after the Biontechvaccine,the patient was admitted to the hospital with complaints of widespread body pain and excessive sweating,and pancytopenia was detected.His CBC showed Hg= 8.0 g/dl, platelets= 146.000/$mm^3$,WBC 2.2 x $10^3/mm^3$. A bone marrow aspirate and biopsy (BMAB) were performed to evaluate his pancytopenia. The aspirate showed 25% blasts.He was diagnosed with acute myeloid leukemia. He received Cytarabine/Etoposide as induction chemotherapy and high dose Cytarabine as consolidation chemotherapy. After achieving remission,he received HLA-haploidentical peripheral blood (PB) SCT with the regimen of Busulfan/Fludara/Cyclophosphamide. Since neutrophil and platelet engraftment could not be achieved 30 days after PBSCT, STR analysis and a BMAB were performed. Chimerizm was detected as 2% by STR analysis. The aspirate was hypocelular.The current clinical situation was accepted as primary graft failure. A second PBSCT with the regimen of Cyclophosphamide/Fludara was planned from the same donor. Neutrophil engraftment was achievedon the 21th day of PBSCT. Eltrombopag was started because thrombocyte engraftment could not be achieved in the follow up. Platelet values > 20.000/$mm^3$ are observed after eltrombopag. HIV was not detected in the patient during this period.

**Discussion:** HIV-1 needs the CD4 receptor and usually CCR5 coreceptor for entry into the target cell. For this reason, there is HIVnatural resistance in the population with CCR5 delta32 deletion. Clinical gaps exist in the effectiveness of current treatment options in HIV-positive patients with a hematologic malignancies. Allo-SCT with a donor with CCR5 mutation as a hematologic malignancy and HIV binary treatment seems intriguing. Gero Hütter, et al, report a successful transplantation of allogeneic stem cells homozygous for the CCR5 delta32 allele to a patient with HIV. Despite the withdrawal of the HAART after the engraftman, HIV reactivation was not seen in this reported case. His AML remained in remission. In this case, PBSCT was planned with the expectation of dual treatment for HIV and AML. However, CCR5 delta32 deletion in the donor could not be screened because it could not be studied inour center. As CCR5 delta32 donor deletion status is unknown, discontinuation of antiretroviral treatment was not anticipated. The patient is being followed in remission for AML and HIV. When this case and other reported cases are evaluated together, Allo-SCT with a donor with CCR5 delta32 deletion shows promise in the treatment of AML and HIV.

# Experience with Inotuzumab in a Patient with B-All who Relapsed after Haploidentic Bone Marrow Transplant

**Sercan UNAL[1], Elif Naz CELIK[2], Olgu Erkin CINAR[1], Batuhan ERDOGDU[1], Mine KARADENIZ[1], Fatma Tuğba CATAN ERDEKLI[1], Umit Yavuz MALKAN[1], Hakan GOKER[1]**

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

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**Introduction:** Relapsed/Refractory B-cell acute lymphoblastic leukemia (B-ALL) shows poor prognosis in adults. Despite various salvage treatments, remission rates have been reported in the range of 22-42% and remission times are typically short. Complete remission rates are higher with inotuzumab than with standard salvage treatments for B-ALL. In this case, we would like to present that a complete remission was achieved after inotuzumab in a haploidentic posttransplant relapsed pre B-ALL patient.

**Case Report:** A 20 year old patient was admitted 2 years ago with complaints of involuntary loss of 4-5 kilograms in 2 months. The white blood cell and lymphocyte count were 111.800 $\mu$l/ml and 108.400 $\mu$l/ml. Bone marrow biopsy was performed and the patient was diagnosed with CALLA+ pre B-ALL.The patient had no cranial involvement. After the diagnostic procedures,was started on the BFM protocol. The MRD result of the patient whose bone marrow was in remission after the BFM protocol was determined as 1.8/10000. During this period, the patient was given brain-sparing radiotherapy, 8 times in total. Approximately 4 months later, lymphocytosis was detected in the patient during routine controls. Bone marrow biopsy performed on this was evaluated as blastic infiltration. The FLAG-IDA protocol was started as a salvage treatment for the patient. After the protocol, 6-7% blasts were detected in the patient's bone marrow biopsy. Bone marrow transplantation preparations were started for the high-risk relapsed/refractory B-ALL patient.The patient did not have a fully compatible donor. For this reason, the patient underwent haploidentic bone marrow transplantation in January 2021. The blast rate was found to be less than 5% in the control bone marrow samples. The chimerism of the patient had been observed as 99-97-98-93%. The patient was followed up in this way for approximately 11 months. In the patient's routine controls, hypocellular bone marrow with diffuse blastic cell infiltration was observed in the bone marrow aspiration biopsy performed in November 2021. The chimerism of the patient was found to be 45%. The patient was considered to have relapsed B-ALL .It was planned to administer 2 courses of Inotuzumab to the patient. In January 2021, the patient underwent bone marrow aspiration biopsy to evaluate treatment response.The blast rate was found to be < 5%. The chimerism of the patient was found to be 95% The MRD result was 0.9/10000.

**Discussion:** In this case, we wanted to present the B-ALL patient after haploidentic bone marrow transplantation. We know that complete remission rates are better with inotuzumab compared to standard salvage treatments. Although the risk of veno-oclusive disease (VOD) increases with inotuzumab treatment, we think that this protocol should play an active role in the treatment of relapsed B-ALL patients.

ABSTRACT

# A Case of Lymphoma-Associated Hemophagocytosis

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**Introduction:** Hemophagocytic lymphohistiocytosis (HLH) is a histiocytic disease characterized by severe systemic inflammation and an excessive immune response. Patients usually present to the clinic with signs of high fever, splenomegaly, bone marrow failure, increased liver enzymes, excessive ferritin level, and hemophagocytosis. Lymphoma-associated HLH is a rare disease with poor prognostic features. Due to the similarity in clinical manifestations of HLH and lymphomas, it may be difficult at the time of diagnosis. In this case report, we wanted to present a patient with ALK+ anaplastic large cell lymphoma who presented with hemophagoistosis in both bone marrow and lymph node biopsy at the time of diagnosis.

**Case Report:** A 29-year-old patient was admitted with fever,night sweats, involuntary weight loss, and swelling in her neck and armpits that had been going on for a few months. In the physical examination of the patient, inguinal axillary lymph nodes (LAP) and hepatosplenomegaly were detected. In the ultrasonography (US), the largest one is approximately 41 x 20 mm in size in the right inguinal region, the cortex is thick, hilar structures are in silicified conglomerate, numerous LAPs, in the bilateral anterior cervical chain, the largest ones in the submandibular area are 12 x 4 mm in the right and 21 x 5 mm in the left, a few sonographically reactive lymph nodes with a vertical length of 165 mm on the liver midclavicular line, the long axis of the spleen was 157 mm, and the largest one was approximately 45 x 21 mm in the paraaortic area, and many LAPs were observed, with thick cortex and hilar structures with indistinct conglomerate appearance. In the laboratory values of the patient, HB 7.0 g/dL, leukocyte-2.5 x $10^3/\mu$L, neutrophil 1.4 x $10^3/\mu$L, platelet 66 x $10^3/\mu$L, lactate dehydrogenase 1773 U/L, Beta-2 Microglobulin 4696 ng/mL, ferritin: 1250, ALT/AST: 135/182. Excisional biopsy was performed for the inguinal lymph node detected in the patient for diagnostic purposes. Afterwards,bone marrow biopsy was performed on the patient. The patient's lymph node biopsy report was consistent with ALK positive anaplastic large cell lymphoma and hemophagocytosis. Similar to this, in the bone marrow biopsy, macrophage activation, findings consistent with hemophagocytosis and lymphoma involvement were reported. After the diagnosis of hemophagocytosis and ALK- positive anaplastic large cell lymphoma, the patient was promptly started on the R-CHOEP chemotherapy protocol. Patient's fever and liver enzymes ferritin began to regress in a short time. Clinical response was observed.

**Discussion:** HLH has many causes, for example infections, rheumatological diseases, immunodeficiencies and malignancies. Lymphoma associated HLH is a disease with a poor prognosis due to difficulties in diagnosis. We believe that there should be studies on lymphoma-associated HLH for early diagnosis and treatment.

# A Rare Case of Patient with T-LGL and Graves' Disease

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**Introduction:** Graves'disease (GD) is the most common cause of hyperthyroidism(1).Untreated hyperthyroidism causes various hematological side effects including leukopenia and rarely pancytopenia. T-cell large granular lymphocyte (LGL) leukemia results from clonal proliferation of cytotoxic (CD8+) T cells. T-LGL is associated with many autoimmune diseases. Herein,we report a neutropenic patient with T-cell large granular lymphocyte leukemia and GD.

**Case Report:** A 29-year-old female patient was evaluated by hematology for isolated neutropenia in 2020. Viral and rheumatological markers were negative; the causes of nutritional anemia were excluded.As a result of flow cytometry sent from peripheral blood" Peripheral blood smear, some of which contains 20% lymphocytes of LGL type,molecular findings supporting the presence of clonal T lymphocytes. The patient,who was diagnosed with T-LGL, was followed up without treatment.Until 11/2021, the patient applied with complaints of palpitation, sweating, weight loss.In the laboratory examination TSH < 0.01 IU/mL, free T4 > 100 pmol/L, free T3 > 50 pmol/L and thyroid stimulating hormone receptor Antibody (TRAB): 40.6 U/L. Scintigraphy was found to be consistent with toxic diffuse goiter. Vitti 3 blood flow pattern was found on ultrasonography (US). According to the criteria of the European Graves' Orbitopathy Group (EUGOGO), stage 1 orbitopathy with bilateral exophthalmos was detected. Since the patient had known T-LGL leukemia, the absolute neutrophil count (ANC) was determined as: 1.10 x $10^9$/L. Radioactive iodine therapy was not planned because she had GD orbitopathy and the gland size was large. Total thyroidectomy was planned after the operation preparation was made with antithyroid treatment, beta blocker and lugol solution and euthyroidism was achieved. However, because the patient was neutropenic, hematology was consulted before starting methimazole. The patient was started on methimazole with GCSF in line with the recommendations of hematology. Methimazole dose adjustment was made by monitoring free T4 and free T3 and daily ANC follow-up. She needed 48 mu GCSF 3 times in total. Free T4 and free T3 values were normalized, and the surgery was performed. No complications developed in the perioperative period. The pathology result was reported as "follicular hyperplasia, it is compatible with Graves' disease". The patient's postoperative ANC count was 1.40 x $10^9$/L.

**Discussion:** Autoimmunity is a known phenomenon during T-LGL disease. However, its relationship with thyroid autoimmunity, especially GD,has not been clearly defined. Pre-treatment neutropenia may complicate the treatment of Graves' disease.In our patient, a significant increase was observed after GCSF, which allowed the initiation of antithyroid medication. Methimazole was continued with repeated doses of GCSF and euthyroidism was achieved in the patient within 10 days. This is a a case suggesting that the use of GCSF in the management of pre- treatment neutropenia in GD seen during TLGL is safe.

ABSTRACT

# Autologous Stem Cell Transplantation in Isolated Amyloidosis of the Bladder

**Tarik Onur TIRYAKI[1], Dilek Ozden OZLUK[1], Mustafa Murat OZBALAK[1], Mesude Yasemin OZLUK[2], Isin KILICASLAN[2], Beyza OLUK[1], Ipek Yonal HINDILERDEN[1], Meliha NALCACI[1]**

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**Introduction:** Amyloidosis is a group of diseases resulting from the accumulation of misfolding proteins in tissue and organs. Deposition of amyloid is localized or systemic. In case of progression, it may result in failure of the involved organ. Amyloidosis may involve many tissues including liver, spleen, kidney, heart, nerves and blood vessels. Depending on the subtype, the treatment decision may vary. The most common subtype is AL amyloidosis. The backbone of therapy for AL amyloidosis is autologous stem cell transplantation (ASCT) with high-dose melphalan in eligible patients. A patient presenting with isolated AL amyloidosis of the bladder is described.

**Case Report**: A 71-year-old male patient was examined for a 15 day history of macroscopic painless hematuria. His medical history was not significant and he used no regular medications. Laboratory tests including complete blood count, biochemistry analysis and coagulation tests were normal. Urinalysis showed 103 erythrocytes, 15 leukocytes. Urine culture remained sterile. Abdomen CT showed thickening of the anterosuperior bladder wall with no abnormal findings in the upper urinary tract (Figure 1). Cystoscopic biopsy demonstrated acellular amorphous material under the bladder epithelium and in the vessel wall, which stained strongly positive with Congo red and showed strong lambda light chain monoclonality by immunohistochemistry (Figure 2A-B, 3). Serum and urine immunfixation electrophoresis showed no monoclonal chains. Bone marrow biopsy showed a polyclonal 5% plasma cell infiltration. F-18 FDG PET scan and echocardiography showed no abnormal findings. No other systemic involvement associated with AL amyloidosis was identified. Diagnosed with isolated bladder amyloidosis, induction treatment with bortezomib, cyclophosphamide and dexamethasone regimen was started. After 4 cycles, ASCT was performed with high dose melphalan (200 mg/m$^2$) as the conditioning regimen. Neutrophil and platelet engraftment were achieved on day +13 and day +14, respectively. No ASCT related complication observed.

**Discussion:** Isolated bladder amyloidosis is a rare manifestation of amyloidosis. Tissue biopsy is vital for the differential diagnosis of bladder carcinoma. Treatment varies according to subtype. Treatment of AL amyloidosis is similar to multiple myeloma. ASCT with high-dose melphalan increases survival in transplant eligible patients.

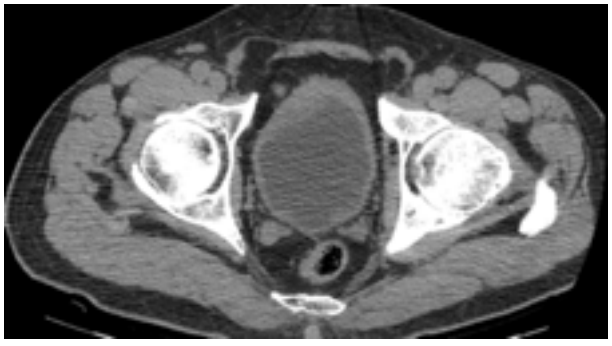

**Figure 1.** Thickened anterior-superior bladder wall in the patient with primary amyloidosis of bladder

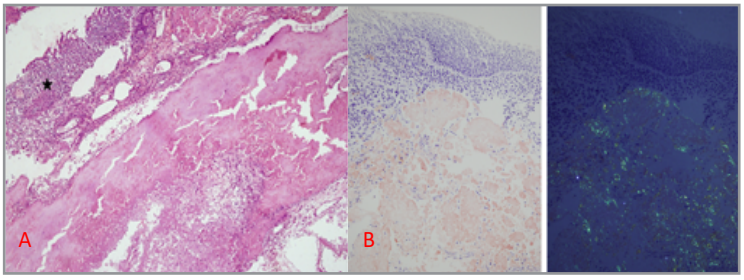


**Figure 2. (A)** Eosinophilic amorphous extracellular material beneath the surface epithelium (black star: hyperplastic urothelial epithelium) (HE).
**(B)** Congo red positive amorphous deposits. Apple green birefrengance under polarized light (right).

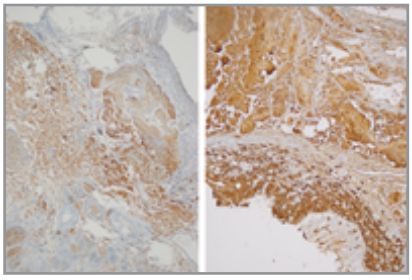

**Figure 3.** Deposits showing strong positivity for lambda light chain (right) whereas kappa staining is weak (left).

ABSTRACT

# Castleman's Disease Case with Concomitant HHV-8 and EBV Infection

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**Introduction:** Castleman's Disease (CD), also known as angiofollicular lymph node hyperplasia, is a heterogeneous lymphoproliferative disease with common histopathological characteristics. Although the relationship between human herpes virus 8 (HHV-8) and human immunodeficiency virus (HIV) to CD is better known, the role of Epstein-Barr virus (EBV) in CD is not clear. In this article, we referred to a young immunosuppressive case with HHV-8 and EBV infection.

**Case Report:** A patient who underwent a living donor liver transplant due to primary sclerosing cholangitis two years ago and was hospitalized for fever, and pneumonia consulted us because of his progressively deepening cytopenias. It was learned that the patient who had been treated with tacrolimus and everelolimus. In physical examination, there was anasarca-like oedema, lymphadenopathies, and palpable spleen. PET-CT showed that pleural and intra-abdominal free fluids, the diffuse lymphadenopathies with dimensions of 1-1.5 cm and SUVmax values between 2.4-6.5, increased spleen and bone marrow activity. At the bone marrow biopsy, no additional findings other than hypercellularity were detected, and the lymph node material of the patient was reported as "consistent with angiofollicular lymphoid hyperplasia". 1 mg/kg/day methylprednisolone treatment was started for the patient with pre-diagnosis of multicentric-CD/TAFRO syndrome. Hemophagocytic cells were detected in the new bone marrow aspiration and biopsy performed on the patient due to increased lactate dehydrogenase and ferritin levels with deepening cytopenias despite steroid use. Therefore, high-dose IVIG was given. The lymph node pathology referred to an external centre was compatible with HHV-8 positive CD. Although EBV IgG positivity and IgM negativity were detected previously, the patient's, whose EBV PCR level was found to be 10487 copy/ml, HHV-8 and IL-6 levels that were sent to an external centre simultaneously were also found to be high. The patient for whom treatment with Rituximab and Etoposide was planned died due to multi-organ failure.

**Discussion:** The acceleration of hematopoiesis and angiogenesis by VEGF concomitantly with IL-6 that was overproduced by B-cells in CD is accepted as the basic pathophysiology. While cases caused by immunosuppression and/or HHV-8 infection are generally in the preliminary plan in the literature, EBV-associated CD is very rarely mentioned. As far as we could detect, our case was the first case of multicentric-CD with both HHV-8 and EBV infection. The absence of such a case in the literature may be due to the fact that EBV infection was not investigated by PCR test in patients with previous EBV infection serology and/or diagnosed HHV-8.

# A Case of Acute Lymphoblastic Lymphoma Developing Thrombotic Microangiopathy after Hematopoietic Stem Cell Transplantation

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**Introduction:** Allogeneic stem cell transplantation (ASCT) is a key treatment option in many malignant hematological diseases. However, many transplant-related complications may develop in patients receiving ASCT. Transplant-associated thrombotic microangiopathy (TA-TMA) is a complication with a high mortality rate that is difficult to diagnose and manage, as it can be confused with other HSCT-related complications. Here, we present a case who developed TA-TMA in the second month of ASCT.

**Case Report:** A 55-year-old female was diagnosed with Philadelphia-chromosome positive B-ALL. HSCT was performed by applying a myeloablative preparation regimen (fludarabine+busulfan) from an unrelated 9/10 matched donor. ATG, cyclosporine and methotrexate were used in the prophylaxis of graft-versus-host disease (GVHD). Acute skin GVHD developed on the 23rd day post-transplant. One week after the lesions were controlled with steroid therapy, she was hospitalized with a preliminary diagnosis of gastrointestinal GVHD as she complained of diarrhea. Ruxolitinib was started in the patient, whose steroid dose was increased after endoscopic imaging and biopsy, and cyclosporine treatment was continued. Thrombocytopenia, reticulocytosis, high LDH, and low haptoglobin (0.01 g/L (0.3-1.9) developed and peripheral smear showed diffuse schistocyte and a few erythroblasts. Considering TA-TMA, cyclosporine was changed to MMF, GVHD treatment was continued. CMV viremia was detected and valganciclovir treatment started. Additionally, the ADAMS TS-13 activity of the patient, whose therapeutic plasma exchange was initiated, was found to be normal. Myocardial infarction secondary to hypotension and multiorgan dysfunction developed after massive gastrointestinal bleeding. Thrombosis also developed in the deep veins of the left upper extremity. After a while, confusion developed and no pathology was detected in the central nervous system imaging. Eculizumab treatment was started in the patient who did not benefit from plasma exchange. However, the patient, who was only in the first week of treatment, died of multiple organ failure.

**Discussion:** Often, there is a precipitating factor for TA-TMA such as priming regimens, calcineurin inhibitors, infections or GVHD. Although the definitive diagnosis is obtained through tissue biopsy, algorithms have been developed to help diagnose TA-TMA using various clinical and laboratory criteria due to the difficulty of this patient group. Primarily, correction of triggering factors in the treatment process should be done. The prominent options in the treatment process seem to be therapeutic plasma exchange, eculizumab, defibrotide, and rituximab. It is a transplant-related complication that is difficult to manage and has a high mortality. Therefore, early diagnosis and determination of the treatment strategy are of vital importance.

ABSTRACT

# A Case of Adrenoleukodystrophy, a Rare Disease in which Hematopoietic Stem Cell Transplantation is a Hope

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**Introduction:** Adrenoleukodystrophy (ALD), which is caused by the dysfunction of the peroxisomal membrane-associated adrenoleukodystrophy protein, results in the accumulation of exceptionally saturated, very long chain fatty acids in tissues, and is an X-linked neurodegenerative disease seen in approximately 1 in 21000 men. The ability to utilize hematopoietic stem cell transplantation (HSCT) to correct such rare inherited metabolic disorders that are caused by enzyme or protein defects has shown promise for ALD patients. Here, we wanted to talk about our HSCT experience in an ALD case.

**Case Report:** A 32-year-old male patient with the diagnosis of ALD was referred to us for HSCT in 2018 due to the progression of his neurological complaints and findings. The patient, who was diagnosed with adrenal insufficiency and followed up in 2005, was diagnosed with ALD in 2015 and was using a regimen of hydrocortisone, fludrocortisone, Lorenzo's oil, baclofen, and gabapentin. The patient presented with marked ataxic spasticity and clonus in bilateral lower extremities and could not mobilize without support. After applying to the patient a myeloablative regimen consisting of busulfan (3.2 mg/kg/day, between -8 and -6 for 3 days), fludarabine (30 mg/m$^2$/day, between -6 and -3 days), ATG (2.5 mg/kg/day, between -5 and -2 for 4 days), and cyclophosphamide (60 mg/kg/day -3 and -2 doses), 6 x 10$^6$ CD34+/kg stem cells were transplanted from an unrelated full-matched donor. Prophylactic immunosuppressive therapy was administered with methotrexate, cyclosporine, and mycophenolate mofetil. Immunosuppressive treatment of the patient who did not have significant signs of graft versus host disease after transplantation was stopped in a controlled manner starting from the third month. It was observed that the patient, who completed the third-year post-transplant without complications and used a single crutch, had a significant improvement in functions such as walking and climbing stairs, and his findings such as ataxia and spasticity were under control.

**Discussion:** Hematopoietic stem cell transplantation can be used therapeutically for many non-malignant diseases, including severe thalassemia syndromes, severe sickle cell disease, Hurler syndrome, and the cerebral form of adrenoleukodystrophy. Cerebral adrenoleukodystrophy is a devastating neurodegenerative form of ALD where only allogeneic hematopoietic cell transplantation has been shown to increase long-term disease stabilization and survival. Additionally, Cartier et al recently administered lentiviral-mediated genetically corrected autologous CD34+ cells after myeloablative chemotherapy to two male cALD patients who had failed to obtain HLA-matched allografts. It has been reported that both patients survived two years after autologous hematopoietic stem cell transplantation.

# Solitary Clear Cell Acanthoma Developing on the Background of Chronic Skin Graft-Versus-Host Disease: A Case Report

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**Introduction:** Clear cell acanthoma (CCA), first described by Degos et al. in 1962, is a rare, benign epidermal lesion. It is usually seen in middle age, peaking at 50-60 years, the female-male ratio is similar, and no ethnicity-related difference has been detected. Its etiopathogenesis is not clear. Here, we present a case of acute myeloid leukemia (AML) who underwent allogeneic stem cell transplantation (ASCT) and developed CCA, a rare skin lesion, while being followed up for chronic skin graft versus host disease (GVHD).

**Case Report:** In 1998, patient, who was diagnosed with AML when he was only 45 years of age, after induction and consolidation treatments underwent ASCT from his brother who was full-matched donor. The patient developed sclerodermic skin GVHD two years after transplantation and was given steroid-based immunosuppressive therapy for about one year. In 2014, 1 cm diameter, hyperkeratotic and vegetative raised nodular lesion was developed on the right ankle. The pathology showed that severe dysplastic changes with clear surgical margins. Patient, who was in remission for 20 years but was followed up with due to chronic skin GVHD, presented with a new tumoral lesion of around 3 cm in the right ankle in June 2019 (Figures A and B). There was extensive scar tissue in both lower extremities, especially on the ankles, due to previous surgery, ulcerated lesions, vegetations and GVHD. The lesion of the patient, who also had a history of dysplasia in a similar region, was biopsied again for the preliminary diagnosis of squamous cell carcinoma. His biopsy reported findings consistent with clear cell acanthoma. Mild to moderate dysplasia and keratoacanthoma were observed in the pathology after total excision of the primary mass. The patient's dysplasia continued to be positive at the surgical margin and was followed up without surgical expansion recommended (Figures C and D).

**Discussion:** Although CCA, which can present as solitary (most common) and as multiple forms, is detected in various regions, it is most frequently observed in the lower extremity (75%). Although our case is falls into the most common group with a solitary lesion and the lesion is located in the lower extremity, it is the first in the literature on the basis of the development of CCA in the background of chronic skin GVHD. It can be discussed whether skin GVHD is an etiological cause in the development of CCA.

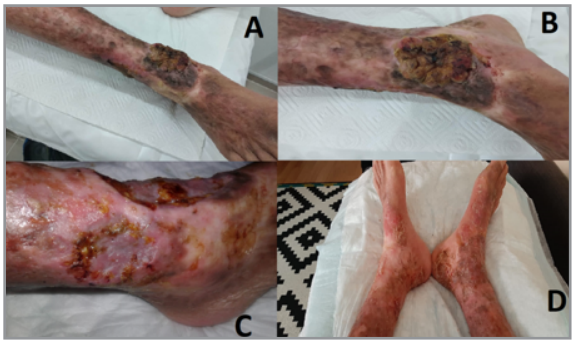


**Figure.** A, B, C, D

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