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A Case of Adult-onset Still's Disease Complicated with Macrophage Activation Syndrome and Diffuse Alveolar Hemorrhage

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Abstract

Adult-onset Still's Disease (AOSD) is a rare inflammatory disease of unknown etiology characterized by high fever, skin rash, arthritis, elevated ferritin and organ involvement. Macrophage Activation Syndrome (MAS) can be seen as a rare, potentially fatal complication in AOSD. Here, we presented a case who was diagnosed with MAS due to general condition disorder, increased ferritin and cytopenia while being followed up with the diagnosis of chronic articular form ESH, and then developed diffuse alveolar hemorrhage (DAH) after a short time. We aimed to draw attention to rare complications after AOSD with this case report that showed a dramatic response to corticosteroid and tocilizumab treatment.

Key Words: Adult-onset Still's Disease, Diffuse alveolar hemorrhage, Macrophage Activation Syndrome, tocilizumab

Makrofaj Aktivasyon Sendromu Ve Difüz Alveolar Hemoraji ile Komplike Olan Erişkin Still Hastalığı Olgusu

Özet

Erişkin Still Hastalığı (ESH) yüksek ateş, deri döküntüsü, artrit, ferritin yüksekliği ve organ tutulumuyla karakterize etyolojisi tam olarak bilinmeyen, nadir görülen inflamatuar bir hastalıktır. ESH'de nadirde olsa, potansiyel olarak ölümcül bir komplikasyon olarak Makrofaj Aktivasyon Sendromu (MAS) görülebilir. Biz burada kronik artiküler form ESH tanısıyla takip edilirken genel durum bozukluğu, ferritin artışı ve sitopeni gelişmesi üzerine MAS tanısı alan ve kısa bir süre sonra da Diffüz alveoler hemoraji (DAH) gelişen bir olguyu sunduk. Kortikosteroid ve tosilizumab tedavisine dramatik cevap veren bu olgu sunumu ile ESH sonrası gelişen nadir komplikasyonlara dikkat çekmeyi amaçladık.

Anahtar Kelimeler: Erişkin Still Hastalığı, Diffüz alveoler hemoraji, Makrofaj Aktivasyon Sendromu, tosilizumab

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INTRODUCTION

Adult-Onset Still's Disease is a systemic inflammatory disease characterized by high fever, transient salmon-colored skin rash, arthritis, leukocytosis, and elevated ferritin. Although the etiology of ESR is not clear, it is thought that viral infections may be the trigger. The diagnosis of the disease is clinical, with patients most commonly having a fever and typically rising in the evening (>39ºC) (1).

Macrophage Activation Syndrome (MAS), also known as Hemophagocytic lymphohistiocytosis (HLH), can be seen as a rare but serious, potentially fatal complication in the course of Adult Still's Disease (2). MAS is a clinical syndrome characterized by systemic hyperinflammation in which histiocyte proliferation cannot be controlled. High fever, hepatosplenomegaly, pancytopenia, deterioration in liver function tests are among the important clinical and laboratory features of MAS (3).

Diffuse alveolar hemorrhage (DAH) is a clinicopathological syndrome, which is defined as the passage of erythrocytes from alveolar capillaries into the alveoli, often leading to acute respiratory failure. The classic triad includes anemia, hemoptysis, and newly revealed bilateral alveolar infiltrates on chest X-ray (4).

We wanted to present the our case, which was complicated with MAS while being followed up with the diagnosis of AOSD and developed DAH after a short time. We aimed to draw attention to rare complications that showed a dramatic response to tocilizumab treatment.

CASE REPORT

A 69-year-old female patient, who was followed up with the diagnosis of chronic articular form AOSD, was hospitalized and followed closely due to increased joint pain, dyspnea, and general condition deterioration while continuing the maintenance treatment (40 mg/day methylprednisolone and methotrexate 15 mg/week). C-reactive protein (CRP): 84 mg/L and Ferritin > 40000ng/mL were found in routine blood tests performed at an external hospital. In our clinic, laboratory tests revealed hemoglobin (Hb): 8.7 g/dL platelets: 24000/mm3 Total Leucocyte count: 950/mm3, CRP: 259 mg/L.No atypical cells were seen in the peripheral blood smear test. After exclusion of infectious pathologies and malignancy, MAS as a complication of AOSD was diagnosed. Posteroanterior (PA) chest X-ray of the patient at the first presentation was given (Figure-1). In the treatment of the patient, 250 mg iv pulse steroid was initiated for 3 days, and then anti-IL-6 receptor antibody (tocilizumab) treatment at 8 mg/kg was planned. The patient, whose general condition and laboratory tests results improved after the tocilizumab treatment.

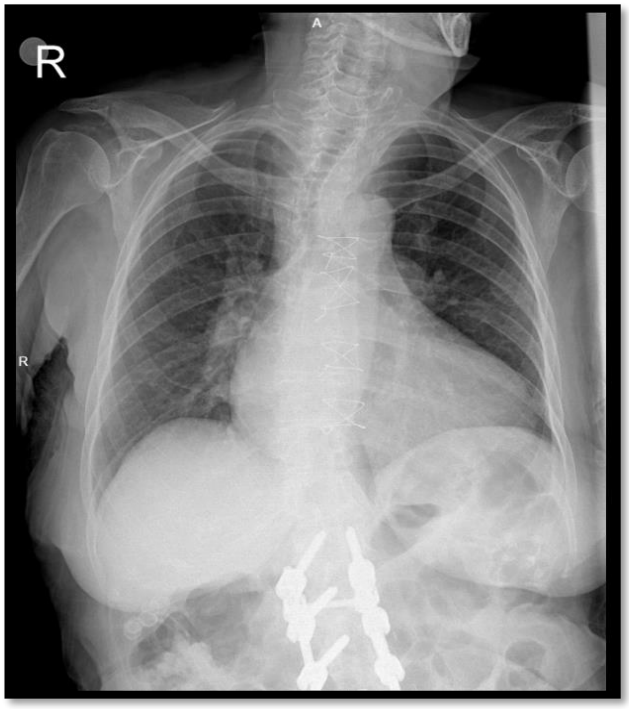

Figure-1. Posteroanterior chest X-ray of the patient at the first presentation

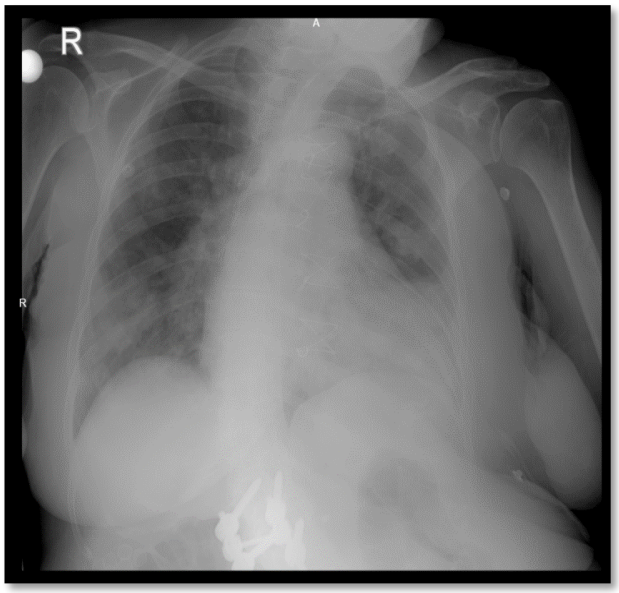

Figure-2. PA chest X-ray shows increased opacity in the middle-lower zone of the right lung and the middle-upper zone of the left lung after intro alveolar hemorrhage.

Ten days after discharge, the patient had a sudden onset of cough and shortness of breath. PA chest X-ray showed diffuse, patchy infiltration in both lung parenchyma, which was more prominent on the left (Figure-2). In the laboratory tests revealed, Hb: 6.7 g/dL platelet: 82000 / mm3. DAH was considered in the patient because of the sudden decrease in Hb and the patient's lung involvement. In her treatment, pulse steroid was given for 3 days and then 1 mg/kg per day oral dose was given. There was no decrease in the Hb value of the patient who was clinically stable in the follow-ups. It was observed that the opacities on the PA chest X-ray regressed (Figure-3).

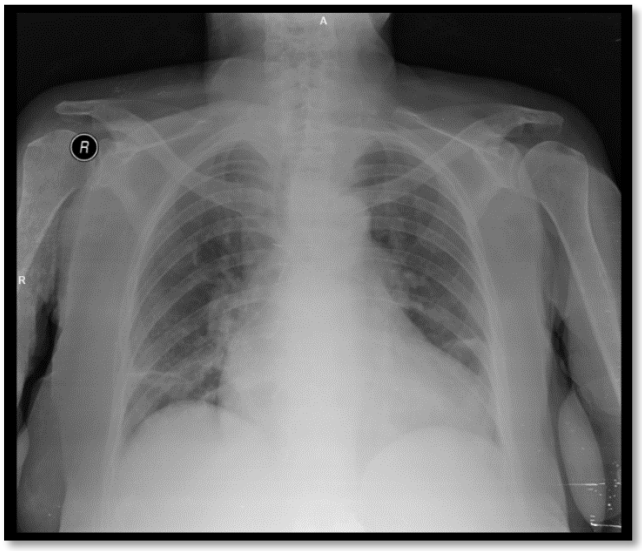

Figure -3. After the treatment, it is seen that the opacity in the middle lower zone of the right lung and the upper zone of the left lung disappeared.

Tocilizumab treatments were continued in the following months. Her disease responded well with those treatments; she achieved remission.

DISCUSSION

Adult-Onset Still's Disease is a rare systemic inflammatory disease of unknown origin, mostly seen in young adults. AOSD is a diagnosis of exclusion. Although there is no specific diagnostic

test, the diagnosis is made according to the Yamaguchi criteria (5). She was diagnosed to have AOSD based on Yamuguchi criteria after the exclusion of other potential diagnoses. Serum ferritin level is a useful tool for diagnosis.

Although macrophage activation syndrome has been reported during the course of many rheumatological diseases, it is a rare complication that can occur in AOSD MAS is a condition that can progress to multi-organ failure and can be fatal. Although bone marrow data are significant in the diagnosis of MAS, it was seen in 70% of the retrospective series (3,6).

Diffuse Alveolar Hemorrhage is a medical emergency that can also be seen in systemic vasculitis, drug-related factors and infections. Cough, hemoptysis, fever and dyspnea are common initial symptoms. However, hemoptysis may not be present in one third of the patients. In DAH, chest X-ray is nonspecific, and most usually show newly formed patchy or diffuse alveolar opacities (7). In the pathogenesis of DAH, IL-6 is believed to be overproduced in the acute phase of the disease. It is also thought that increased IL-18 levels in both blood and lungs may cause lung damage (8). In our patient, low hemoglobin level, dyspnea and cough were prominent. There were also patchy infiltrates in the chest X-ray. Initiation of systemic glucocorticoid therapy in DAH due to rheumatic disease is part of the accepted regimens (9). In our patient, a significant regression was observed in the clinic and X-ray after iv pulse steroid treatment.

Adult-Onset Still's Disease, generally responds well to nonsteroidal anti-inflammatory drugs and corticosteroids. Disease-modifying antirheumatic drug (DMARD) should be used in patients dependent or resistant to glucocorticoids. The greatest experience has been with methotrexate, it has been observed in studies that it is effective in reducing the steroid dose (10). In patients who do not respond to other treatments, anti-tumor necrosis factors such as IL-1 blocking anakinra, and sometimes infliximab and etanercept are also included in the treatment (11). In the literature, tocilizumab has shown benefit in a small randomized trial compared to placebo in AOSD. In resistant cases, tocilizumab can be used at an initial dose of 4 to 8 mg/kg every two to four weeks. The efficacy and safety of tocilizumab in patients with resistant AOSD, improvement was observed in the majority of patients in the fourth week (12). We also applied tocilizumab treatment at similar doses and intervals in our case.

CONCLUSION

Although Adult Still's Disease should be kept in mind in terms of making a differential diagnosis from other diseases and iniating treatment quickly. In this case, we presented a case of resistant AOSD that was resistant to systemic corticosteroids and complicated by MAS and DAH. The use of tocilizumab after corticosteroids in the treatment of such complicated cases seems promising.

Ethics Committee Approval: Case report

Informed Consent: Verbal and written consent was obtained from the patient who participated in this study

Author Contributions:

Concept: KAA, ÖSG, Design: KAA, Supervision: KAA, ÖSG, Data Collection and/or Processing: KAA, ÖSG Analysis and/or Interpretation: KAA, Writing: KAA, ÖSG.

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