Pulmonary Hemorrhage as the Initial Manifestation in Systemic Lupus Erythematosus with Active Nephritis: Case Report

Sistemik Lupus Eritematozusta Aktif Nefritle Birlikte İlk Bulgu Olarak Pulmoner Hemoraji

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ABSTRACT Pulmonary hemorrhage is the most devastating pulmonary complication of systemic lupus erythematosus. It has rarely been reported to occur as the initial presentation in lupus patients. We report a 50-year-old male who presented with pulmonary hemorrhage and nephritis as the initial manifestation of systemic lupus erythematosus. He presented with dyspnea, hemoptysis and pretibial edema. He responded to early intravenous pulse methylprednisolone therapy and cyclophosphamide therapy, but his pulmonary hemorrhage relapsed 20 days later. He was given intravenous methylprednisolone, intravenous cyclophosphamide and 5 sessions of plasmapheresis, resulting in temporal stabilization of his condition. Pulmonary hemorrhage in this connective tissue disease is an uncommon but serious complication with high mortality rates in spite of intensive treatment.

Key Words: Systemic lupus erythematosus; lung diseases; lupus nephritis

ÖZET Pulmoner hemoraji sistemik lupus eritematozusun en yıkıcı pulmoner komplikasyonudur. Lupus hastalarında ilk bulgu olarak pulmoner hemorajinin görülmesi nadir olarak bildirilmiştir. Biz, sistemik lupus eritematozusun ilk bulgusu olarak pulmoner hemoraji ve nefrit ile gelen 50 yaşında bir erkek hastayı sunduk. Hasta, dispne, hemoptizi ve pretibial ödemle başvurdu. Erken intravenöz pals metilprednizolon tedavisine ve siklofosfamid tedavisine yanıt verdi fakat pulmoner hemorajisi 20 gün sonra tekrarladı. İntravenöz metilprednizolon, intravenöz siklofosfamid ve 5 seans plazmaferez verildi, durumunda geçici bir düzelme gözlendi. Bu bağ doku hastalığında pulmoner hemoraji yoğun tedaviye rağmen yüksek mortalite hızı olan, sık görülmeyen fakat ciddi bir komplikasyondur.

Anahtar Kelimeler: Sistemik lupus eritematozus; akciğer hastalıkları; lupus nefriti

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Pulmonary hemorrhage (PH) is a rare and frequently fatal condition with mortality rates as high as 50-90%.1-3. The occurrence of massive PH as the initial and sole clinical manifestation of systemic lupus erythematosus (SLE) with active nephritis has rarely been reported.4,5 Treatment of PH in SLE remains controversial because no randomized trials are available. The experience from a number of case series suggests that high dosage of pulse corticosteroids with plasmapheresis, cyclophosphamide (CP) or both improves survival.1,6. We report a 50-year-old male with PH as the initial clinical manifestation of SLE, who had clinical response to early aggressive pulse methylprednisolone and CP therapy but whose PH relapsed later.

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CASE REPORT

A 50-year-old male patient was admitted to our hospital with complaints of dyspnea, hemoptysis, pretibial edema lasting for 10 days. On physical examination on admission, he was afebrile, tachycardic (102/min) and tachypneic (28/min) and his blood pressure was 170/100 mmHg. The palpebral conjunctiva was mild anemic. Pretibial pitting edema was observed. On auscultation, loud crackles were heard in the lower part of bilateral lungs. Initial laboratory data revealed the following: arterial blood gas pH 7.54; PaO_2 60 mmHg, $PaCO_2$ 45.1 mmHg; HCO_3 38 mmol/L, oxygen saturation (SaO_2) 90 %, hemoglobin 11.5 g/dL; hematocrit 35.3%; reticulocyte index 1; white blood cell count 11 400/mm³; platelet count 253 000/mm³; C-reactive protein 9.4 mg/dL; C3 71.9; C4 1.09 mg/dL; blood urea nitrogen 45 mg/dL; serum creatinine 0.9 mg/dL; urinalysis with proteinuria 4810 mg/dL and microscopic hematuria; antinuclear antibody (ANA) was positive with a titer of 1:320 homogenous pattern, anti-dsDNA was positive; anti-neutrophil cytoplasmic antibody (ANCA) was negative (MPO-ANCA-and PR3-ANCA); anticardiolipin antibodies IgG and IgM were negative. Electrocardiogram showed a normal sinus rhythm. Chest roentgenogram revealed diffuse reticular infiltration of both lower lungs. Chest computed tomography revealed bilateral pleural effusion, alveolar infiltration pattern of both lower lungs.

The diagnosis of vasculitis with PH and nephritis were made and intravenous pulse methylprednisolone therapy of 1 g was given immediately on the first day of admission.

Renal biopsy was performed on the third day of the patient's hospitalization. In addition to immune complex deposits plus mesangial proliferation on light microscopy, there were variable combinations of IgG,IgM,IgA,C1q,C4c (full-house IF) on immunofluorescence. These pathological findings were considered as lupus nephritis (stage IIB).

Intravenous CP 1 g and mesna 0.5 g to prevent the urotoxicity of CP were added on the third day after the pathology result. Intravenous pulse methylprednisolone therapy of 1 g was given daily for three consecutive days resulting in a dramatic improvement in his clinical, oxygenation, radiographic and hematological status on the 12th day. Twenty days after treatment, the patient was readmitted due to dyspnea, hemoptysis, increased pretibial edema, decreased hemoglobin levels, increased hematuria and proteinuria. He did not need mechanical ventilatory support. He was given intravenous methylprednisolone, intravenous cyclophosphamide and 5 sessions of plasmapheresis, resulting in temporal stabilization of his condition. He developed hemorrhagic cystitis on the second day of his second cyclophosphamide treatment. So that a third cyclophosphamide treatment was not used. He was given 2 g/day mycophenolate mofetil instead of cyclophosphamide. His hemoglobin level returned to normal, respiratory distress improved, hematuria and proteinuria decreased and no further episodes of hemorrhage occurred. He was discharged on the 15th day of admission in a stable condition.

DISCUSSION

SLE is an autoimmune chronic systemic disease which can involve several organs such as skin, lung and heart. Pulmonary disease is a common manifestation of SLE and is reported to occur in over half of the patients throughout the course of their disease.[7] Pulmonary manifestations of SLE can include a wide spectrum of diseases such a pleuritis, pneuomonia, pulmonary embolism, pneumothorax and pulmonary hemorrhage.[8,9]

Pulmonary hemorrhage is a rare and catastrophic complication in patients with SLE. Its frequency ranges from <2 to 4.7% in lupus patients.[1-3] Among the rheumatologic diseases, pulmonary hemorrhage most frequently occurs in patients with SLE and the systemic vasculitis.[10-12] In one study of biopsy confirmed PH, Wegener's granulomatosis (WG) was the most frequent underlying condition, followed by Goodpasture's syndrome, idiopathic pulmonary hemosiderosis and collagen vascular diseases. Overall, vasculitis (either WG or microscopic polyangiitis) was the most frequent, representing 41% of cases.[12] Testing for ANCA,

anti-glomerular basement membrane antibodies and anti-phospholipid antibodies should be obtained to exclude other etiologies such as systemic vasculitis.[13]

In most patients with PH, the diagnosis of SLE has already been established. In the majority of cases, the diagnosis of SLE is already established an average of 36 months before occurrence of pulmonary bleeding.[14] PH, as initial clinical manifestation of SLE, like in our patient, is rarely seen and often lethal with a reported mortality rate as high as 70-90%.[15] Diagnosis of PH is suggested by hemoptysis, cough, progressive dyspnea, generalized fatigue, abrupt fall in hemoglobin and diffuse bilateral alveolointerstitial infiltrates on initial chest radiograph.[1,2] Severe nephritis is frequently found at the time of PH, being the most common concurrent systemic finding in SLE patients with PH.[15] Our patient also had abnormal renal function we suggested the possibility of lupus nephritis.

A kidney biopsy was performed in our patient, the pathology revealed lupus nephritis. In SLE patients with PH, there was no clear indication about which treatment modality influenced the outcome of the patient. Corticosteroids were the mainstay of therapy, but additional immunosuppressive treatments and supportive ventilation were often required.[16] Immunosuppresive agents such as CP, azathioprine, mycophenolate mofetil and etanercept may be used in PH, especially when the condition is severe and when first-line therapy with steroids has failed.[3,17] The use of CP in SLE patients with PH is still controversial.[15] Plasmapheresis is added if the patients have an inadequate clinical response to high-dose corticosteroid and CP therapy.[1]

In summary, PH is a rare but lethal complication of SLE. A rapid and aggressive treatment with high-dose corticosteroids and cytotoxic agents, such as CP, mycophenolate mofetil may benefical in SLE patients with PH.

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