Idiopathic pulmonary hemosiderosis in an adult patient responded well to corticosteroid therapy

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ÖZET

Erişkin bir hastada kortikosteroid tedavisine iyi yanıt veren idiyopatik pulmoner hemosiderozis

İdiyopatik pulmoner hemosiderozis (İPH) tekrarlayan ya da kronik hemoraji ile karakterize etyolojisi bilinmeyen çok nadir görülen bir hastalıktır. Hastalığın klinik seyri hastadan hastaya değişebilmektedir, ancak genel olarak hastalığın prognozu kötüdür. Tedavisi semptomatik ve destekleyicidir. İPH tedavisi için kortikosteroidler ve diğer immünsüpresif ilaçlar kullanılır. Çocuklarda yaygın olarak gözlenebilir ancak erişkinlerde de görülür. Hastalığın klinik belirtileri sebebi bilinmeyen demir eksikliği anemisini, hemoptiziyi, dispne öksürüğü ve akciğer grafisinde parankimal lezyonları içerir. Erişkinlerde çok nadir görüldüğünden ve hastalığın klinik seyri kişiden kişiye değişebildiğinden klinik ve radyolojik olarak steroid tedavisine iyi yanıt veren İPH'li erişkin bir hastayı sunduk.

Anahtar Kelimeler: *Hemosiderozis, akciğer, YRBT, steroid.*

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SUMMARY

Idiopathic pulmonary hemosiderosis in an adult patient responded well to corticosteroid therapy

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Idiopathic pulmonary hemosiderosis (IPH) is a very rare disorder of unknown etiology characterized by recurrent or chronic hemorrhage and accumulation of hemosiderin in the lung parenchyma. It is most common in children but can occur in adults. Clinical manifestations of the disease include iron deficiency anemia without any known cause, pulmonary symptoms such as hemoptysis, dyspnea and cough, and parenchymal lesions on chest X-ray. The clinical course of the disease may vary from patient to patient however, in general, the prognosis of the disease is worse. Treatment is symptomatic and supportive. Corticosteroids and other immune suppressive agents were used for the therapy of IPH. Since it is seen rarely in adults and the clinical course of the disease vary from patient to patient we presented an adult male patient with IPH responded well to steroid therapy clinically and radiologically.

Key Words: *Hemosiderosis, lung, HRCT, steroid.*

Idiopathic pulmonary hemosiderosis (IPH) is a very rare disorder of unknown etiology characterized by recurrent or chronic hemorrhage and accumulation of hemosiderin in the lung parenchyma. IPH is considered to be an immune mediated disease even though its etiology is unknown. IPH is a disease of childhood and usually occurs in children before 10 years of age but can occur in adults. It has an incidence of 0.24 and 1.23 in some selected populations there is no gender difference in prevalence. Clinical manifestations of the disease include iron deficiency anemia without any known cause, pulmonary symptoms such as hemoptysis, dyspnea and cough, and parenchymal lesions on chest X-ray (1,2).

The clinical course of the disease may vary from patient to patient however, in general, the outcome of the disease is worse. Death often results from massive pulmonary hemorrhage. Treatment is symptomatic and supportive. Corticosteroids (CS) and other immune suppressive agents such as azothioprine, hydroxtychloroquine, cyclophosphamide were used for the therapy of IPH (1-8).

Since it is seen rarely in adults and the clinical course of the disease vary from patient to patient we presented an adult male patient with IPH responded well to steroid therapy clinically and radiologically.

CASE REPORT

A twenty years old male patient referred to our service for dyspnea, palpitation and easy fatigability. His complaints started three weeks before admission. Treatment with antibiotics had not improved his symptoms. On admission the patient was afebrile (36.7°C) but looked fatigue and his skin was pale. The blood pressure was 100/60 mmHg, the heart rate was 125/min and rhythmic. Examination of the lungs revealed crepitations on auscultation on both hemi thoraces. Complete blood count revealed anemia with a hemoglobulin value of 8.29 g/dL and with a haematocrit value of 28.4%. Platelet count was 518.000 µg/L and leucocyte count was 10.100 µg/L. Blood chemistry was normal except low serum lipid values. Serum Fe level was 15 µg/dL (range 53-167) and serum Fe (transferrin) satu-

ration was 5.30% (range 20-50). Serum ferritin, folat and B-12 values as following 91.85 ng/mL, 8.75 ng/mL and 315.3 pg/mL respectively.

An X-ray of the chest revealed bilateral subtle reticulonodular infiltration particularly on middle and upper lung zones (Figure 1). A high resolution computerized tomograph (HRCT) scan showed micronodular infiltration of alveolar pattern in all segments of both lungs. Some nodules became confluent in some areas and ground glass opacity was seen among the nodules (Figure 2). The distribution of micronodules compatible with a random pattern since the nodules appeared evenly distributed throughout the lung, and involve both lungs almost symmetrically however there was the lack of the subpleural predominance often seen in patients with a perilymphatic distribution even though some of the nodules were seen to involve the pleural surfaces and fissures.

Rheumatological markers (antinuclear, antineutrophil cytoplasmic, anticardiolipin, ant-jo-1 and anti-dsDNA, anti-ssA (Ro), anti-Sm, anti-ssB (LA), antisentromer, anti-Sol-70 and anti-LKM-1 antibodies) were all negative and serum rheumatoid factor and immunoglobulin levels were also

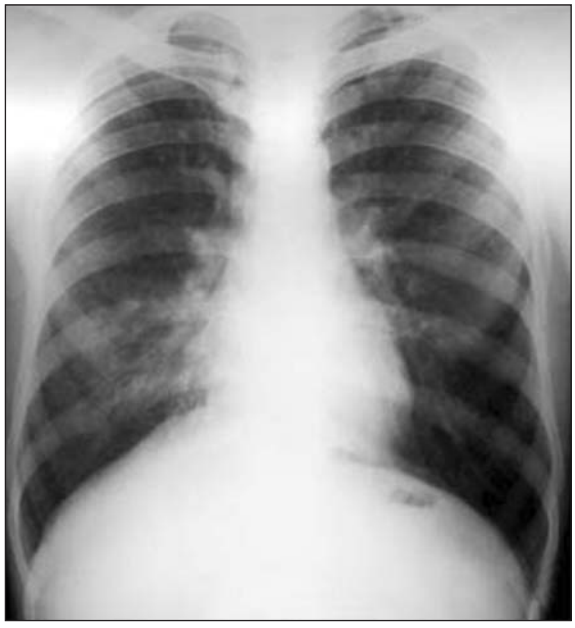

Figure 1. Bilateral subtle reticulonodular infiltration particularly on middle and upper lung zones is seen on admission chest X-ray.

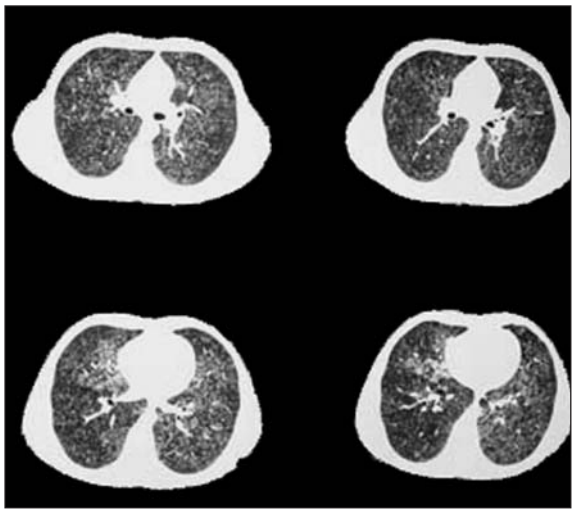

Figure 2. A HRCT scan showed micronodular infiltration of alveolar pattern in both lungs. Some nodules became confluent in some areas and ground glass opacity was seen among the nodules.

in normal limits. A skin prick test was applied and an atopy was not detected. Renal function was normal and serum antiglomerular antibodies were negative. Cardiac examination and an echocardiogram of the patient were normal. Spirometric values were in normal limits except a FEF_{25-75} value of 70% predicted and arterial blood gas analyses revealed hypoxemia and hypocapnia.

Supplemental blood had to be infused to the patient two times since serum Hb values dropped lower than 8 g/dL and, the patient had palpitations and orthostatic hypotension.

Fiberoptic bronchoscopy performed in two different times. Bronchial mucosa was observed as hyperemic, edematous otherwise normal. Bronchial lavages revealed no evidence of acid-fast organism, fungi or malignancy and no haemosiderin laden macrophages were detected. However transbronchial biopsy specimens revealed peribronchial hemosiderin laden macrophages but it was not diagnostic. Open lung biopsy was performed and histopathological examination of wedge biopsy was consistent with pulmonary hemosiderosis (PH) and focal interstitial thickening but there was no evidence of pulmonary vasculitis, nonspecific/granulomatous inflammation, or deposition of immunoglobulins. In Figure 3, histopathological lung specimen

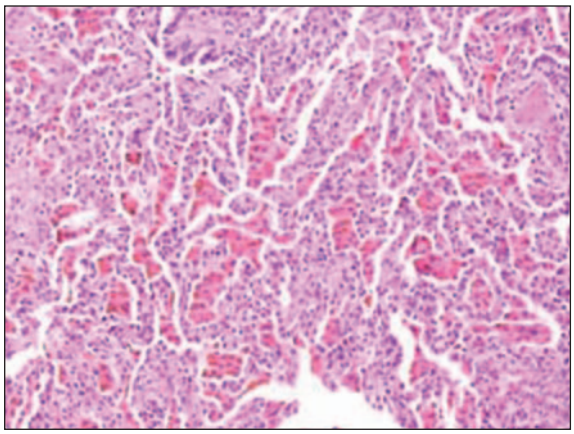

Figure 3. Histopathological lung specimen showing alveoli filled with collections of hemosiderin-laden macrophages.

showing alveoli filled with collections of hemosiderin-laden macrophages is seen. In Figure 4, iron deposition in macrophages with prussian blue is seen. A duodenal biopsy was performed, it was consistent with low grade nonspecific duodenitis. In addition, serum antigliadin IgA and antigliadin IgG antibodies were negative.

Since no cause was found to be responsible for this entity, we considered the PH as idiopathic. After the diagnosis of IPH had been made, the patient was started on prednisolon 1 mg/kg. A control HRCT obtained one month after steroid therapy revealed a marked regression of aforementioned lesions seen in previous HRCT (Figure 5). Chest X-ray was also improved (Figure 6). The patient was checked four months after therapy

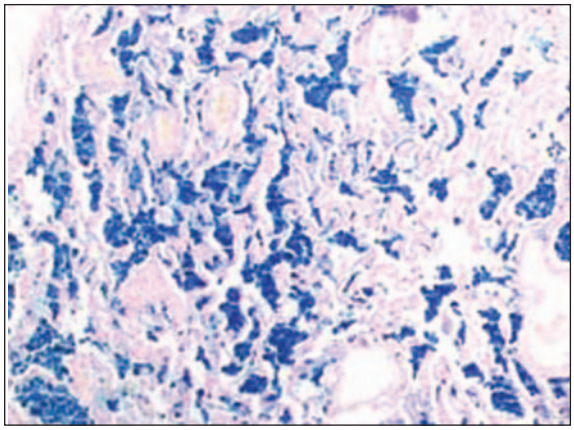

Figure 4. Iron deposition in macrophages with prussian blue.

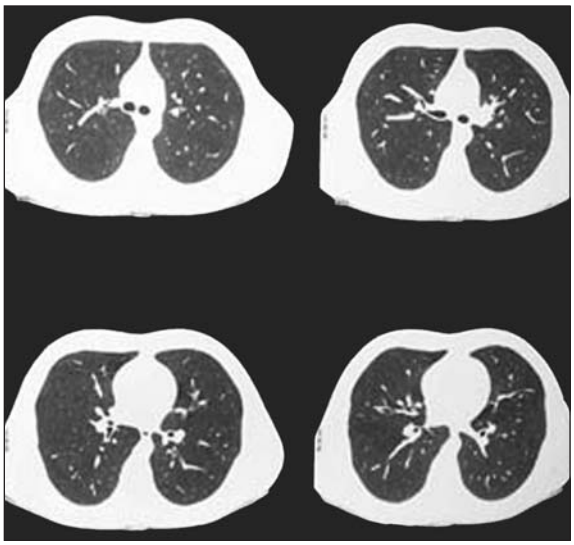

Figure 5. Abnormalities were markedly regressed on control HRCT.

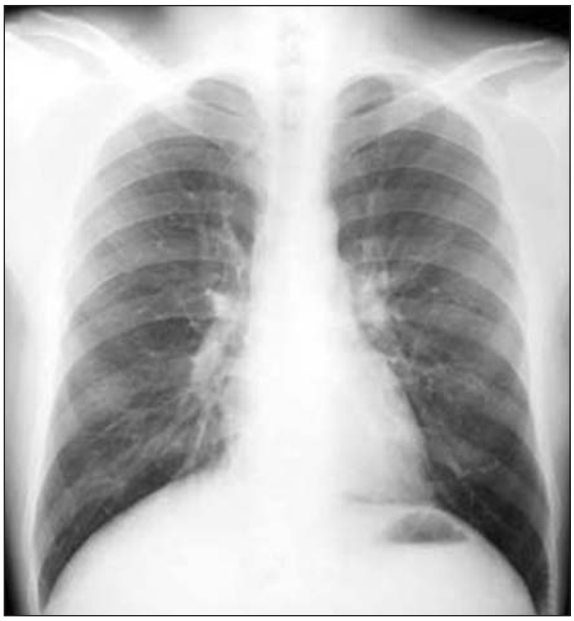

Figure 6. Abnormalities were regressed on control chest X-ray.

with a new HRCT and no new lesion was seen. The patient was also clinically improved and had no complaints except some skin lesions attributed to CS use.

DISCUSSION

We have shown an adult case with a rare disorder with its clinical presentation, course and an immediate response to CS treatment. Our pati-

ent showed a marked improvement clinically and radiologically with the CS therapy suggesting a good prognosis compatible with the reports that an early response to steroids might be seen however we found the response of our patient to CS therapy is dramatic. On the other hand, IPH generally results in chronic respiratory failure due to progressive pulmonary fibrosis caused by recurrent intrapulmonary hemorrhage and in some patients, it results in sudden death from acute pulmonary hemorrhage (1-8). Thus, even an immediate response to CS, we could not predict the prognosis of our patient.

Excluding the patients dying suddenly due to acute hemorrhage, theoretically the fibrosis caused by recurrent hemorrhage might be prevented particularly by using CSs in a general meaning by using immune suppressive agents such as azothioprine, hydroxtychloroquine, cyclophosphamide. We believe this condition was somewhat valid for our case since lesions seen HRCT almost completely regressed. In addition, arterial blood gas values improved and became normalized. In an other point of view, if we consider the decrease in serum Hb values as a clue of intra pulmonary hemorrhage in IPH, our patient's serum Hb values did not decrease after initiation of CS therapy however before commencement of the therapy, supplemental blood had to be infused to the patient two times. Cessation of the drop in serum Hb values, alone, might be considered as an indicator of the improved clinical picture of our patient. Supporting this finding it was suggested that patients having lower Hb levels tend to have shorter survival than patients having relatively higher Hb (3).

Histopathologically diffuse infiltration with hemosiderin-containing macrophages is characteristic, however hemosiderin deposition occurs in many other disorders. Pulmonary capillaritis (neutrophilic infiltration of alveolar septa) may occur. Patients who live for several years may develop pulmonary fibrosis due to blood in interstitial spaces (9). In our patient there was some evidence of mild fibrotic process on obtained wedge biopsies.

On the other hand, the HRCT findings of IPH were not fully described in the current literature. Different HRCT patterns of IPH were reported. Ground glass opacity micronodules, interlobular septal thickening, peribronchovascular interstitial thickening and consolidation might be seen. On HRCT, acute hemorrhage is characterized by ground glass opacity or consolidation. In the subacute/chronic phase, discrete pulmonary nodules of almost uniform size distributed throughout the lungs is a characteristic feature (10-12). In our case mainly a randomly distributed micronodular and confluent nodular appearance was outstanding and some other findings such as ground glass opacity among the nodules, peribronchovascular interstitial thickening and some fresh parenchymal bants were also detected but no features of fibrosis such as honeycombing, bronchiectasis and no kinds of emphysema were detected. Our case was consistent with subacute/chronic phase of IPH radiologically. However findings on HRCT immediately subsided during steroid therapy.

Even our patient with IPH responded well to steroid therapy clinically and radiologically in a short-term and despite some reports indicating steroids might cause substantial improvements in recovery of symptoms and early prognosis, effect of steroids on long-term prognosis is not known. There are some survival data about IPH in one of them five-years survival was found as 86% and in another, it was shown that average survival was 2.5 years after onset of symptoms (2,3). However, these data could not lead us to suggest effect of steroids on long-term prognosis.

As a result our case, again, reminds us to bear IPH in mind in the differential diagnosis of micronodular appearance on HRCT particularly in an adult patient with associative anemia. Secondly this study indicates a good example of well response to CS therapy clinically and radiologically in short-term in an adult patient with IPH.

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