Pulmonary hemosiderosis with juvenile rheumatoid arthritis: a case report

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Pulmonary hemosiderosis may rarely be associated with juvenile rheumatoid arthritis or can develop during the course of the disease.

We present a three-year-old boy with severe iron deficiency anemia (without any pulmonary symptoms) and arthralgia at the time of diagnosis. Two years after the initial diagnosis he developed pulmonary hemosiderosis and pauciarticular type of juvenile rheumatoid arthritis which progressed to seronegative polyarticular juvenile rheumatoid arthritis. He responded very well to prednisolone and was maintained well on low-dose alternate-day prednisolone and naproxen sodium treatment. This is the only case of association of these two diseases in our experience in both the Pediatric Rheumatology and Pediatric Respiratory Diseases Departments.

Key words: pulmonary hemosiderosis, juvenile rheumatoid arthritis, associate disease.

Pulmonary hemosiderosis is characterized by an abnormal accumulation of hemosiderin following diffuse alveolar hemorrhage. It may occur either as a primary disease of the lungs, idiopathic pulmonary hemosiderosis (IPH) or as secondary to cardiac, hemorrhagic and collagen diseases[1].

Juvenile rheumatoid arthritis (JRA) is the most frequent pediatric collagen disease. Extra-articular manifestations of JRA include uveitis, pericarditis, myocarditis, central nervous system disease, renal glomerulitis, pleuropulmonary disease and pulmonary hemosiderosis[2-7]. We report a patient with pulmonary hemosiderosis associated with pauciarticular JRA and progressed to polyarticular JRA.

Case Report

A three-year-old male patient presented with fatigue, tachycardia with a heart rate of 125/minute, and tachypnea with a respiratory rate of 38/minute. He had a low-grade systolic murmur; the remainder of the physical examination was unremarkable. The laboratory investigations revealed a hemoglobin (Hb) of 2.3 g/dl, hematocrit of 12%, white cell count of 18,000/mm^3, reticulocyte count of 3.85% and hypochromic microcytosis on peripheral smear. The serum iron level and iron binding capacity were 13 mg/dl (normal 60-80) and 404 mg/dl (normal 200-400), respectively, with a transferrin saturation of 3%. The serum ferritin level was 32.1 ng/ml (normal 17-230). The direct and indirect Coombs' tests were negative and the hemoglobin electrophoresis and osmotic fragility tests were normal. The chest X-ray was normal. He was diagnosed as having iron deficiency anemia of unknown cause. The patient responded to iron replacement therapy. Seven months later the patient presented with anorexia and cough. His hemoglobin level and hematocrit were normal (14.2 g/dl and 42%, respectively). Two years later the patient was found to have arthritis and arthralgia of this right knee. He had minimal clubbing and both the liver and spleen were palpable 2 cm below the costal margin. His Hb was 8.6 g/dl, white blood count 12,300/mm^3, erythrocyte sedimentation rate (ESR) 56 mm/hour and C-reactive protein (CRP) (+). Antinuclear antibody test and rheumatoid factor were

negative. Serum complement 3 and 4 were normal. Within a month he developed arthritis of right elbow and ankle along with right knee. His ESR and CRP levels remained elevated. He was put on non-steroidal anti-inflammatory treatment with a diagnosis of JRA. Two months later the patient was admitted to hospital with chest pain and cough. His physical examination revealed tachycardia, tachypnea, clubbing, suprasternal and intercostal retractions and hepatosplenomegaly. Chest X-ray revealed bilateral diffuse reticulo-nodular infiltrates (Fig. 1) with a hemoglobin level of 6 g/dl. His family did not give permission for a lung biopsy but hemosiderin-laden macrophages were found in the gastric washing. Further laboratory examinations revealed serum anti-glomerular basement membrane antibody (anti-GBM) and anti-nuclear cytoplasmic antibody (ANCA) as negative. The pulmonary function test by spirometry (Mirato AS-600 Autospiro) revealed a mild obstructive and moderately restrictive pattern. He was put on 2 mg/kg/day prednisolone with a diagnosis of pulmonary hemosiderosis and JRA. He responded to prednisolone showing a normal chest X-ray (Fig. 2) and pulmonary function test, and the hemoglobin level increased to 12.7 g/dl. The patient continued to have joint symptoms and progressed to polyarticular JRA and was put on naproxen sodium 10 mg/kg/day with alternate-day 5 mg prednisolone. On long term follow-up of five years there was no recurrence of either arthritis or pulmonary hemosiderosis.

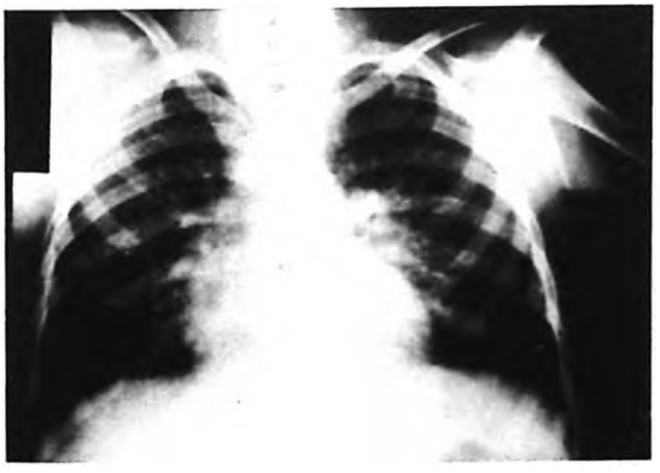

Fig. 1. Chest X-ray showing bilateral fine reticulonodular infiltrates in mid and lower zones.

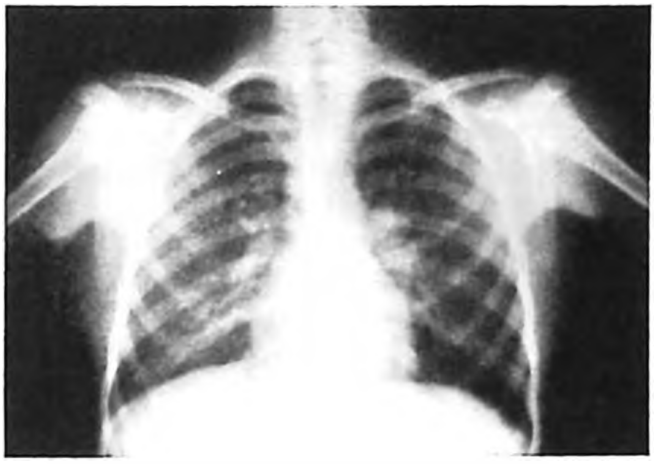

Fig. 2. Note the desappearance of diffuse reticulonodular infiltrates after prednisolone treatment.

Discussion

Manifestations of the pleuropulmonary disease in JRA include transient pneumonitis, interstitial reticular and nodular infiltrates, pleural effusion and patchy pleural infiltrates and, very rarely, hemosiderosis[2,6,8]. Most RA patients with signs of pleuropulmonary disease have other clinical evidence of RA, but in some instances the lung disorder may precede the usual clinical manifestations of RA. In such circumstances, the diagnosis is suggested by serologic tests or may not be suspected until the other obvious manifestations of RA have become evident.

Idiopathic pulmonary hemosiderosis (IPH) is a disease of unknown etiology, usually occurring in children and young adults. Even though the favorable results of immunosuppressive therapy in this disease support the presumed association of the disease with an autoimmune disturbance, this does not necessarily indicate that idiopathic pulmonary hemosiderosis itself is due to an immune disturbance[3]. Damage to pulmonary alveolar tissue by a variety of agents might initiate in some individuals an autoimmune process, or patients with IPH may have a type III immune response with irregular deposition of immune complex material along the basement membrane. In these cases there is no specific antigen-antibody reaction to basement membranes as seen in Goodpasture's syndrome, but instead the basement membranes appear to act as a site for deposition of toxic complexes resulting in tissue damage[3]. On the other hand, whether or not immune deposits in the lung are necessary for pulmonary hemorrhage is controversial. Pulmonary hemorrhage can develop with no detectable immune complex deposits in lung[9].

The association of IPH and RA was first noted by Karlish[4]. Lemley and Katz[3] claimed in their report that as in three other previously reported cases, pulmonary hemosiderosis was not idiopathic but rather a presenting manifestation of rheumatoid arthritis. JRA also may rarely present with pulmonary hemorrhage in children[2,8]. Furthermore, Cunnigham et al.[10] reported a five-year-old female with JRA who developed pumonary hemosiderosis and hematuria two years later and died in respiratory failure. Our patient first presented with iron deficiency anemia with no accompanying pulmonary findings until about seven months later when he had only a cough. Two years later he had developed pauciarticular JRA that progressed to polyarticular JRA. The full-blown picture of alveolar hemorrhage was seen two months after the joint manifestations. He is the only patient to present with JRA and pulmonary hemosiderosis in our experience at the Pediatric Nephrology and Rheumatology Department in the last 20 years. He is also the only patient to have the association out of 23 patients with idiopathic pulmonary hemosiderosis treated between 1980-1998 at the Pediatric Respiratory Diseases Department[11].

Although the significance of the association remains to be elucidated, this case, as do the others previously published, shows the possibility of the association of pulmonary hemosiderosis and rheumatoid arthritis. Associated diseases should be borne in mind in severe iron deficiency anemia of uncertain etiology as well as in IPH.

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