Severe iron deficiency anemia in a child with idiopathic pulmonary hemosiderosis: a case report

Murat Derbent, Figen Özçay, Ümit Saatçi, Namık Özbek

Department of Pediatrics, Başkent University Faculty of Medicine, Ankara, Turkey

SUMMARY: Derbent M, Özçay F, Saatçi Ü, Özbek N. Severe iron deficiency anemia in a child with idiopathic pulmonary hemosiderosis: a case report. Turk J Pediatr 2002; 44: 258-260.

We report a case of idiopathic pulmonary hemosiderosis (IPH) in a three-year-old male patient who presented with severe iron deficiency anemia. The child had been diagnosed with iron deficiency anemia nine months earlier and had received multiple blood transfusions, but the cause of his anemia had not been established. The diagnosis of IPH was made after a biopsy of the left lung showed large numbers of hemosiderin-filled macrophages in the alveoli. He did not respond to standard dose corticosteroid (CS) treatment (2 mg/kg/d). However, high-dose short-term CS treatment was successful in two episodes of acute respiratory hemorrhage in this patient. We conclude that IPH should always be considered when investigating the cause of iron deficiency anemia. A more rapid diagnosis in this case could have prevented unnecessary investigations and blood transfusions. We also suggest that high-dose short-term CS treatment should be kept in mind, especially in patients who do not respond to a standard dose.

Key words: idiopathic pulmonary hemosiderosis, high-dose corticosteroids, iron deficiency anemia.

Idiopathic pulmonary hemosiderosis (IPH) is a rare disorder of unknown etiology that is manifest by iron deficiency anemia, recurrent or chronic pulmonary symptoms such as cough and hemoptysis, and diffuse pulmonary infiltrates[1]. The incidence of IPH is reported to range from 0.24 to 1.23 cases per million[2]. Although its specific cause is unknown, the disease is considered to be an immune-mediated condition[2]. The clinical course of IPH is highly variable, and most patients continue to experience episodes of pulmonary hemorrhage despite treatment. Affected individuals often present with anemia, coughing and radiological evidence of pulmonary infiltrates. Symptoms such as fever, respiratory distress and clubbing are usually seen at later stages of the disease, but may also be the first signs observed[2,3].

In this report, we describe a pediatric patient with IPH who presented with severe iron deficiency anemia.

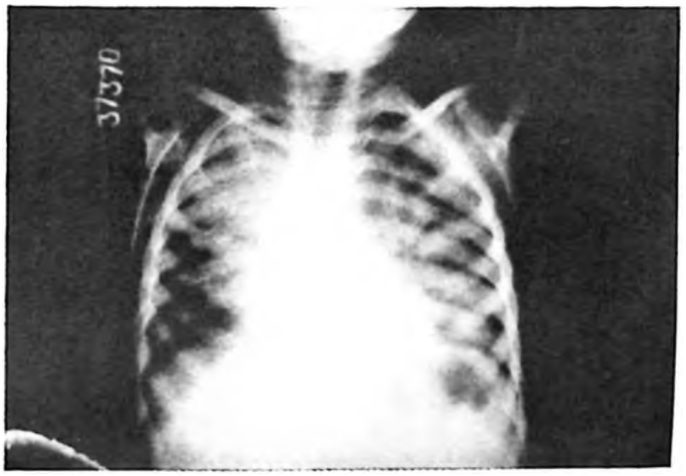
Case Report

A three-year-old male patient was referred to our hospital for severe anemia of unknown cause. He had a nine-month history of pallor and fatigue that had gradually worsened with time, and was suffering from severe fatigue at presentation. There was no history of hemoptysis or dyspnea. The patient's anemia had been investigated at a number of other hospitals. These work-ups had revealed iron deficiency anemia and the child had received multiple blood transfusions, but the underlying problem could not be determined.

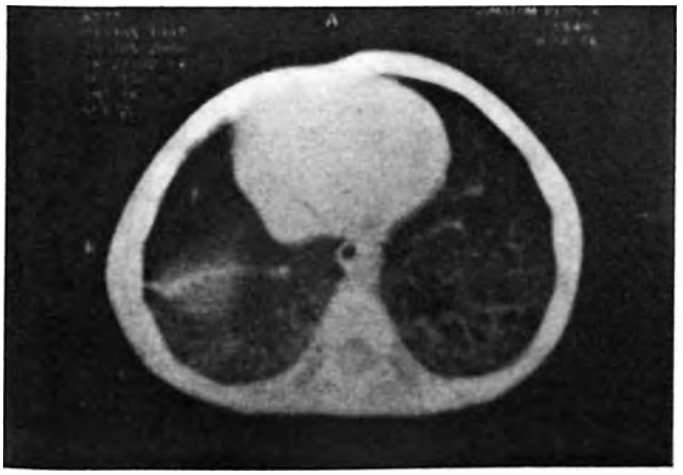
Physical examination at our center revealed marked palor, dyspnea, tachycardia, ronchi, a symmetrical pattern of decreased breath sounds over both lung fields and clubbing of the fingers. The child's size and weight were within normal limits for his age. The laboratory findings were as follows: hemoglobin 4.6 g/dl, hematocrit 14.6%, leukocyte count 12.4×10^9/L (differential

This study was presented at the IVth National Hematology Congress, 1-4 November 2000, İzmir, Turkey

85% polymorphonuclear leukocytes, 15% lymphocytes), platelet count 240x10^9/L, reticulocyte count 4.6%, serum iron 28 μg/dl (normal, 50-140 μg/dl), serum iron binding capacity 410 μg/dl (normal 130-350 μg/dl), and ferritin 293 ng/ml (normal, 15-300 ng/ml). A chest X-ray (Fig. 1a) and thoracic computed tomography (Fig. 1b) demonstrated a symmetrical diffuse pattern of pulmonary infiltrates bilaterally. Examination of gastric aspirate specimens showed no hemosiderin in the macrophages present, but biopsy of the left lung revealed large numbers of hemosiderin-filled macrophages in the alveoli (Fig. 2). A direct Coombs' test, and testing for cold agglutinins, antinuclear antibody, anti-DNA antibody and glomerular basement membrane antibody were all negative. Complement 3 and 4 levels and urine analysis were normal. A radioallergosorbent test (RAST) for cow's milk indicated the patient was sensitive to milk protein.



(a)



(b)

Fig. 1a and 1b. The patient's chest X-ray (1a) and computed tomography (1b) show a symmetrical diffuse pattern of pulmonary infiltrates bilaterally.

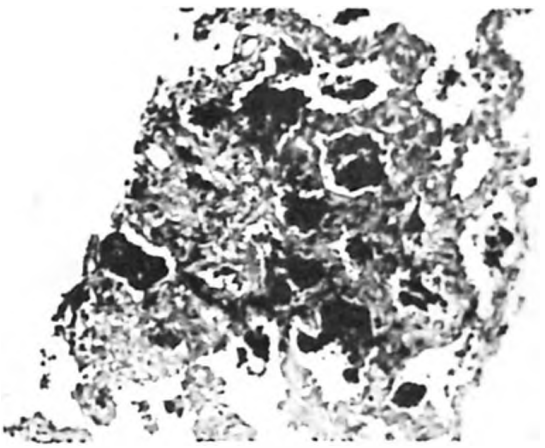


Fig. 2. Biopsy of the left lung showed the large numbers of hemosiderin-filled macrophages in the alveoli (Prussian blue, x 115).

Once the diagnosis of IPH was confirmed by the lung biopsy and other findings, we initiated a course of standard-dose corticosteroid (CS) treatment (2 mg/kg/d). Since the patient's RAST for cow's milk was positive, dietary restriction of milk and milk products was another important element of treatment. However, the patient encountered two episodes of acute respiratory hemorrhage and distress under this treatment regimen. On both occasions, he responded to high-dose short-term methylprednisolone, given as 30 mg/kg for 3 days, 20 mg/kg for 4 days, and tapered to a 2 mg/kg maintenance dose.

Discussion

Idiopathic pulmonary hemosiderosis is a disorder of unknown etiology that is characterized by recurrent or chronic hemorrhage and accumulation of hemosiderin in the lung alveoli. The disease can affect individuals of any age, from neonates through to adults, and occurs with equal frequency in males and females[3,4]. The many experimental, morphologic, and ultrastructural studies that have been done of IPH have not revealed the mechanisms behind this condition[3]. The response to immunosuppressive therapy in some patients suggests that the disease may have an immunological basis[2,5]. In addition, some familial cases have been reported, and Kiper and colleagues[3] found that 43% of their IPH patients had consanguineous parents, indicating a possible genetic component as well[2,6].

The three main findings associated with IPH are as follows: 1) iron deficiency anemia of no other apparent cause; 2) pulmonary symptoms,

including cough, dyspnea and hemoptysis; and 3) transient diffuse pulmonary infiltrates or a miliary pattern on the chest radiograph. Diagnosis of IPH is established only when hemosiderin-filled macrophages are identified in multiple gastric aspirate specimens and/or on histological examination of a lung biopsy[3]. Our patient presented with severe iron deficiency anemia, and the diagnosis of IPH was confirmed by the finding of hemosiderin-filled macrophages in lung biopsy material (Fig. 2). We ruled out other causes of pulmonary hemorrhage, including rheumatological diseases, with appropriate laboratory testing. Goodpasture's syndrome was also excluded based on a negative test for antibody to be glomerular basement membrane and on normal urinalysis.

Diagnosis tends to be more difficult in cases of insidious onset. Kiper and associates[3] studied 23 children with IPH between 1979-1994, and noted there was often a long delay (range, 4 months to 10 years) between the start of symptoms and the time when the correct diagnosis was made. We attribute the nine-month delay in our case to the fact that the patient exhibited no respiratory symptoms of hemoptysis, cough or dyspnea in the earlier stages.

Interestingly, reports have noted a connection between IPH and sensitivity to cow's milk[2]. Individuals with IPH who exhibit this form of sensitivity have a better prognosis than those who do not have milk protein sensitivity. The former category of patients may not need long-term immunosuppression. Saeed and coauthors[2] reported one patient who was successfully treated with a milk-free diet only, without any medication. Still, it is not known what role milk precipitins play in the pathogenesis of IPH[2].

Studies indicate that patients show varied response to immunosuppressants such as corticosteroids, azathioprine, cyclophosphamide, and hydroxychloroquine. Recent work has revealed that long-term, low-dose CS therapy prevents respiratory crises and prolongs survival in most cases[2]. Based on these findings, we initially prescribed standard-dose CS combined with dietary milk restriction for our patient. However, standard-doses of CS were insufficient in this case, and he responded well to treatment with higher doses of CS.

We wish to emphasize that IPH should always be considered a possible cause of iron deficiency anemia, especially in patients who require multiple blood transfusions and exhibit reticulocytosis. Our case is important in that it exemplifies how the diagnosis can be overlooked, and how this can lead to serious deterioration. We would like to suggest high-dose short-term CS treatment as one form of therapy, especially in patients who do not respond to standard-dose CS treatment.

REFERENCES

1. Milman N, Pedersen FM. Idiopathic pulmonary hemosiderosis. Epidemiology, pathogenetic aspects and diagnosis. Respir Med 1998; 92: 902-907.
2. Saeed MM, Woo MS, MacLaughlin EF, Margetis MF, Keens TG. Prognosis in pediatric idiopathic pulmonary hemosiderosis. Chest 1999; 116: 721-725.
3. Kiper N, Göçmen A, Özçelik U, Dilber E, Anadol D. Long-term clinical course of patients with idiopathic pulmonary hemosiderosis (1979-1994): prolonged survival with low-dose corticosteroid therapy. Pediatr Pulmonol 1999; 27: 180-184.
4. Cassimos CD, Chryssanthopoulas C, Panagiotidous C. Epidemiologic observation in idiopathic pulmonary hemosiderosis. J Pediatr 1983; 102: 698-702.
5. Chryssanthopoulas C, Cassimos C, Panagiotidous C. Prognostic criteria in idiopathic pulmonary hemosiderosis in children. Eur J Pediatr 1983; 140: 123-125.
6. Beckerman RC, Taussig LM, Pinnas JL. Familial idiopathic pulmonary hemosiderosis. Am J Dis Child 1979; 133: 513-517.