The Turkish Journal of Pediatrics 1997; 39: 111-115

CHLOROQUINE IN IDIOPATHIC PULMONARY HEMOSIDEROSIS*

A Case Report

*Adalet Meral MD***, Ünsal Günay MD***, Aygün Küçükerdoğan MD****
*Yakup Canıtez MD****, Sema Özuysal MD*****

SUMMARY: Meral A, Günay Ü, Küçükerdoğan A, Canıtez Y, Özuysal S. (Departments of Pediatric Hematology and Pathology, Uludağ University Faculty of Medicine, Bursa, Turkey). Chloroquine in idiopathic pulmonary hemosiderosis: a case report. Turk J Pediatr 1997; 39: 111-115.

This report describes an 11-year-old boy with idiopathic pulmonary hemosiderosis. His only presenting symptom was severe anemia due to iron deficiency. Idiopathic pulmonary hemosiderosis was diagnosed nine years after the onset of symptoms. During this period many invasive and non-contributory investigations were performed. This report describes the patient's diagnostic problems, clinical features and dramatic improvement with chloroquine (250 mg/day) after failing to respond to megadose methylprednisolone (30 mg/kg). One year later, chloroquine was discontinued. The patient has remained in remission since March 1994. Chloroquine should be used for this life-threatening conditon since it is less toxic than other immunosuppressive drugs.
Key words: iron-deficiency anemia, idiopathic pulmonary hemosiderosis, chloroquine.

Iron-deficiency anemia is common in childhood and usually dietary in origin[1]. If a deficient diet is not the cause, diagnostic attention focuses on the gastrointestinal tract. Respiratory causes are rare, and occult pulmonary hemorrhage is often not considered. We describe a case with idiopathic pulmonary hemosiderosis leading to iron-deficiency anemia in order to draw attention to both the difficulties in making this diagnosis and the response to chloroquine.

Case Report

An 11-year-old boy was hospitalized in February 1993 with fatigue and pallor. He had these complaints since he was three years old and frequently received iron treatment for iron-deficiency anemia. He had also been transfused three times in the previous five years for severe anemia. Despite being transfused, his anemia had recurred, and further investigations including fecal occult blood, barium meal and follow-through, esophagoscopy and colonoscopy were found to be negative. His family history was not notable.

* From the Departments of Pediatric Hematology and Pathology, Uludağ University Faculty of Medicine, Bursa.

** Pediatrician, Uludağ University Faculty of Medicine.

*** Professor of Pediatrics and Pediatric Hematologist, Uludağ University Faculty of Medicine.

**** Research Assistant in Pediatrics, Uludağ University Faculty of Medicine.

***** Pathologist, Uludağ University Faculty of Medicine.

On admission to the hospital, his body weight was 31 kg (10^{th}-25^{th} percentile), height was 135 cm (10^{th} percentile), temperature was 36.5 °C, pulse was 80 beats/min, respiratory rate was 24 breaths/min and his blood pressure was 100/80 mm Hg. Physical examination revealed 2 cm hepatomegaly, a soft systolic ejection murmur and rales over both lung field. The other systems were found to be normal.

Complete blood count was as follows: white blood cell count 6200/mm^3 (78% polymorphonuclear cells, 2% eosinophils, 20% lymphocytes), hemoglobin 5.1 g/dl, mean corpuscular volume 59.9 fl, mean corpuscular hemoglobin 26.3 pg, mean corpuscular hemoglobin concentration 24 percent, platelets 202,000/mm^3 and reticulocyte count 2.8 percent. The peripheral blood smear showed hypochromic microcytic erythrocytes. The low level of serum iron (3 µg/dL) and increased iron-binding capacity (838 µg/dl) suggested iron-deficiency anemia. Bone marrow aspiration was normocellular with erythroid activation and no stainable iron. Chest x-ray and high-resolution thorax computerized tomography showed bilateral, widespread reticulogranular infiltrates, suggesting hemosiderin deposition in the alveolar space (Figs. 1 and 2).

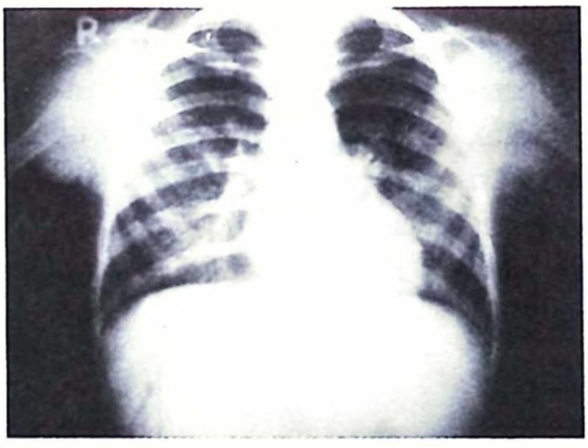

Fig. 1: Plain chest radiogram on admission.

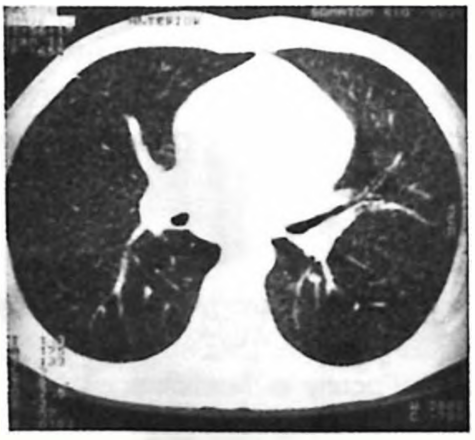

Fig. 2: High resolution computerized thorax tomography demonstrating bilateral reticulogranular infiltrates which indicate hemosiderin deposition in alveolar space.

Autoantibodies were negative. Immunoglobulins A, G, M and E were within normal limits. Our presumptive diagnosis was idiopathic pulmonary hemosiderosis (IPH). To confirm this diagnosis, fiberoptic bronchoscopy was performed. Both the transbronchial biopsy specimen and bronchoalveolar lavage iron-stainable, hemosiderin-laden macrophages (Fig. 3).

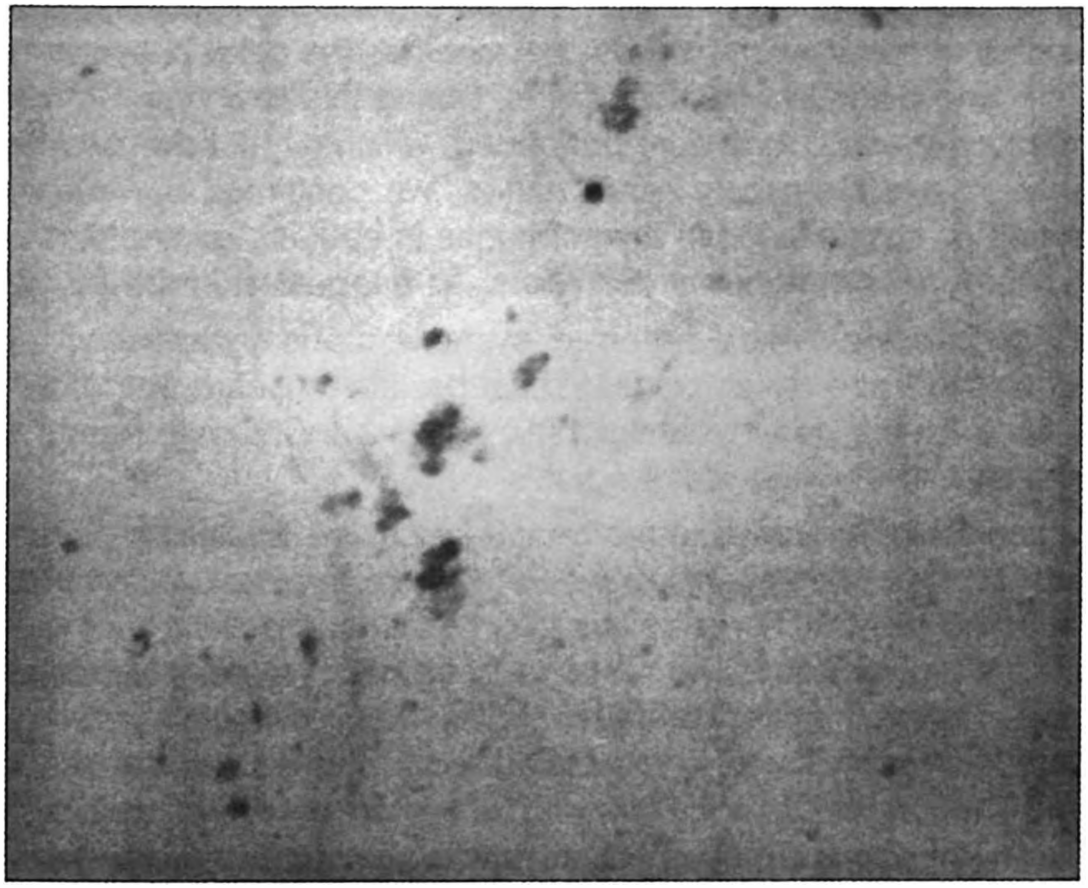

Fig. 3: Bronchoalveolar lavage showing iron stainable hemosiderin-laden macrophages.

The differential diagnosis of Good-Pasture Syndrome, collagen vascular diseases and celiac syndrome was made by normal urinary hemosiderin, sediment, renal function tests, complement, immunoglobulin levels and negative antiglomerular basement membrane antibody, autoantibodies and antigliadin antibodies. The patient was first treated with megadose methylprednisolone (MDMP: 30 mg/kg) tapered off within one month. There was no improvement in the chest films or hematological findings.

Chloroquine sulfate 250 mg PO daily was then initiated. In one month the patient's hemoglobin level increased to nine g/dl and the reticulocyte count decreased. The clinical and laboratory findings returned to normal in the second month of treatment. The final blood count was as follows: Hb 14 g/dl, Hct 38.4%, MCV 84 fl, MCH 34 pg, MCHC 32%, Plt: 254,000/mm^3 and reticulocyte count 1%.

One year later the chloroquine was discontinued. The patient has been in remission since March 1994.

Discussion

The term pulmonary hemosiderosis indicates an abnormal accumulation of iron as hemosiderin in the lungs. Half of affected children have no pulmonary symptoms[2, 3]. Our patient did not have obvious clinical respiratory symptoms; his only presenting symptom was iron-deficiency anemia. The delay between the onset of symptoms and diagnosis was nine years. During this time many invasive and non-contributory investigations were performed, which might have been avoided if the diagnosis had been considered earlier. We confirmed our diagnosis by demonstrating hemosiderin-laden macrophages in sputum, gastric washing and more specifically in the bronchial epithelium, as suggested in the literature[3].

Glomerulonephritis, vasculitis syndromes, systemic lupus erythematosis, juvenile rheumatoid arthritis and celiac disease must be differentiated from IPH[4]. In our case, the complement and immunoglobulin levels were normal. Autoantibodies and gliadin antibodies were also negative.

There are various approaches to the treatment of IPH. Exclusion of cow's milk from the diet in infancy has been suggested[5]. Corticosteroids, cyclophosphamide, azothioprine and plasmapheresis have been tried for the control of pulmonary bleeding[3, 6]. Our patient failed to respond to MDMP. We selected chloroquine for the second-line therapy because of its lack of toxicity compared to immunosuppressive regimens and isolated reports of a dramatic response in childhood[7]. The use of chloroquine may be limited by retinal toxicity; regular ophthalmic examinations are essential and were normal in our case. The possible action of the drug is suppression of lymphocyte proliferation, inhibition of antigen presentation by alveolar macrophages and the effect of immune complex formation[8]. Our patient responded to the drug after two weeks of oral intake and is now in complete remission without any serious complications after having discontinued the treatment.

These findings suggest that a therapeutic trial of chloroquine could be considered in children with IPH who do not respond to MDMP because of its lack of toxicity compared to other regimens.

REFERENCES

1. Dallman PR, Yip R, Oski FA. Iron deficiency and related nutritional anemias. In: Nathan O, Oski FA (eds). Hematology of Infancy and Childhood (4th ed) Vol: 1. Mexico: WB Saunders Co; 1993: 413-450.
2. Kjellman B, Elinder G, Garwicz S, Svan H. Idiopathic pulmonary haemosiderosis in Swedish children. Acta Paediatr Scand 1984; 73: 584-588.
3. Heiner DC. Pulmonary hemosiderosis. In: Chernick V, Kendig EC (eds). Kendig's Disorders of the Respiratory Tract in Children (5th ed). Philadelphia: WB Saunders; 1990: 498-508.

4. O'Donohue WJ Jr. Idiopathic pulmonary hemosiderosis with manifestations of multiple connective tissue and immune disorders. Am Rev Res Dis 1974; 109: 473-479.
5. Stafford HA, Polmar SH, Boat TF. Immunological studies in cow's milk induced pumonary hemosiderosis. Pediatr Res 1977; 11: 898-903.
6. Colombo JI, Path FCCP, Stoiz SM. Treatment of life-threatening primary pulmonary hemosiderosis with cyclophosphamide. Chest 1992; 102: 959-960.
7. Bush A, Shappard MN, Warnwe JO. Chloroquine in idiopathic pulmonary hemosiderosis. Arch Dis Child 1992; 67: 625-662.
8. Prasad RN, Mahajan RC, Ganguly NK. Effect of chloroquine on cellular immune responses of normal and P. knowlesi-infected rhesus monkeys. Immunol Cell Biol 1987; 65: 211-216.