IDIOPATHIC PULMONARY HEMOSIDEROSIS

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Idiopathic pulmonary hemosiderosis has long been considered a rare disease, occurring mainly in childhood, however an increasing number of cases are currently being diagnosed and reported.

The patient whose case is reported here had been treated for atypical pneumonia, pulmonary tuberculosis and asthma in several different hospitals over a period of six years. The clinical picture, together with the presence of hemosiderin in macrophages obtained by gastric lavage, suggested idiopathic pulmonary hemosiderosis but it was decided to perform a lung biopsy for a conclusive diagnosis.

The reasons for publishing this case are twofold : one, because it is the first recorded case of its kind in Turkish medical literature and two, because it is a case in which steroid therapy was used without apparent success.

Case Report

An eight year old boy was admitted to Hacettepe Children's Hospital on April 4, 1961, with palpitations and difficulty in breathing which had persisted for 3-4 days. He had had similar spells off and on for a year prior to admission. In 1955 he had been treated for atypical pneumonia and six months later, in another hospital, it was suspected that he had tuberculosis and antituberculous therapy was tried without success. Following this the possibility of bronchial asthma was suggested by the staff of the same hospital.

The patient was the second child of a healthy family, no other member of which had similar complaints.

Physical Examination on Admission : The patient was found to be a pale, active child with normal turgor and tonus. No lymphadenopathy was detected. His lips and fingernails were cyanotic and clubbing of his fingers was noted. His chest was barrel-shaped with prominent precordium. There were pathological sounds in his cardiovascular and respiratory systems and examination of other systems revealed nothing unusual.

His temperature was 36.5 C., respiration 28, pulse 140. He weighed 21 Kg. and his blood pressure was 130/40. His electrocardiogram showed sinus tachy-

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cardia and right ventricular hypertrophy. A roentgenogram revealed hypertrophy of the right ventricle and widespread interstitial infiltration in both lung fields. These shadows were prominent in the medial parts especially in the paracardiac region.

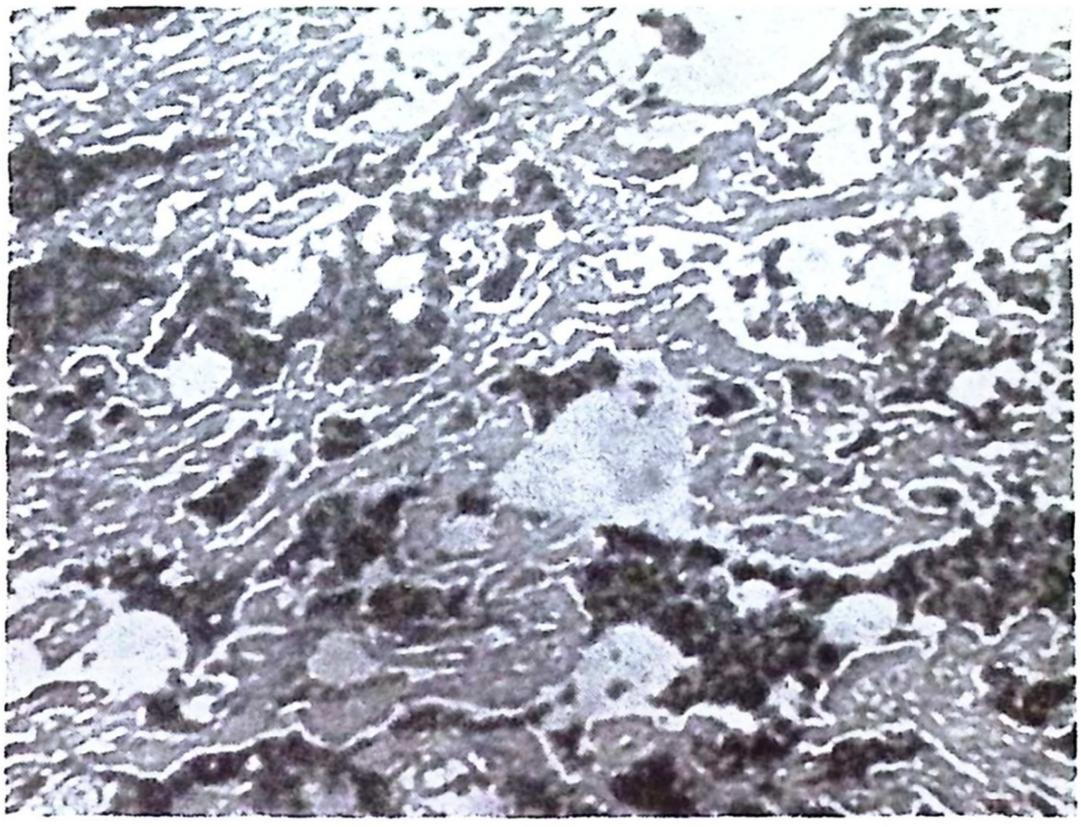

Figure 1. Shows fibrous thickening of the interalveolar space and iron positive macrophages (siderophages) in the alveoli (X 100).

Note : Perl's test for hemosiderin used in all slides and all were counter stained with hematoxylin and eosin.

Laboratory : The laboratory examination showed serum iron to be 39 gamma per 100 cc., hemoglobin 10.4 - 11.52 Gm./100 ml. and erythrocyte fragility 0.36 - 0.20. Prothrombin time was 31 seconds, control 20 seconds. Bilirubin was 0.8 mg./100 ml. (direct 0.3 mg., indirect 0.5 mg.). All skin tests for tuberculosis, histoplasmosis, coccidioidomycosis, and toxoplasmosis were negative. Cold agglutinin test was negative. A test for circulating precipitins to cows milk was not done.

Repeated gastric washings were positive for macrophages containing hemosiderin. It was this which prompted the lung biopsy. Biopsy material was taken from the lingula and consisted of a piece of firm red-brown lung tissue measuring $1.4 \times 1.2 \times 0.6$ cm. Histologic examination showed numerous iron-containing macrophages in the alveoli, both by hematoxylin-eosin stain and by perlingual Prussian blue reaction. The same procedure also revealed iron impregnation of the elastic tissue of the interalveolar walls, in the walls of the vessels, and in the peribronchial connective tissue. The interstitial connective tissue was conspicuously increased and contained a nonspecific inflammatory infiltrate consisting mainly of lymphocytes and a few plasma cells.

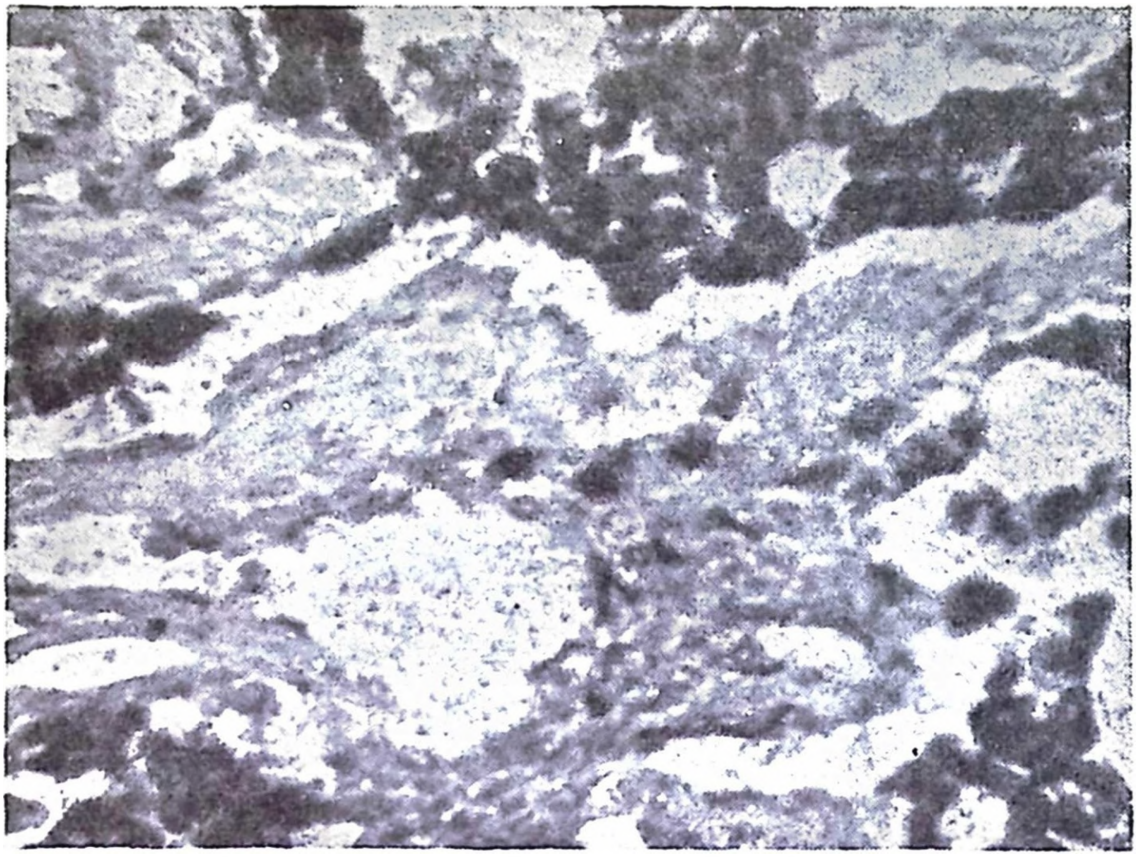

Figure 2. Same field as figure 1 under high power (X 430).

The patient had a typical attack on the 20 th day of hospitalization with marked dyspnea and temperature elevated to 38.6 C. Following this attack, treatment with prednisolone, 40 mg./day, was instituted. Eight days later the prednisolone was reduced to 30 mg./day owing to the presence of side effects. The patient was discharged on May 21, 1961, to be followed in the out-patient department. He was advised to report in once a week and was, in fact, seen three times · 5/30/61, 6/27/61, and 7/3/61, each time in good condition. On the last visit prednisolone was reduced to 5 mg./day. On July 6, 1961, he was brought back to the hospital with another severe attack and died four hours after admission.

Discussion

Idiopathic pulmonary hemosiderosis was thoroughly reviewed by Soergel[1] in 1957. For this reason no attempt will be made here to repeat his survey of the literature. Apparently the first case was reported by Virchow[2] in 1864 although credit for the first detailed description of the disease goes to Ceelen.[3]

Soergel himself collected 81 reported cases prior to 1957 but discarded 16 adult cases as having insufficient data for definite diagnosis. Among the remaining 65 patients, 53 were children. Since 1957, an increasing number of cases has been reported and, in our opinion, this is due to an increasing familiarity with the disease on the part of pediatricians in general.

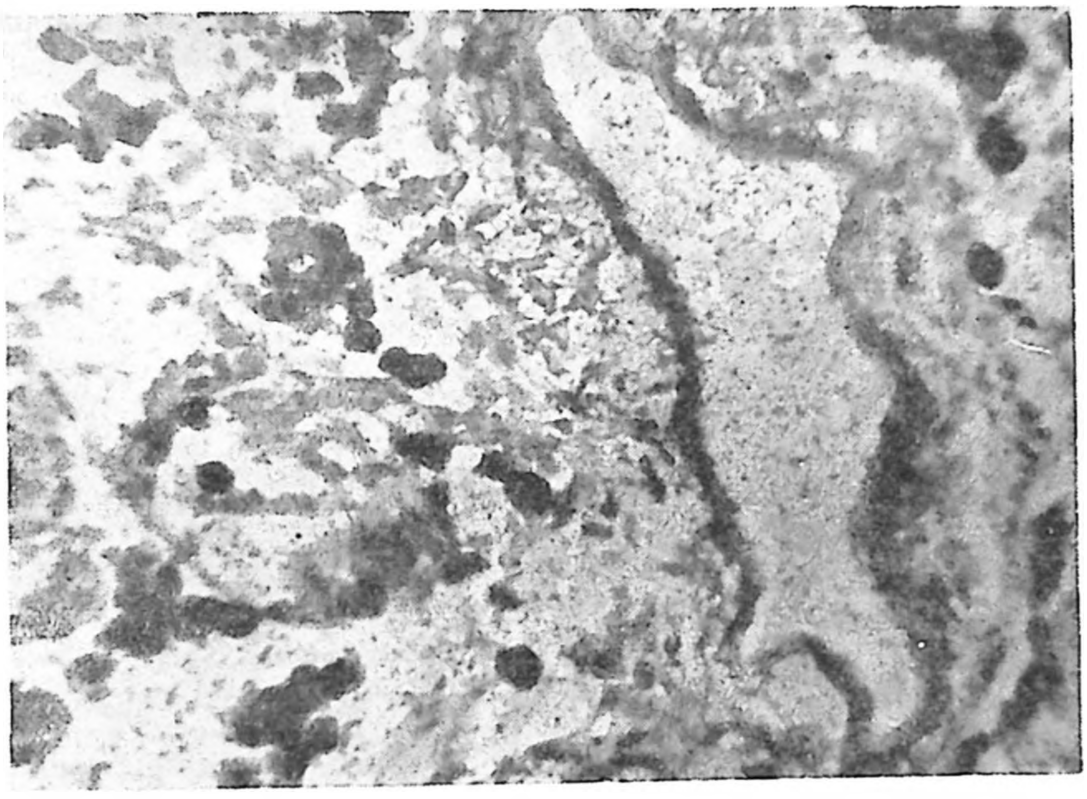

Figure 3. Shows iron impregnation of the elastic tissue of vessel walls (X 250).

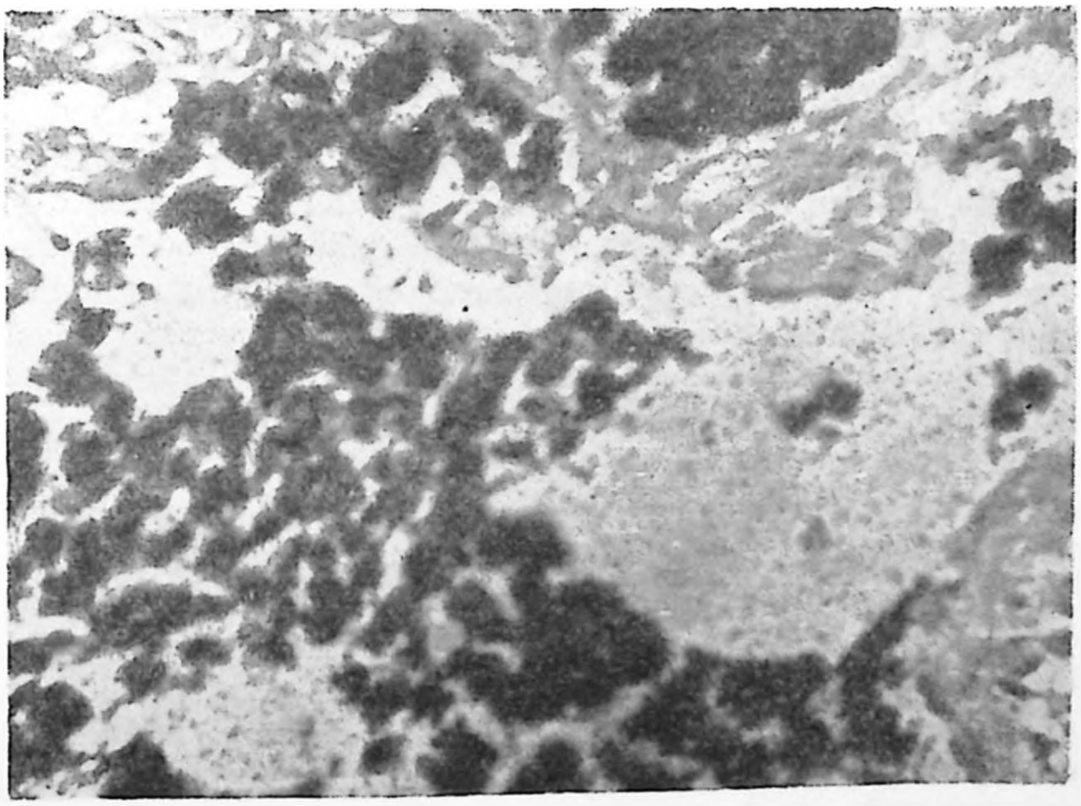

Figure 4. High power appearance of siderophages (X 430).

The presenting symptoms include such complaints as pallor, loss of appetite, easy fatigability and frequent colds. Some cases may be diagnosed as virus pneumonia as happened to our patient. Probably the most characteristic feature of the disease is the onset of an acute attack. Due to intra-alveolar hemorrhage the patient suddenly becomes critically ill. He shows marked dyspnea, coughs often and may vomit. His temperature may rise and hemoptysis may occur. In some cases, a slight jaundice may be noted several days after the attack. Diagnosis during an attack is not difficult if one keeps the possibility of idiopathic pulmonary hemosiderosis in mind. Quite a few patients die during these attacks, in other cases recurrent but less severe attacks have been reported.

Clinical observations in these cases are similar to those in any chronic lung condition. In the chronic stage right-sided heart failure is noted. Roentgen ray examination of the lungs reveals little perihilar patching but occasional diffuse interstitial infiltration.

Since the clinical observations in idiopathic pulmonary hemosiderosis are similar to those in any common type of pulmonary pathology the possibility of this disease must be kept in mind when one is confronted with a case of chronic lung disease. In such a situation it is recommended that specific laboratory studies, such as examination of gastric and bronchial washings and sputum for hemosiderin containing macrophages and a test to demonstrate circulating precipitins against cows' milk be performed. For a conclusive diagnosis however we feel it is preferable to obtain a lung biopsy specimen since any bleeding in the pulmonary system may result in the finding in the lungs of cells of this type, which are essentially macrophages and are normally present throughout the body. Their presence in the lungs may therefore be non-specific or may indicate a chronic condition such as tuberculosis (which should be considered in the differential diagnosis). Morphologically speaking the most striking change in pulmonary hemosiderosis is the retrogressive alteration of the lung tissue itself, which may be manifested as fibrosis or elastic tissue degeneration, and can be discovered by examination of biopsy specimens. In this condition, mild to moderate non-specific chronic inflammatory infiltrations are secondary in nature and are a response to the retrogressive changes of unknown etiology. Much attention has been paid to the hemolytic processes of hemorrhage into the lungs by various means but the presence of hemosiderin is merely an expression of the phagocytic activity of otherwise inert macrophages. It is not certain that the toxicity of the iron compounds

can account for the tissue changes. We emphasize these points because there are those who feel that the clinical picture, together with roentgen-ray examination and demonstration of the hemosiderin - containing macrophages, should be enough to establish the diagnosis. We have purposely omitted a few conditions with similar morphology, such as rheumatic heart disease, since these can easily be eliminated as diagnostic possibilities by proper clinical and laboratory examinations.

Etio - pathogenesis : Ceelen[1] and Wyllie[4] suggested a complete deficiency of the elastic tissue in the lungs while Pilcher and Eitzen[5] thought the cause of pulmonary fibrosis was congenital or acquired low grade inflammation of the lungs. McLetchie[6] postulated a defective vasomotor control of the pulmonary vessels. Steiner[7] introduced the concept of autoimmunization and Manderson[8] suggested a circulatory defect. Recently Wilson et al.[9] demonstrated that in children with iron deficiency anemia there is some degree of functional or anatomic gastrointestinal abnormality which permits passage of whole cows' milk proteins through the wall of the gastrointestinal tract, leading to secondary sensitization to these proteins. In some cases they felt that this produced a further train of events resulting in pulmonary hemosiderosis. In other cases they postulated that some children might be sensitized to cows' milk early in life without having iron deficiencies and that this, too, could lead to pulmonary hemosiderosis and eventually to other conditions such as iron deficiency anemia, due to blood loss, and hypoproteinemia.

Treatment : Besides supportive treatment including iron, blood transfusions and, during attacks, antibiotics to prevent secondary infections, there are two main types of treatment : one is splenectomy, the other is the use of steroids.

There are reports of four cases in which splenectomy was performed : three of these showed some degree of improvement, no improvement was noted in the fourth.

A review of the literature reveals that ten patients have been treated with steroids. Five of these showed improvement while no change was observed in the other five. Since information on the final outcome in the five patients showing improvement was unobtainable it seems impossible to make a judgment on the value of steroid treatment on the basis of these five cases. We can only mention that our experience with steroids was disappointing.

In our opinion, it is unlikely that successful treatment for this condition will be developed until such time as we have a better understanding of its pathogenesis. The work of Wilson et al. seems very promising in this regard and further work along the same lines should prove fruitful.

Summary

A case of idiopathic pulmonary hemosiderosis, established by lung biopsy, in an eight year old boy is presented. The unsuccessful use of steroid therapy is reported.

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