CASE REPORT

Essential Pulmonary Hemosiderosis

By B. JONSSON, M.D., B. VAHLQUIST, M.D. AND K. AGNER, M.D.

ESSENTIAL PULMONARY HEMOSIDEROSIS presents a very characteristic disease picture with involvement of the lungs and anemia as leading signs. The disease was first described by Ceelen. The first case diagnosed during life was published by Waldenström. A good survey of the disease has been published by Wyllie et al. In all, it is now possible to summarize from the literature about 25 cases.

We have had the opportunity to follow a typical case with fatal termination in a 5 year old boy and to carry out certain special investigations, e.g., chemical analysis of the iron deposits in the lungs.

HISTORY

The patient, a boy, was born on November 14, 1943. He was said to have been perfectly normal up to the age of 2 years. At that time a physician was consulted several times because of the development of anorexia. No organic disease was found. Anemia was not present at that time. In the spring of 1948 (at the age of 4 years), the patient became increasingly tired and pale. In June, he was admitted to a local hospital. At that time his hemoglobin was 3.7 Gm. per cent. Since then, he showed constantly pronounced hypochromic anemia with increased reticulocyte values. The anemia was temporarily improved by blood transfusions. Continuous treatment with iron, liver extract and folic acid gave no definite effects. His general condition varied and at times was fairly satisfactory.

In January, 1949 he became ill with fever, cough and pronounced dyspnea. At the same time the anemia became more marked. X-rays of the lungs showed cloudy, small, patchy shadows which improved after a few weeks. In March a new attack developed with hemoptysis. Five weeks later he was admitted to the Norrtull Hospital. On examination he showed a pronounced pallor of the skin and mucous membranes. In the second intercostal space on the left side a soft, systolic murmur was audible. Pulse rate was 120/minute. There was no enlargement of the liver or spleen, and the remainder of the examination was essentially negative.

Laboratory investigations: April, 1949. Hb. 4.9 Gm. per cent. Erythrocytes 1.98 1'si./mm.³. Hematocrit 15 per cent. Mean red cell diameter 6.7 μ. Mean corpuscular volume 75 cu. micra. Mean Hb. content 25 Gm. × 10⁻¹². Mean hemoglobin concentration 33 per cent. Reticulocytes 9.0 per cent. White cell count 8,600/mm.³. Differential count: band form polymorphs 16 per cent, segmented polymorphs 38 per cent, lymphocytes 24 per cent, metamyelocytes 2 per cent. Thrombocytes 280,000. Coagulation time 2 min. 45 sec. Bleeding time 2 min. 30 sec. Retraction of the clot 52 per cent in 2 hours. Prothrombin index 87. Fragility test: total hemolysis at 0.22 per cent, beginning at 0.42 per cent sodium chloride. Serum bilirubin 0.3 mg. per cent. Cold agglutinin reaction negative. Wassermann reaction negative. Microsedimentation rate 20 mm./hr. Serum iron 50 micrograms per cent. Direct Coombs test negative. No hemolysins in serum (test according to Wintrobe¹⁰).

Marrow puncture determination: "leukopoiesis normal. Erythrocytes mainly small and pale, and show pronounced anisocytosis, moderate poikilocytosis. The majority of the

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ESSENTIAL PULMONARY HEMOSIDEROSIS

eerythroblasts are small with a dense nucleus and often a scanty, oxyphile protoplasm. Although they are numerous the impression nevertheless is that of a torpid reaction, where the rapidly proliferating immature forms are reduced in number. Howell-Jolly bodies and mitosis are lacking. Otherwise normal picture." (Dr. E. Segerdahl.)

Plasma proteins (estimated by Kjeldahl's method) 6.7 Gm. per cent. Electrophoretic analysis gave the following relative per cent: albumin 54.0, globulin alpha 9.9, beta 12.7, gamma 6.0, delta 17.1. Basal metabolism, +9 per cent. ECG normal. Mantoux negative to 1 mg.


Course of the disease: The condition was stationary during the first few weeks. On May 7 a new acute attack with severe dyspnea and hemoptysis occurred and on this occasion about 100 ml. of blood were lost with the sputum. The patient's general condition was very poor but improved after blood transfusion. The excretion of urobilin in the urine increased and the serum bilirubin rose to 1.1 mg. per cent. After a few days the attack was over and his condition was the same as it had been before the attack. The course of the hemoglobin and reticulocyte counts are shown in figure 1. Complete hematologic data are listed in table 1.

X-ray of the lungs on April 16 showed only vague, mottled shadows which were diffusely spread out over both lungs, but most pronounced at the bases and in the paramediastinum. On May 9 (two days after the hemoptysis) widespread, miliary, mottled shadows had appeared. On renewed investigation on May 12, 16 and 22 a progressive improvement could be observed, but mottled shadows of the lungs were still present. X-ray of the other organs showed normal pictures (heart, liver, spleen, skeleton).

By means of differential agglutination with various Rh typing sera it could be demonstrated that the blood which the patient obtained by transfusion on May 8 was still present to some extent, on May 31 (after twenty-three days) but had disappeared completely on June 10 (after thirty-three days).

On June 10, the patient developed another hemoptysis and died within a few hours.

Autopsy. (Dr. H. Ryd.)

Lungs: large, firm, with a generalized increased consistency. The pleural surface thin, dark red, unevenly colored with a great number of dark red, sometimes confluent small petechiae. Some parts in the upper lobes less dark. The surface on section was somewhat

Fig. 1.—The course of the hemoglobin and reticulocyte counts
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Hemoptysis; ad mortem.

Blood transfusion 150 cc.
Blood transfusion 80 cc.
Blood transfusion 130 cc.
Blood transfusion 300 cc.
Blood transfusion 225 cc.
Blood transfusion 250 cc.
Blood transfusion 150 cc.
Blood transfusion 200 cc.
Fig. 2.—X-ray of the lungs two days after an hemoptysis showing cloudy, widespread shadows

Fig. 3.—Lung tissue stained with Perls' Berliner reaction showing hemosiderin macrophages
hardened but smooth and homogeneous of dark red-brown color. All over the lungs large amounts of brown fluid, clear, and poor in air, were expressed. There was somewhat more air in the lighter parts. No pus in the bronchi. Both pleurae contained about 50 ml. of clear, serous, dark red fluid.

No changes in other organs.

Microscopic examination. Many sections from different parts of the lungs were examined and showed the same picture. The alveoli were diffusely crowded with large cells containing large amounts of brown pigment in the cytoplasm. In some areas, groups of alveoli were observed containing heavy amounts of laked, red blood corpuscles. The walls between the alveoli were moderately increased in thickness with dilated capillaries, were slightly fibrosed and contained numerous hemosiderin macrophages. In the smallest and medium-sized pulmonary arteries the elastic substance was formed into coarse, thread-like structures which were stained dark grey with Weigert's elastin stain, dark blue-grey with hematoxylin, clear blue with Perls' Berliner blue reaction, and black-grey with Kossas' Carbol method. In many places single thread-like structures were seen in the alveolar walls, which gave the same color reactions. In many places these threads were completely or partially surrounded by either single or grouped large multinucleated giant cells of the type of foreign body cells.

Pathologic Diagnosis. The liver showed a slight fatty infiltration. Sections of the spleen, kidney, adrenals, testis, thyroid gland and the skin were normal. Hemosiderin containing cells were found, except for the lungs, to some extent only in the lymph glands.

Diagnosis: hemosiderosis pulmonum idiopathicum.

Chemical analysis of the lung tissue (Dr. K. Agner) showed that there was 1.97 mg. hydrolyzable iron per gram of tissue. Lung tissue from 5 patients, who had died as the result of accidents and who had no evidence of lung or heart disease, contained 0.03 mg. hydrolyzable iron per gram.

DISCUSSION

The characteristic signs and symptoms of essential pulmonary hemosiderosis can be summarized as follows:

Heredity: no evidence. Sex distribution: even. Age at onset: almost always in childhood. Course of the disease: long standing, often over many years. Prognosis: serious, many cases fatal. Lung signs: relapsing attacks with hemoptysis and a picture simulating pulmonary edema. Eventually a chronic insufficiency of the lungs with dyspnea and cyanosis may appear. Autopsy findings in the lungs: diffuse bleeding due to diapedesis. Hemosiderosis. Changes in the elastic tissue of the blood vessels. Blood picture: anemia of iron deficiency type (low mean corpuscular hemoglobin, low serum iron) but with unusually pronounced reticulocytosis. Blood picture otherwise normal. No abnormal general bleeding tendency. During the attacks an increase in the serum bilirubin and urobilinogenuria may occur. The anemia is frequently influenced by iron therapy. Cases with severe chronic lung insufficiency may show polycythemia.

In the present case a pronounced anemia was observed seven months before the first pulmonary attack. This appeared in January, 1949, and was followed at a one to two month interval, by new attacks; the last one in June of the same year was fatal.

The anemia of essential pulmonary hemosiderosis has been interpreted as an anemia due to blood loss. The survival time of transfused red blood corpuscles was in our case shortened to between three and five weeks. This finding may, however, perhaps be explained by continuous blood loss through the lungs and is not necessarily an expression of increased hemolysis. The same is true for the
reticulocytosis, the normoblastic reaction in the bone marrow and the slight bilirubinemia. Pathologic agglutinins could not be demonstrated by the Coombs test.

As is evident from the results of the chemical analysis, the lungs contained quantities of hydrolyzable iron, which were increased a hundredfold above normal. Garsche estimated the iron content of lung tissue in a case of hemosiderosis of the lung. He found that there was 11.51 Gm. iron per 100 Gm. ash, compared with 0.0061 Gm. in a normal case. The histo-chemical reactions demonstrated, in agreement with earlier investigations, that the iron was mainly deposited as hemosiderin in the cells, and these were partially excreted into the lumen of the alveolae. Evidently it was available for the normal iron metabolism and could not be used for blood regeneration. This would explain why the anemia was of a microcytic type and the serum iron low.

The hemoptysis and the attacks simulating pulmonary edema form a very characteristic disease picture. In childhood such signs are very rare. Evidently the attacks coincide with diffuse blood loss in the lung parenchyma and the alveolae and this would explain the intensification of the anemia at the same time. The roentgenologic pulmonary signs in connection with the attacks are mainly caused by hyperemia and bleeding into the alveolae and smaller bronchi. When the blood is absorbed or expectorated there is a marked regression of the roentgenologic changes. But even in the latent phase miliary shadows may be observed which are caused by pulmonary fibrosis.

Histologic studies of the lungs at autopsy show, besides the diffuse diapedesis bleedings and massive hemosiderosis, a marked change in the elastic tissue of the vessels. Several authors have tried to explain the disease picture by considering these as primary changes; they looked upon the bleedings and the anemia as a consequence of the fragility of the vessels. The characteristic attacks with deterioration must, however, be explained in another way. It should be stressed further that in the hemosiderosis of stasis, e.g., in connection with mitral valve failure, changes in the elastic tissue of the vessels are also found. The fundamental cause of this peculiar disease picture is still unexplained.

Characteristic changes in organs other than the lungs are not observed. Histo-chemical iron deposits are not found in liver, spleen or other organs.

SUMMARY

The authors report a fatal case of essential pulmonary hemosiderosis in a 5 year old boy. The child showed typical signs of the disease with relapsing pulmonary attacks with hemoptysis and pronounced anemia of iron deficiency type. Huge amounts of hydrolyzable iron were found in the lungs.

REFERENCES

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