Idiopathic Pulmonary Hemosiderosis Associated with Renal Changes and Abnormal Serum Proteins

Report of a Case

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Idiopathic Pulmonary Hemosiderosis is now a well recognized clinical syndrome. It was first described by Virchow in 1851. Ceelen in 1931 reported the first detailed study of two cases in children. It affects both sexes and any group ranging from childhood to middle age.

It is manifested by periodic attacks of cough, either dry or productive, dyspnea, hemoptysis and cyanosis associated with hypochromic anemia and evidence of hemolysis. Hemoptysis, hematemesis and abdominal pain occurred in cases described by Wyllie et al. Other features described elsewhere are pyrexia, headaches, clubbing of digits, gastrointestinal upset, hematuria, hematosplenomegaly, jaundice, cardiac enlargement, congestive cardiac failure, lymphadenopathy and vague aching pain in left pectoral region unrelated to breathing and exertion.

It is characterized by remissions and relapses. Time interval between onset and death varied from three months to 20 years (mean 5.4 years).

Etiology

Several hypotheses:

1. Ceelen (1931) suggested that there is a primary defect in the pulmonary vessels particularly involving the elastic fibers. Wyllie et al. postulated that decrease of elastic fibers in the pulmonary interstitial tissue leads to lack of distensibility of the lungs with consequent peripheral vascular stasis. This is followed by "hemorrhage by diapedesis" and deposition of hemosiderin.

2. Mcletchie and Colpitts (1949) postulated that the primary abnormality is one of defective vasomotor control of capillary tone.

3. Steiner (1954) considered an auto-antibody antigen reaction with the lung as the "shock-organ."

4. Soergel and Sommers (1962) suggested that the primary pathogenic mechanism is a congenital abnormality of alveolar growth and function.

Case Report

A Pakistani laborer, aged 42 years, who had been in this country for a year, was admitted to Poole Hospital, Nunthorpe, Middlesbrough, on March 9, 1963, complaining of: cough with scanty whitish phlegm and slight shortness of breath on climbing up hills (Gr. II dyspnea), for a week; and blood stained sputum for a day. No history of chest pain. He had a poor appetite and history of loss of weight.

There was no history of any serious illness, previous blood transfusion or iron-therapy. No previous chest x-ray film inspection had been made. There was no history of previous dusty occupation. He was a non-smoker.

On admission he appeared pale, but there was no cyanosis, jaundice or clubbing of digits, no lymphadenopathy and no evidence of congestive cardiac failure. His pulse rate was 72 and regular; blood pressure—180/80. Heart sounds were normal. No abnormality was detected in the respiratory system, gastrointestinal system or central nervous system.

Investigations: Routine blood examinations revealed hypochromic anemia (Hemoglobin=63 per cent and serum iron=51 micrograms per cent, normal serum iron=60 to 160 micrograms per cent).

All the investigations, including failure to detect ova, cysts or parasites in the feces, negative occult blood tests, presence of free gastric acid, normal barium meal study, negative Hess's test, normal bleeding time, clotting time and prothrombin activity and normal sternal marrow picture, failed to show any obvious cause of hypochromic anemia. Dietetic factor was excluded by careful history.

White blood cell count=6,000/cmm.; normal differential count. Erythrocyte sedimentation rate (Westergren) was persistently high.

Sputum—No acid or alcohol-fast bacilli were found either on film or after culture isolated on
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Foura 1: X-ray film of chest showing increased reticulation occupying the lower two-thirds of both lung fields.

several occasions. No macrophages containing hemosiderin were seen after repeated attempts. No malignant cells were detected.

X-ray film of the chest on admission (March 11, 1963)—Increased reticulation occupying the lower two-thirds of both lung fields. No other abnormality was detected.

Electrocardiogram was within normal limits.

Miscellaneous: Tuberculin (Mantoux method) 1 in 1,000 was strongly positive. Latex slide, Rose-Waaler and slide L. E. tests were all negative (titre 1 in 2).

Liver function tests revealed normal serum bilirubin, alkaline phosphatase and serum transaminase, but abnormal thymol turbidity and colloidal gold test. Bilirubin, urobilinogen and urobilin were not detected in the urine.

Titrated direct and indirect Coombes test was negative. Serum calcium was normal. Among the serologic tests for syphilis, Price's precipitation reaction was only positive which was reported to be non-specific.

Biopsies

Bronchoscopy was normal and bronchial biopsy was negative for sarcoidosis, tuberculosis and malignancy. Cytology for malignant cells (both sputum and aspirate) was also negative.

Liver Biopsy did not reveal any evidence of sarcoidosis or other noteworthy feature. No stainable iron pigment was detected.

Muscle Biopsy was negative for polyarteritis.

Lung Biopsy—"This lung tissue showed patchy atelectasis with some compensatory emphysema. The alveolar walls are thickened, but no true fibrosis is seen. Free iron pigment is demonstrable, but it is obscured by carbon in most sites. The greater part of this iron appears to lie within phagocytes. The appearances are those of pulmonary hemosiderosis."

Abnormal Serum Proteins: The total proteins were uniformly high and the globulins, especially the γ-globulins, rose to a very high level three or four times the normal.

Renal Changes: M. S. U. showed only trace of albumin and on one occasion small number of red blood cells (10 cmm.).

Concentration and dilution test showed defective concentrating power (Sp. Gr. 1015) but normal diluting capacity (Sp. Gr. 1000).

Creatinine clearance was uniformly low.

Blood urea was persistently normal. Bence Jones protein was not detected and I. V. P. was within normal limits.

Figure 1: X-ray film of chest showing increased reticulation occupying the lower two-thirds of both lung fields.

Figure 2: Section of lung showing thickened alveolar walls and free iron pigment, the greater part of which appears to lie within phagocytes.
Renal Biopsy (December 17, 1963)—"There was one sclerotic glomerulus with some surrounding fibrosis. Another glomerulus showed some congestion of the capillaries. There was part of a third glomerulus showing fibrosis of Bowman's capsule and surrounding chronic inflammation. Stain for hemosiderin was only faintly positive."

COMMENTS

(1) The patient concerned has been symptom-free since admission in spite of gross biochemical changes.

(2) Association with renal changes—two types of renal lesion have been reported, one fatal, another like this non-fatal, with no renal symptom whatsoever.

(3) Association with abnormal serum proteins—only one case has been reported in the literature though without association of renal changes. The only abnormality in the case described by Palmer was decreased albumin and raised globulin, but no electrophoretic pattern was given.

(4) Treatment—various treatments have been advocated though the advantage of one over the other has not yet been decided. Besides iron, vitamin C, blood transfusion and antibiotics, steroids and splenectomy are being used with mixed success.

The patient concerned has been treated with steroids (prednisolone 20 mg. daily) and oral and parenteral iron. In this case, it has been very difficult to assess the effects of steroid therapy in spite of improvements in anemia (responded to iron as well; hemoglobin came up to 82 per cent and maintained at that high level until the date of discharge, and serum iron rose to 70 micrograms per cent). Creatinine clearance (came up from 32 ml. per minute to 75 ml. per minute) and x-ray films of chest showed considerable clearing of reticulation; there were persistently high erythrocyte sedimentation rates, abnormal serum proteins and abnormal renal histology even after five months' steroid therapy.

(5) On the basis of findings such as abnormal serum proteins, renal insufficiency, positive flocculation tests and high erythrocyte sedimentation rate, the etiology of the condition could probably be due to "connective tissue disorder," affecting lungs and kidneys only, of "auto-allergic" basis.

REFERENCES


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DIRECT CURRENT COUNTERSHOCK IN CARDIAC ARRHYTHMIAS

In 80 per cent of the patients, the arrhythmia was successfully terminated by synchronized direct current discharge. Failures are attributed to congenital arrhythmia, long-standing arrhythmia, and the persistence of severe underlying heart disease. No complications have been experienced in this group of patients. It is recommended that after a short trial of drug therapy, all patients with serious tachycardia should be treated by synchronized direct current countershock. If the arrhythmia threatens life, then synchronized direct current countershock is the immediate treatment of choice. In patients with atrial fibrillation, direct current shock is effective in restoring sinus rhythm, but unfortunately, relapse is common.