Idiopathic Pulmonary Haemosiderosis in Children

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Idiopathic pulmonary haemosiderosis (IPH) was first described by Virchow in 1865 as 'brown lung induration'. In 1931 Ceelen reported the necropsy findings in 2 children. The clinical picture in association with radiological and pathological findings was reported by Waldenström (1944), and Wyllie *et al.* (1948) reviewed 24 cases in children. Nearly 200 have since been reported.

In the past 5 years, 26 patients with IPH were admitted to the Paediatric Clinic of Athens University, and form the subject of this review.

Material

The sex ratio was about 2 males to 1 female; 2 of the males were twins, most probably monozygotic. Of the 26 patients, 21 were less than 3 years old at the onset of the disease (Fig. 1). The youngest was 6 months and the oldest 9 years.

Diagnosis on admission. IPH was diagnosed in only 5 patients. In 18 patients the initial diagnosis was anaemia (aetiology unknown 12, haemolytic 3, iron deficiency 3) and in 3 patients bronchopneumonia.

Symptoms. Pallor, often extreme, was the most common symptom (24 cases). Fever, cough, and malaise were present in most patients and dyspnoea in 10 patients. In only 5 patients was there a history of blood-stained sputum, only one having had overt haemoptysis.

Physical signs. In more than one-half of the patients the liver and spleen were enlarged. Although all patients were acutely ill, râles were heard in only 7. 3 had moderate jaundice.

Laboratory findings. All patients had hypochromic microcytic anaemia of variable severity, with Hb values ranging between 2 and 11 g./100 ml. Siderophages in the sputum or gastric washings were invariable. A moderate reticulocytosis was usual. Coombs test was negative; Hb electrophoresis normal. G6PD activity determined by Motulsky test in 5 boys and 3 girls was

normal. In 1 case urinary findings (protein, red cells, and granular casts) suggested glomerulonephritis. Occult blood in the faeces was found in 5 out of the 10 patients examined.

Radiological findings. The infiltrations of the lungs during crisis were striking, considering the minimal physical findings. Diffuse homogeneous shadows were seen in all patients during the acute phase, which, characteristically, changed rapidly in size, density, and distribution, and usually cleared within a week or two (Fig. 2).

Treatment and prognosis. Most patients were given blood transfusions, prednisone 2 mg./kg., and full doses of antibiotics during the acute or subacute phase. Subsequently prednisone 1 mg./kg. was given until discharge, after which 5–15 mg. was given daily for an

FIG. 1.—Age of onset in 26 cases (17 male, 9 female) of idiopathic pulmonary haemosiderosis.

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FIG. 2.—Chest x-rays of a 3-year-old boy. (a) Massive infiltration mainly in the right lung. (b) 7 days later: the opacity in the right lung is now much less pronounced, but there is a new large opacity in the left lung. (c) 8 days later note considerable clearing.

indefinite period. A milk-free diet was advised in 19 patients.

Contact was lost with 6 patients after discharge; of the remaining 20 patients, 4 died after an average of 3.5 years following the onset of IPH. Two died in hospital following massive pulmonary bleeding; one also developed pneumothorax. Both were on steroids and milk-free diet. Two patients died at home; we do not know whether they were still on steroids.

Sixteen patients have been followed up for an average of 2.8 years. In 2, steroid therapy was discontinued arbitrarily. Four months later the first had a subacute exacerbation. The second has been in remission for nearly 3 years. One 5-year-old girl had her last subacute episode 4 months after steroid treatment was discontinued. Another patient is still on 10 mg. prednisone per day; he occasionally spits blood-stained sputum but he is free from any other symptom. The remaining 12 patients are still on steroids; they are symptom-free and lead a normal life.

Discussion

IPH is predominantly a disease of childhood. It is not uncommon (Wyllie *et al.*, 1948), and increasing familiarity with its bizarre manifestations will probably lead to the recognition of patients affected by mild forms of the disease (Coates and Bellamy, 1961; Karlish and Hemsted, 1964; Samuels, Howe, and Butler, 1964).

Few patients have overt haemoptysis, and the amount of blood expectorated is considerably less than the amount actually lost, particularly so in infants and young children who swallow their sputum. The typical case presents with symptoms of anaemia (Soergel and Sommers, 1962). Interestingly, a few adults with IPH have been reported who showed no evidence of anaemia over a period of years, despite the presence of persistent pulmonary infiltrations (Ditto and Ognibene, 1964). Some

patients may present with severe dyspnoea, fever, x-ray changes, and anaemia (Lancet, 1963); initially bronchopneumonia is often diagnosed, as was the case in 3 of our patients, though during acute episodes the physical findings in the chest were usually minimal in spite of the alarming symptoms.

In one child urinary findings of glomerulonephritis were present with a normal blood urea; he died 3 months later of acute pulmonary bleeding, the renal pathology being that of active glomerulonephritis. In contrast to adult patients (Azen and Clatanoff, 1964; Canfield, Davis, and Herman, 1963; Saltzman, West, and Chomet, 1962; Walker and Joekes, 1963; Elder, Kirk, and Smith, 1965), only a few of the children reported have developed renal lesions and these were focal (Saltzman *et al.*, 1962).

The aetiology of IPH is still unknown. Various hypotheses such as congenital weakness or fragility of lung capillaries, milk allergy, or immuno-allergy have been suggested (Heiner, Sears, and Kniker, 1962; Soergel and Sommers, 1962). Soergel and Sommers postulated that capillary bleeding in IPH resulted from abnormal growth and function of alveolar epithelial cells (Soergel and Sommers, 1962). Lung biopsy findings have been reported by several authors; haemorrhage with haemosiderosis and fibrosis was striking but not specific. Although interstitial fibrosis is said to develop in IPH, some authors have shown that fibrosis is minimal or even absent in fulminating cases (Grill, Szögi, and Bogren, 1962).

It is reported that IPH occurs sporadically and that it shows no predilection for sex, a particular geographic area, or the season of the year. However, its incidence is perhaps higher in Greece than elsewhere. 13 of our 26 children originated from a small area of central Greece inhabited by an isolated

community in which intermarriage is common. The incidence of haemoglobinopathies and G6PD deficiency is also increased in this area. Hence, it is probable that hereditary factors may be involved in the development of IPH. Two of our patients were twins, most probably monozygotic (Choremis, Messaritakis, and Karpouzas, 1965), while Meadow (1965) has reported a case in a boy who was the product of a consanguineous marriage.

The prognosis of IPH is grave (Coates and Bellamy, 1961; Karlsh and Hemsted, 1964; Ognibene and Johnson, 1963; Spreccace, 1963; Wyllie *et al.*, 1948). Since symptoms are usually intermittent, it is difficult to assess the efficacy of any therapy. Most patients in this study were treated with steroids and were put on a milk-free diet. It was impossible to assess the effect of the latter, since steroids were given at the same time. Steroid therapy during bleeding episodes appeared to speed up recovery and to improve the patient's immediate prognosis. It was our impression that the course of the disease in patients on long-term steroids was milder, but that steroids did not prevent crises or prolong survival.

Summary

Twenty-six children with idiopathic pulmonary haemosiderosis admitted to hospital in the past 5 years have been reviewed. All had hypochromic microcytic anaemia of variable severity. Siderophages in the sputum or gastric washings, and chest x-ray findings were invariably present.

Steroid therapy during the acute phase of the disease appeared to speed up recovery and to improve the immediate prognosis. Long-term steroid therapy did not appear to prevent crises or to prolong survival. The effect of a milk-free diet could not be evaluated.

Of the 26 cases, 20 have been followed up and 4

have died. 16 have been followed for an average of 2.8 years; of these, 12, who are all on maintenance steroid therapy, are free of symptoms.

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