A 1½-year-old girl presented with a four-month history of dry paroxysmal cough associated with breathlessness. She had a history of low-grade fever twice in the past four months; each episode lasted one to two days. There was no other relevant history. She had received various antibiotics without benefit. On examination, she was irritable and had tachypnea and mild cyanosis. There was mild intercostal recession. Chest auscultation revealed bilateral diffuse coarse crepitations. The rest of the examination was normal.

Pertinent laboratory study results included a raised ESR and a WBC count of 12,500/cu mm with 10 percent eosinophils. A chest roentgenogram showed bilateral reticulonodular opacities, more marked in the right lung, associated with a prominent right mediastinal bulge (Fig 1). A differential diagnosis of miliary tuberculosis, sarcoidosis, and histiocytosis X was considered. Since miliary tuberculosis is by far the most common in this subcontinent, the patient was given antituberculosis drug therapy along with steroids, even though the Mantoux and BCG tests were negative. However, the patient’s condition continued to deteriorate, and the breathlessness and cyanosis were more pronounced one month later.

A CT scan performed at this time confirmed interstitial lung disease and also showed small cysts (Fig 2); the solid mediastinal mass, localized to the anterior mediastinum, was of nonspecific morphology even after IV contrast enhancement (Fig 3). A skeletal survey was performed but results were normal. Other investigations, including bone marrow examination and liver biopsy, also did not provide a clue to the diagnosis. A right thoracotomy was performed. At operation there was a hard, caseating mediastinal mass with the adjacent lung adherent to it. The right lung showed multiple small cysts and extensive fibrosis, but the expansion was good. Both the mass and the lung were biopsied.
Diagnosis: Primary pulmonary histiocytosis X

The mediastinal biopsy showed large aggregates of lipid-laden histiocytes with a number of giant cells, lymphocytes, plasma cells, eosinophils, and occasional neutrophils. The surrounding tissue showed fibrosis. The lung biopsy revealed thickening of the alveolar septa with a large number of foamy and solid histiocytes.

Pulmonary involvement in histiocytosis X may occur as a part of the disseminated disease or as a separate entity, called primary pulmonary histiocytosis X (PPHX); the two are indistinguishable pathologically. Any distinction, therefore, must be based on clinical and/or radiologic examination. The former is much more common in children, while PPHX is seen chiefly in young adult males. Only 14 patients of PPHX have been reported so far in prepubertal children. The prognosis of PPHX in the pediatric age group is grave; seven patients had died within one year of diagnosis.

The typical radiologic features in adults include a reticulonodular infiltrate with or without honeycombing, occurring predominantly in the upper lobes; pneumothorax can also occur. Sparing of the costophrenic angles reportedly carries a good prognosis; this was seen in our patient (Fig 1). Nonetheless, these features are nonspecific, and other causes of interstitial lung disease in children should be excluded such as sarcoidosis, Hamman-Rich syndrome, tuberculous sclerosis, and the collagen diseases, although they are equally rare. An open lung biopsy will establish the diagnosis if the clinical features are not distinctive.

Pulmonary involvement is the predominant but not necessarily sole site of involvement in PPHX. An occasional patient may demonstrate extrapulmonary involvement in the form of diabetes insipidus or minor skeletal lesions. PPHX in association with an anterior mediastinal mass has not previously been reported. This combination is even more unusual, because an anterior mediastinal mass itself is rare at the time of presentation in children with histiocytosis X. It is thought that these masses represent thymic infiltration. Certainly, the mass in our patient was at the site of the thymus and was inseparable from it on CT (Fig 3).

Owing to the paucity of pediatric literature on PPHX and to the well-known occurrence of spontaneous remissions in histiocytosis X, a firm opinion on the therapy of these patients is not possible. Our patient deteriorated after receiving steroids, which is at variance with the experience of others. We subsequently treated her with 25 mg/day of mercaptopurine, following which she had a gratifying clinical response—the breathlessness and cyanosis gradually disappeared over six weeks. A plain roentgenogram four months after initiation of mercaptopurine therapy showed marked regression of the mediastinal mass, although the infiltrates persisted almost unchanged. It is known, however, that the radiologic findings may persist unchanged or even progress despite remarkable clinical improvement. Abramson et al described cavitation occurring in the anterior mediastinal masses after therapy in children with histiocytosis X; this was not seen in our patient.

One year after the onset of symptoms, our patient was asymptomatic, growing well, and showed no evidence of skeletal or visceral involvement apart from that of the lungs.

REFERENCES

2 Marcy TW, Reynolds HY. Pulmonary histiocytosis X. Lung 1985; 163:129-50