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CASE REPORT

Sole pulmonary involvement by Langerhans' cell histiocytosis in a child

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Sole pulmonary involvement by Langerhans' cell histiocytosis in a child. J.M. Chatkin, J.C. Bastos, R.T. Stein, A.M. Gaiger. ©ERS Journals Ltd 1993.
ABSTRACT: The case of a boy aged 4 yrs and 7 months, with isolated pulmonary involvement by Langerhans' cell histiocytosis is reported. The presentation of the disease was a sudden pneumothorax, with no previous signs of respiratory disease. The case was confirmed by S-100 and MT1 antibody staining, and was treated with pulse steroids and several pleural drainages, until the boy died after a large bilateral pneumothorax.
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Pulmonary involvement is not an infrequent finding in Langerhans' cell histiocytosis (LCH). It is present in 50% of adults [1], and 32–50% of children [1, 2] with disseminated disease.

Cases of the lung as the only organ affected by LCH were first described by FARINACCI *et al.* [3]. Since then, it has been reported in several series [4–7].

Nevertheless, it is very unusual to find LCH limited to the lungs in children [8–10]. Only 12 cases were reported in the literature until 1987 [1]. BASSET *et al.* [4] described only two patients younger than 15 yrs old with primary disease of the lungs, among 78 cases of LCH reviewed.

We report a case of Langerhans' cell histiocytosis with isolated pulmonary involvement in a boy under 5 yrs of age.

Case report

A white boy aged 4 yrs and 7 months was admitted with a history of intense thoracic pain developed two days before admission. He also presented difficulty in breathing. An X-ray of the chest showed a subtotal left pneumothorax and bilateral multiple small cystic lesions (fig. 1). The pneumothorax was evacuated and breathing improved. Since the symptoms returned, the boy was referred to the University Hospital for a new admission. There were no other important features in his past history, except for a left lower lobe pneumonia when he was 45 days old.

On physical examination, the child was eutrophic (weight 18.8 kg), agitated and sweating. He had no fever and he was breathing fast (respiratory rate 58 bpm).

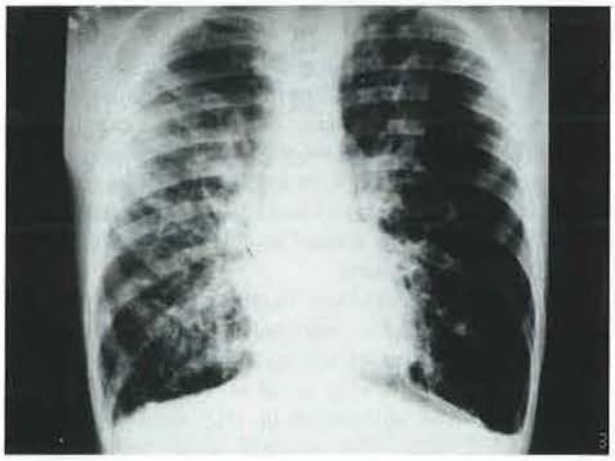

Fig. 1. – Chest X-ray showing subtotal left pneumothorax with bilateral multiple small cystic lesions.

He was not cyanotic and had no clubbing. He had diminished breathing sounds in the left lung and was distressed, with an increased use of accessory muscles. Heart rate was 120 beats·min^{-1}, with normal cardiac sounds. The chest X-ray showed a large left pneumothorax and the same multiple cystic lesions as described previously.

Laboratory data showed a normal leucocyte count, with no abnormalities in blood electrolytes, urea values, and sedimentation rate. Urine cultures, and sputum smears and cultures were all negative. Blood gas analysis showed arterial oxygen tension (Pao_2) 11.3 kPa (85 mmHg), and arterial carbon dioxide tension ($Paco_2$) 4.9 kPa (37

mmHg) breathing at 30% fractional inspiratory oxygen (F_{IO_2}).

The pneumothorax was managed by insertion of a pleural catheter connected to an underwater seal. The child developed several new pneumothoraces in the next 2 weeks, and a persistent bronchopleural fistula was surgically closed. He continued stable over the following days, with a normal respiratory rate. A new series of alternating bilateral pneumothoraces then began, and were initially treated by pleural drainage. A chemical pleurodesis was tried, without success, and after many events the surgeon used venous catheters in underwater seal to drain the pneumothoraces. At that time, with a persistent right pneumothorax, another surgical fistula correction was performed, with lung biopsy and abrasion pleurodesis.

A pulmonary radioisotope perfusion scan showed irregular perfusion in both pulmonary fields, because of multiple subsegmentary defects. Roentgenographic examination of the skull was normal, as was the radioactive bone scan. The report of the Pathology Department produced the diagnosis of Langerhans' cell histiocytosis.

Pulse steroids with methylprednisolone (30 mg·kg^{-1} per dose) were used for 5 doses on alternate days, without any change in clinical, radiological or laboratory data. Continuing oral steroid therapy (prednisone 1 mg·kg^{-1} daily) was then used, but small pneumothoraces continued to occur. After 3 weeks, a bilateral hypertensive pneumothorax developed, and caused an irreversible cardiac arrest.

Pathology report

Microscopy

The main lesion revealed the presence of a cellular infiltrate, with areas of central cavitation and destruction of lung parenchyma. The infiltrate consisted of histiocytes, lymphocytes and scattered eosinophils. A few multinucleated giant cells were also present. The histiocytic infiltration also involved the septal fibrous tissue associated with increased collagen deposition. The histiocytic cells had a pale, sometimes vacuolated, cytoplasm, and an eccentrically placed folded nucleus (fig. 2).

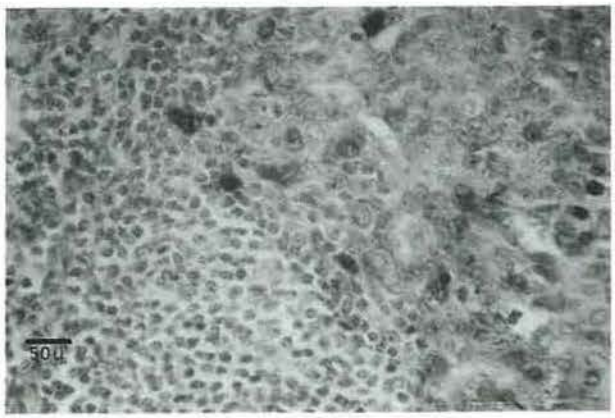

Fig. 2. – Cellular infiltrate consisting of histiocytes, lymphocytes and scattered eosinophils (magnification ×40).

Immunohistochemistry

The abnormal histiocytes showed strong reactivity for S-100 protein, and moderate staining with MT1 antibody. The positive reactivity with these two markers is highly suggestive of LCH affecting the lung.

Discussion

In 1940, LICHTENSTEIN and JAFFE [11], and OTANI and EHRLICH [12] described an entity that presented osteolytic lesions, characterized by intense histiocytic and eosinophilic infiltration, which they called eosinophilic granuloma of the bone. Later, FARBER [13] demonstrated the histological similarities between eosinophilic granuloma, Letterer-Siwe disease and the Hand-Schüller-Christian disease. In 1953, LICHTENSTEIN [14] proposed the integration of this group of lesions, with the designation histiocytosis X. More recent studies, however, have shown that the histiocytic cell common to these different lesions is the same Langerhans' cell histiocyte as found in the skin, oral mucosa and in other organs. The designation of Langerhans' cell histiocytosis (LCH) was then proposed as a better defining term [15].

There is no clear consensus about the natural history of isolated lung involvement in LCH in children, since it is a very uncommon condition [1, 10, 16]. MCDOWELL *et al.* [1] described one type with an initial stage consisting of respiratory symptoms, followed by failure to thrive; the chest radiograph is not suggestive of the disease at that stage. After some time, symptoms improve but the radiological picture remains the same, or becomes even worse. Another type has been described [8, 10, 16], in which there are no prominent clinical signs before the diagnosis is made as a casual finding during routine examination. At this time, a honeycomb lung appearance is often found in chest X-rays because of delayed diagnosis. Our case follows the latter pattern, since the disease presented with no respiratory symptoms until the sudden onset of the pneumothoraces. The boy's weight was adequate, and he thrived, but showed a honeycomb lung at X-ray.

There is no difference between the histological findings in the isolated organ and the disseminated disease. There is an accumulation of atypical histiocytes (Langerhans' cells), eosinophils, and a few lymphocytes in peribronchiolar structures, that may also be present in perivascular and alveolar sites [16]. The histological pattern found in our patient resembles the description of pulmonary eosinophilic granuloma, instead of the Letterer-Siwe disease that usually occurs at this age.

The European Histiocyte Society Writing Group [15] has proposed a classification for the diagnosis of LCH: "presumptive diagnosis", "diagnosis" and "definitive diagnosis". Since our patient had compatible findings of LCH and positive staining for S-100 protein and MT1 antibody, he could be classified as "diagnosis". Some problems in performing the electronmicrographic studies did not allow us to demonstrate the Birbeck granules in the histiocytes, necessary for the definitive diagnosis.

The progression of the disease and the repeated pneumothoraces caused us to evacuate the leaks. This is a complication of LHC occurring in up 10% of adult cases [7]. The macroscopic vision of the lesions makes these clinical events understandable (fig. 3).

The use of steroids for a period of three weeks continuously seemed to be a rational approach. We were considering the use of chemotherapy with vinca alkaloids, when a large hypertensive bilateral pneumothorax developed, leading to irreversible cardiac arrest, and death in a very similar way to some of the cases described by McDowell *et al.* [1].

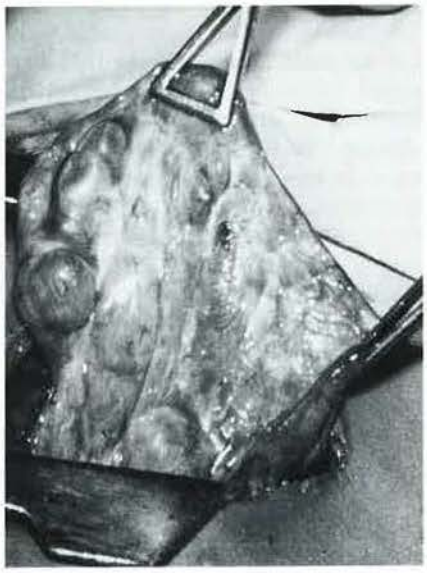

Fig. 3. – Macroscopic view of affected lung during surgery, showing multiple cystic lesions.

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