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Recurrent Bilateral Spontaneous Pneumothorax in Early Infancy: A Case of Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH) is a rare disorder characterized by infiltration of either single or multiple organs by S100 and CD1a positive cells. Patients with pulmonary LCH are predisposed to pneumothorax due to destructive changes in the lung parenchyma. Here, we report a case of multisystem LCH who presented at 2 months of age with simultaneous bilateral spontaneous pneumothorax.

Keywords: Langerhans cell histiocytosis, spontaneous pneumothorax, infancy, congenital, bilateral

Introduction

Langerhans cell histiocytosis (LCH) is a rare disorder characterized by infiltration of either single or multiple organs by a distinct cell type that is S100 and CD1a positive and contains ultra-structural Birbeck granules on electron microscopy. [1]Historically, LCH included 4 main clinical forms: Letter-Siwe disease, Hand-Schuller-Christian disease, eosinophilic granuloma (together grouped as histiocytosis) and Hashimoto-Pritzker disease. The Writing Group of the Histiocyte Society in 1987 proposed the uniform term of "Langerhans Cell Histiocytosis" to encompass all the above mentioned eponymous forms. [1, 2] Lung involvement occurs in up to half of all children with multisystem disease and usually parallels the overall disease activity.[3] Spontaneous pneumothorax (SP) occurs in approximately 10% of children with pulmonary disease and may be a terminal event .[4 - 6] Here, we report a case of multisystem LCH who presented at 2 months of age with simultaneous bilateral pneumothorax.

Case Report

This 2-month-old female infant presented with grunting and respiratory distress and history of skin lesions since birth. On examination, she had eruptions on her trunk and at the diaper area, splenomegaly and dyspnea. Her respiratory rate was 60/min, with intercostal and subcostal retraction evident.

Chest x-ray revealed bilateral reticulonodular shadowing, multiple cystic areas, and bilateral pneumothoraces (Figure1). Also, a lytic bone lesion was observed at the upper end of her right humerus. Chest CT scan of the patient showed diffuse parenchymal nodules with air-filled cysts and bilateral pneumothoraces (Figure 2). A skeletal survey showed multiple lytic lesions in her skull, right humerus, right radius and distal femur bilaterally.

A biopsy of the osteolytic area of her right humerus was performed which was

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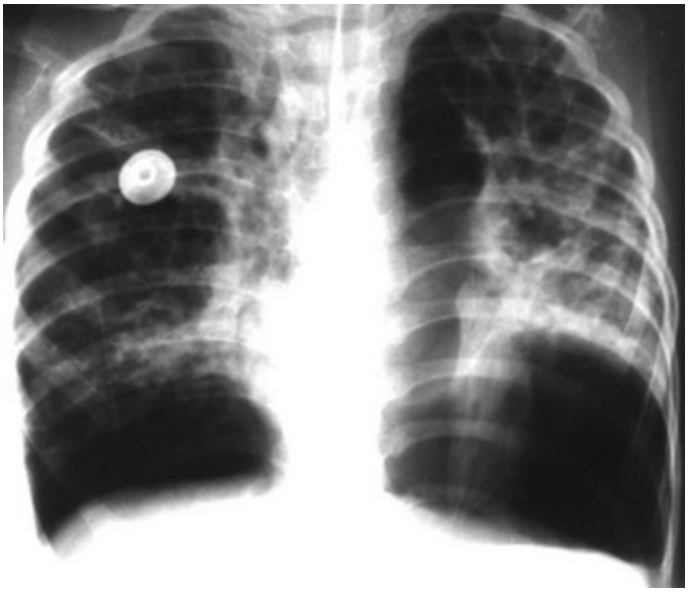

Fig 1. Bilateral pneumothorax superimposed on the background of cystic changes due to Langerhans cell histiocytosis.

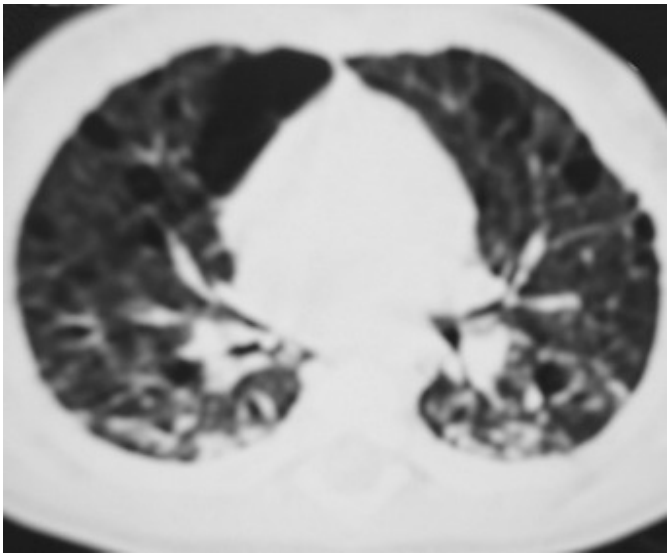

Fig 2. Chest CT scan shows diffuse parenchymal nodules with air-filled cysts, paraseptal bullae, and bilateral pneumothoraces.

diagnostic of LCH with bony trabecular infiltration by mixed histiocytes and inflammatory cells (Figures 3 and 4), positive for CD1a on immunohistochemical staining.

Bilateral chest drains were inserted for the patient. Treatment was started with prednisolone, 2mg/kg/day, and was followed by weekly injections of vinblastin, 3 mg/m^2.

Two months later, the patient developed a swelling on her right arm, which showed a fracture on x-ray of the right humerus (Figure 5). The patient's general and respiratory condition had not improved and she suffered from recurrent bilateral pneumothoraces despite receiving chemotherapy. Repeated air leaks prevented removal of the chest drains. Finally, in an attempt to stabilize her respiratory status at 6 months of age, bleomycin was instilled into both pleural spaces via chest drains to stimulate a chemical pleurodesis. The respiratory situation stabilized and her general condition improved gradually thereafter. Her next CXR revealed a honeycomb appearance in both lungs (Figure 6). No further pneumothoraces did occur. She was discharged from the hospital and was planned to continue the weekly vinblastin plus cyclosporine, 5mg/kg/day. This regimen produced improvement in the general condition of the patient; she gained weight and nearly reached the normal developmental milestones.

At 15 months of age, in an attempt to wean her from corticosteroids, she was readmitted with feverand dyspnea. CXR showed bilateral pneumothoraces on a background of multiple lung bullae. The patient became apparently neutropenic, probably due to a septic process. Her respiratory conditions deteriorated; she became oxygen dependent and mechanical ventilation was needed. She did not respond to broad spectrum antibiotics and mechanical ventilation and died at 15 months of age.

Discussion

Recurrent spontaneous pneumothorax (SP) is a disabling disorder that may present as a primary pneumothorax in young and healthy patients, or as a secondary pneumothorax due to the complications of an underlying lung disease.[7] Simultaneous bilateral spontaneous pneumothorax (SBSP) is a rare condition, mainly seen in patients with an underlying disease. [8, 9] According to literature, 65 cases with SBSP were reported by 2004.[8] In a report from Department of Thoracic Surgery of Istanbul, Turkey, 12 cases of SBSP were presented; 7 out of 12 patients (58%) had an underlying lung disease. SBSP in one of these patients was secondary to LCH. [8]

Lung involvement in multisystem LCH is reported in about 20-40% of cases. [3, 10] Lung involvement in LCH in children is usually a part of a generalized disease. Young children with multisystem LCH often present with nonspecific symptoms including fever, failure to thrive, irritability and loss of appetite.

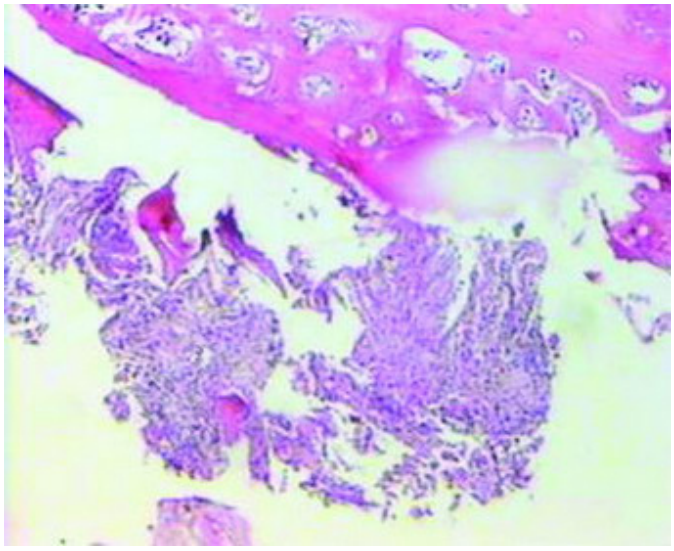

Fig 3. Microscopic view shows inflammatory cell infiltrates in a lytic bone lesion (low-power field)

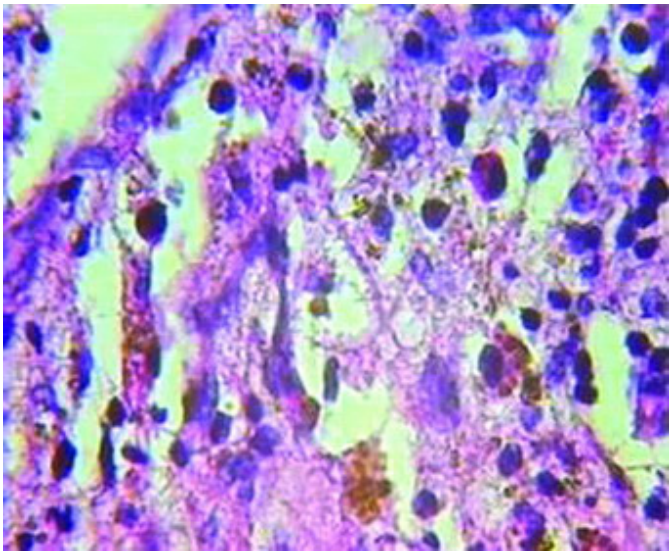

Fig 4. Higher magnification view showing infiltration of lymphocytes, plasmocytes, and histiocytes.

This may be followed by lung, liver and bone marrow failure, which entails a high mortality rate.[11] By contrast, isolated pulmonary LCH is mainly seen in young adults. [4, 12] Development of pneumothorax secondary to pulmonary LCH in young adults has been frequently reported. Indeed, pulmonary LCH is an interstitial lung disease characterized by development of cystic changes, which predispose to pneumothorax.[13-16]

Patterns of lung involvement on chest radiography of children with lung disease is that of reticulonodular shadowing secondary to interstitial alveolar infiltration by Langerhans cells .[12] Disease progression is accompanied by the appearance of small cysts and bullae with subsequent fibrosis and honeycomb appearance.[4] The infiltration is usually bilateral and symmetric. Either cystic changes may occur as the chief finding, or more commonly superimposed on a background of reticulonodular changes.[5] Spontaneous pneumothorax is thought to arise from the rupture of these cysts.

Pneumothoraces occur more frequently in adult patients, who have isolated progressive lung disease. [4] However, SP occurs in approximately 10% of children with pulmonary LCH. [4, 13] Other most etiologies of spontaneous pneumothorax in children are asthma, cystic malformations, cystic fibrosis, post-infectious bullae and infectious pneumonias.[17] A relatively high recurrence rate (58%) was observed in a group of adults with pulmonary LCH when pneumothorax was managed without pleurodesis. [13]

According to literature, there are few reports of bi-

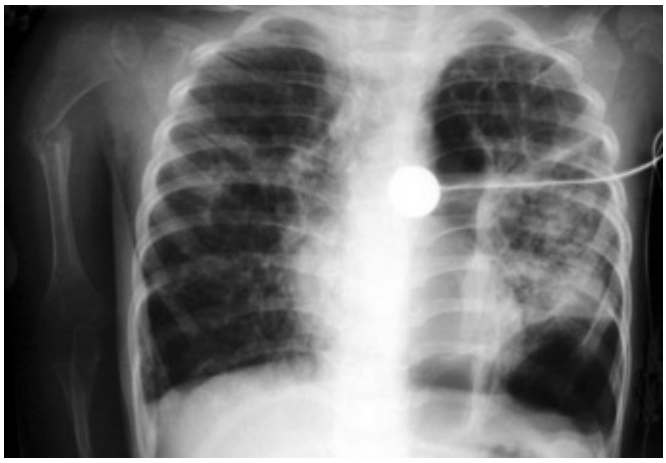

Fig 5. Areas of loculated pneumothorax in both lungs, cystic changes and a pathologic fracture due to lytic expansive lesion of right humeral proximal diaphysis.

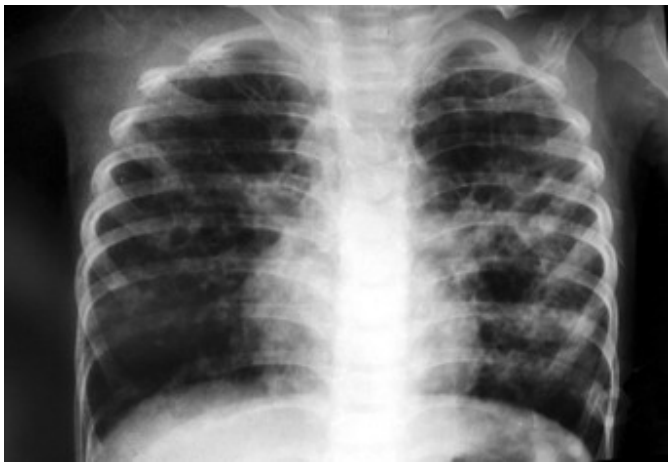

Fig 6. Honeycomb appearance due to progressive interstitial fibrosis

lateral pneumothorax due to LCH in adolescence. [18-20] One example is a 16-year-old girl presented with sudden onset of shortness of breath followed by loss of consciousness and sudden death due to bilateral pneumothorax. Post mortem microscopic sections of the lung showed LCH. [18] To our knowledge, the youngest patient who has developed sudden pneumothorax due to LCH was a 4-month-old girl who presented with hepatosplenomegaly and respiratory distress. [21]Three more cases have been reported already, including a 4-year-old, a 3-year-old, and a 16-month-old boy. [4, 22, 23]

The noteworthy feature of our patient was the presentation of SBSP in early infancy combined with vesicular eruptions over her trunk and diaper area since the neonatal period. Congenital self-healing Langerhans cell histiocytosis (CSHLCH) is a variant of LCH that presents with cutaneous lesions at birth or during the neonatal period. [1] So far, 40 cases of CSHLCH have been reported in the literature.[1] The clinicopathologic lesions that characterize the disease are congenital skin lesions in an otherwise healthy infant with mild or no systemic symptoms and spontaneous involution of the skin lesions. [24] We do not know of any SBSP reported in the setting of this entity. Although our patient presented with skin rash during the neonatal period, involvement of other organ systems and the progressive course of the disease are not compatible with CSHLCH. To the best of our knowledge, there are no reported SBSP due to LCH immediately after neonatal period. Accordingly, Langerhans cell histiocytosis should be considered in differential diagnosis of spontaneous pneumothorax, even among neonates.

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