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# LANGERHANS CELL HISTIOCYTOSIS ASSOCIATED WITH RECURRENT PNEUMOTHORAX*

## A Case Report

*Ayşenur Ökten MD***, *Hilal Mocan MD****, *Erol Erduran MD*****
*Yakup Aslan MD******, *Halit R. Gümele MD*******, *Yavuz Özoran MD********

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**Pulmonary involvement of Langerhans cell histiocytosis (LCH) is an uncommon but important cause of pulmonary fibrosis and honeycombing in young adults. Rarely, pulmonary LCH may be complicated by spontaneous pneumothorax. It may be isolated or associated with multiple organ involvement. We describe here a case of LCH with diabetes insipidus, skin lesions and pulmonary involvement in a 15-year-old boy. The case was complicated by four episodes of spontaneous pneumothorax with typical radiologic findings of pulmonary LCH. His presentation, radiologic findings, treatment and clinical course during three-years of follow-up are discussed.** *Key words: Langerhans-cell histiocytosis, recurrent pneumothorax.*

Eosinophilic granuloma of bone, Hand-Schüller-Christian disease and Letterer-Siwe disease constitute a complex of diseases of unknown cause. They are grouped under the term of histiocytosis X, now more correctly called Langerhans-cell histiocytosis (LCH)[1,2]. LCH has extremely variable presentations, and may be localized or disseminated[2].

Pulmonary involvement of LCH is uncommon and may rarely be complicated by spontaneous pneumothorax[3]. We present here a case of LCH with diabetes insipidus (DI), skin lesions and bilateral pulmonary involvement with honeycombing. This case was complicated by four episodes of spontaneous pneumothorax in the three-year follow-up period.

* From the Department of Pediatrics, Radiology and Pathology, Karadeniz Technical University Faculty of Medicine, Trabzon.

** Associate Professor of Pediatrics, Karadeniz Technical University Faculty of Medicine.

*** Professor of Pediatrics, Karadeniz Technical University Faculty of Medicine.

**** Assistant Professor of Pediatrics, Karadeniz Technical University Faculty of Medicine.

***** Research Assistant in Pediatrics, Karadeniz Technical University Faculty of Medicine.

****** Associate Professor of Radiology, Karadeniz Technical University Faculty of Medicine.

******* Professor of Pathology, Karadeniz Technical University Faculty of Medicine.

## Case Report

A 15-year-old boy was admitted to our pediatric clinic with a six-month history of polyuria and polydipsia. His past history was unremarkable. Physical examination revealed a dozen discrete 1-2 mm reddish-brown papules on the trunk. No lymphadenopathy, hepatosplenomegaly, or respiratory difficulty was noted. His neurologic status was also normal.

Complete blood count and bone-marrow aspirate findings were normal. Skeletal survey showed no lytic lesions, and liver function tests were within normal limits. Immunologic testing revealed normal serum immunoglobulin levels. The number of circulating T-cells (E-rosette forming = 64%) were within normal limits, but the $T_4$:$T_8$ lymphocyte ratio (4.3) was very high, suggesting a deficiency of $T_8$-positive cells. The urinary volume was 3650 ml/$m^2$/day, and the water deprivation and arginine vasopressine tests were interpreted as neurogenic DI[2].

The chest x-ray displayed a "honeycomb" pattern (Fig. 1), and the most severe abnormalities identified on the pulmonary computerized tomography (CT) scan were cysts and nodules (Fig. 2). Magnetic resonance (MR) examination showed thickening of the pituitary stalk and absence of the normal hyperintense signal of the posterior hypophysis, which shows antidiuretic hormone supply of the hypophysis (Fig. 3).

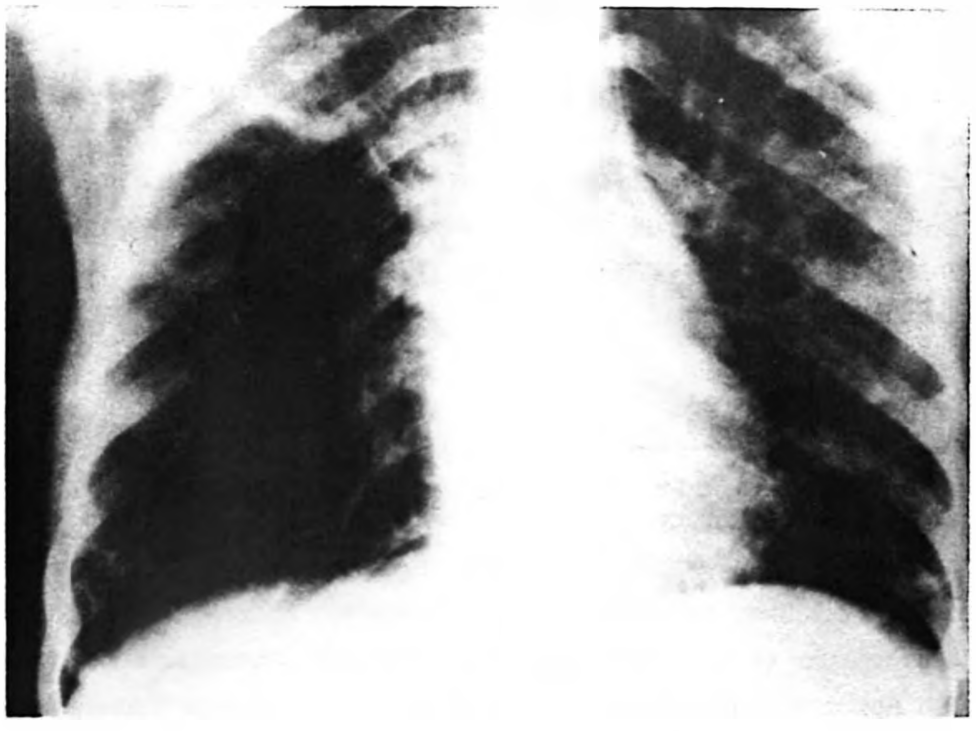

Fig. 1: Posteroanterior radiograph showing typical reticular, cystic and nodular abnormalities of pulmonary LCH, termed honeycomb pattern.

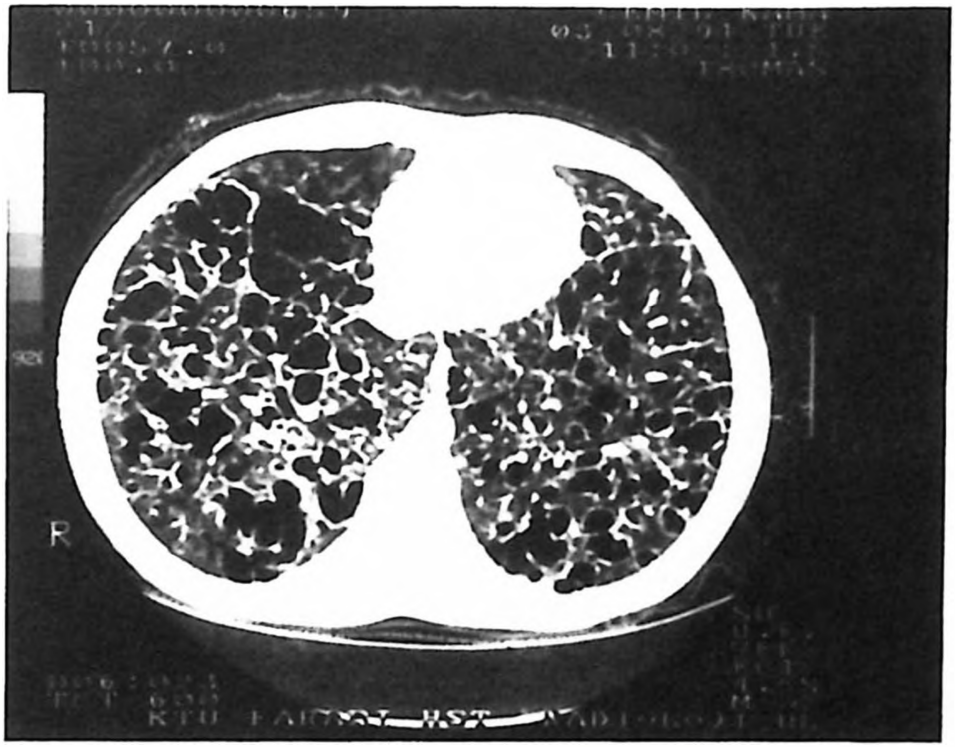


Fig. 2: CT scan showing cysts of various sizes with distinct, thin walls. Intervening lung tissue is normal.

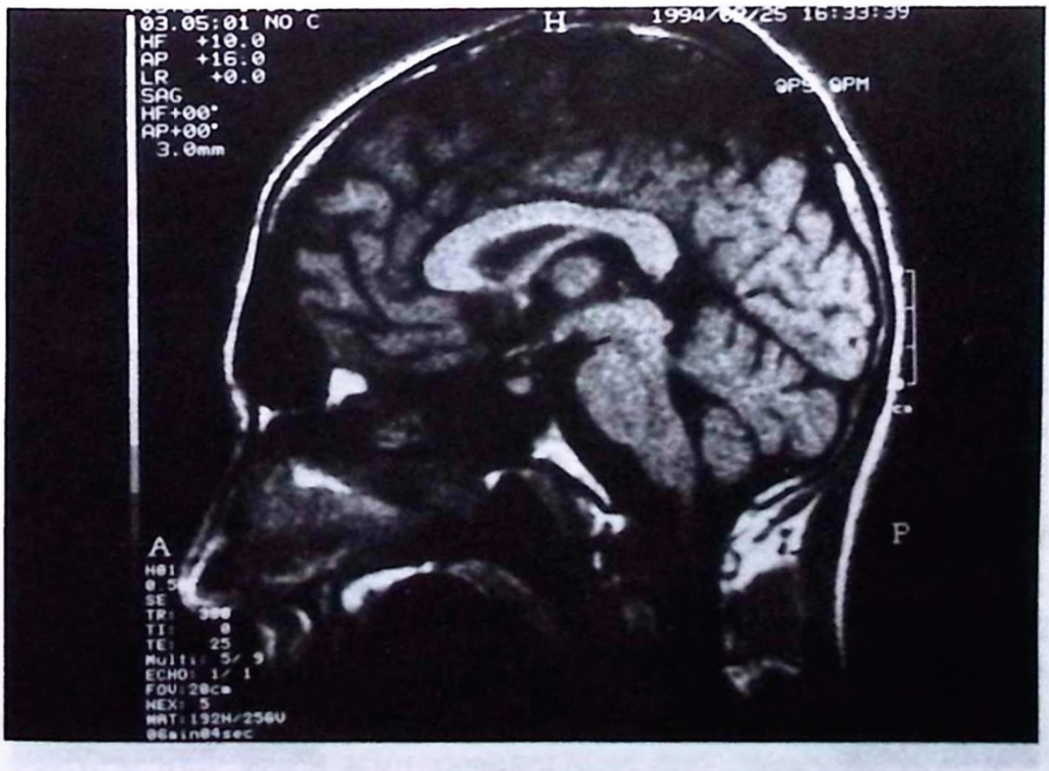


Fig. 3: MR examination showing thickening of the pituitary stalk and the absence of the normal hyperintense signal of the posterior hypophysis (arrow).

Forced vital capacity was reduced to 61 percent. The diagnosis of LCH was made by skin biopsy (Fig. 4) along with the other supporting clinical and laboratory findings.

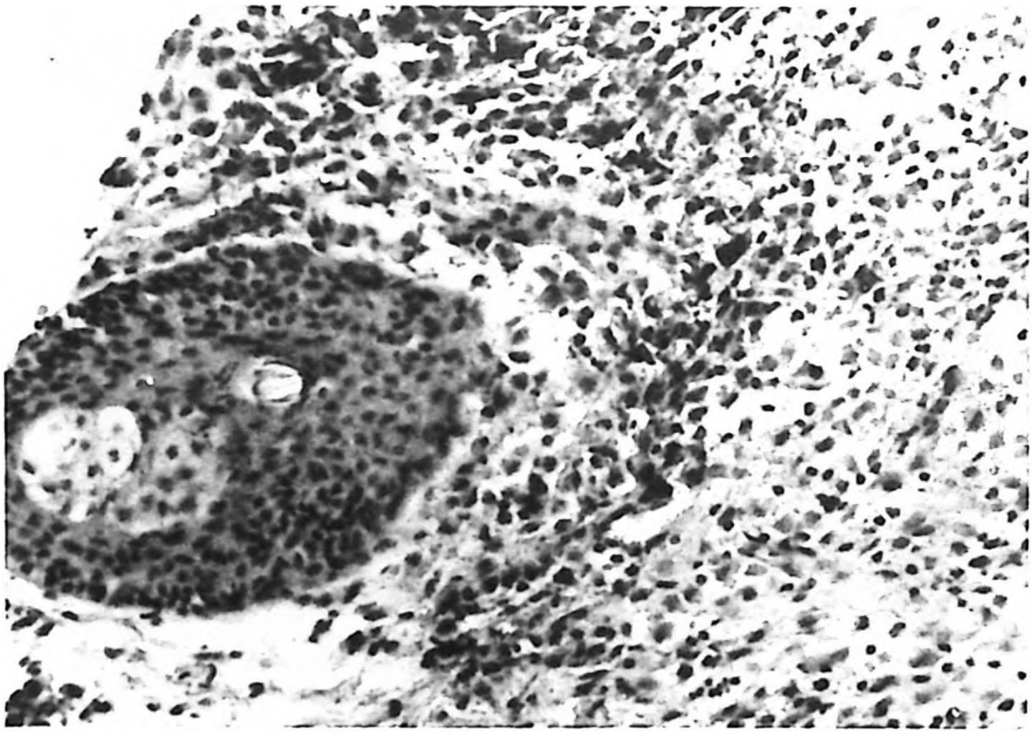

Fig. 4: The superficial dermal infiltrate consists of mononuclear histiocytes with indented nuclei.

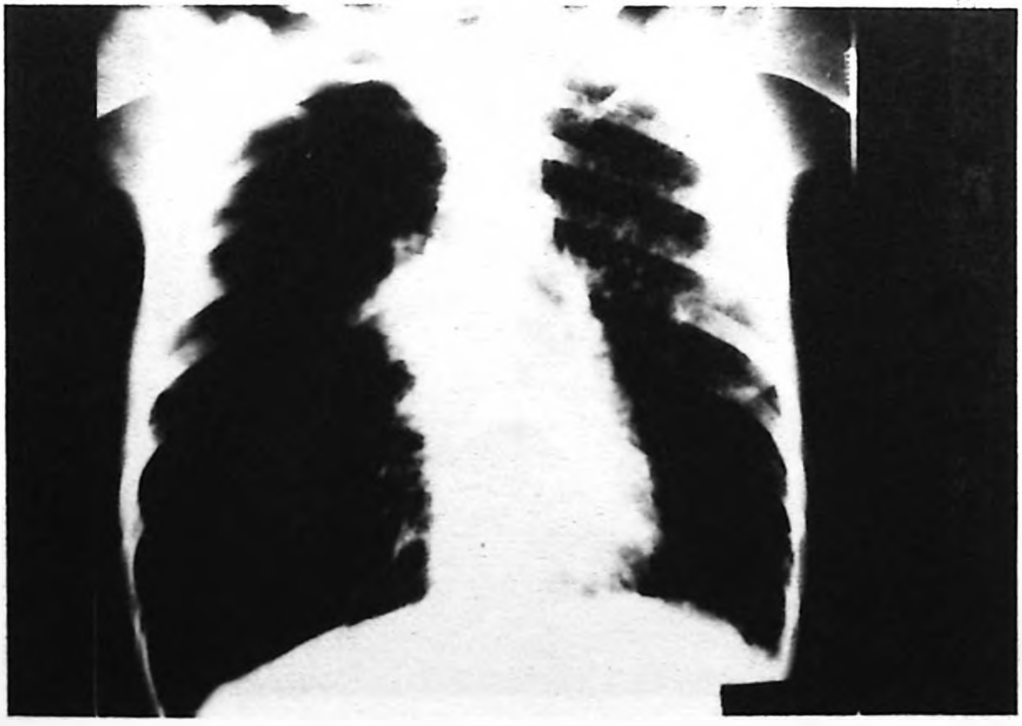

Fig. 5: Chest radiograph showing unilateral pneumothorax with typical findings of pulmonary LCH.

The patient was given a combination of arginine-vasopressine, prednisolone and vinblastine. Although prednisolone and vinblastine were discontinued three months after initiation of the therapy, arginine-vasopressine administration continued. Radiologic abnormalities of the pulmonary disease were not improved by the therapy, and the disease was complicated by four episodes of spontaneous pneumothorax which were treated with tube drainage during the three-year follow-up period (Fig. 5).

## Discussion

Pulmonary involvement of LCH is an uncommon but important cause of pulmonary fibrosis and honeycombing in young adults[3]. It is suggested that 40 percent of patients with multisystem LCH have clinical and/or radiological evidence of lung pathology[4]. The most common functional disturbance is reduced lung or respiratory compliance with reduced lung volume and abnormal lung perfusion[4, 5]. In our case, vital capacity was found to be decreased. The main pathologic feature of pulmonary LCH is peribronchiolar inflammation leading to fibrosis and cyst formation. Although pulmonary LCH may be suspected on the basis of chest radiographic findings, the CT findings of predominantly upper lobe nodules and cysts are virtually pathognomonic[3, 5, 6]. All of these abnormalities were demonstrated in our case.

Diagnosis can be established by transbronchial or open lung biopsy[2]. However, Ha et al.[4] suggested that biopsy is unnecessary in most cases because lung involvement is often mild and transient and usually parallels overall disease activity. Lung biopsy should be considered when radiologic and clinical signs progress during follow-up[4]. We did not attempt an open lung biopsy because of the stable course of disease in our patient.

As pulmonary LCH progresses, the nodules decrease in number, leaving multiple thin-walled cysts. Rarely, cysts may be complicated by spontaneous pneumothorax. Januszkiewicz et al.[7] reported a case with three episodes of spontaneous pneumothorax due to pulmonary LCH. The present case was complicated by four episodes of spontaneous pneumothorax during the three-year follow-up period. Tube drainage was performed for each recurrence of spontaneous pneumothorax.

Pulmonary LCH may be isolated or associated with multiple organ involvement such as bone, hypothalamus, skin, etc[2]. Diabetes insipidus is a well-recognized component of LCH, with a reported prevalence of 5-50 percent in different series[8]. It is thought to be a result of infiltration of the posterior pituitary by Langerhans cells[9]. Only a few patients have DI on presentation with LCH, but it may develop during the first four years after presentation and diagnosis of LCH[9]. On MR examination, thickening of the hypothalamus and the pituitary stalk in the absence

of the posterior pituitary bright signal is seen in children with overt DI[10], as in our patient. Systemic drug therapy is generally offered only when there is complicating failure to thrive or gross organ dysfunction[5].

Treatment programs incorporate a variety of chemotherapeutic agents, including prednisolone, etoposide, methotrexate, cyclophosphamide and vinblastine[2]. It has not been possible to estimate a clear benefit from any particular treatment. The majority of cases resolve partially or completely, but some deteriorate[5]. Although in our case the lung function tests improved, radiologic improvement was not detected during prednisolone and vinblastine therapy, and the disease was complicated by four episodes of spontaneous pneumothorax.

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