Isolated Pulmonary Langerhans-Cell Histiocytosis Mimicking Miliary Tuberculosis

Miliyer Tüberkülozu Taklit Eden İzole Pulmoner Langerhans Hücreli Histiositoz Olgusu

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Abstract

Isolated involvement of lungs in the course of Langerhans'-cell histiocytosis (LCH) is very rare in childhood. Spontaneous pneumothorax (PTX) may occur during the course which necessitates rapid intervention. We present a 17 months-old girl who was sent with the pre-diagnosis of miliary tuberculosis. Despite antituberculosis therapy, her pulmonary function deteriorated. The chest tomography showed a different lung pattern which is suggestive of LCH. The biopsy findings and immunohistochemistry staining supported the diagnosis. She experienced recurrent pneumothorax incidences which were managed by drainage. She responded well to chemotherapy. Although rare, isolated pulmonary LCH should be remembered in differential diagnosis of cystic lung disease in childhood. On time diagnosis, appropriate therapy and rapid intervention for pneumothorax have important impacts on patient prognosis.

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Key words: Langerhans'-cell histiocytosis, pulmonary involvement

Özet

Çocukluk döneminde, LCH hastalığı sırasında sadece akciğerlerin tutulması nadir olarak görülen bir tablodur. Kendiliğinden oluşan pnömotoraks atakları hastalık esnasında görülebilir ve hızlı şekilde müdahale edilmelidir. Bu yazıda kliniğimize miliyer tüberküloz ön tanısı ile sevk edilen 17 aylık bir kız çocuğunun klinik takibini sunmak istedik. Antitüberküloz tedavi kullanmasına rağmen, hastanın akciğer fonksiyonları bozulmaya başladı. Çekilen göğüs tomografisinde hastanın akciğer dokusunda LCH ile uyumlu bir görüntü mevcuttu. Biopsi bulguları ve immunohistokimyasal boyama sonuçları da LCH tanısını destekledi. Klinik seyri esnasında su altı drenajı ile tedavi edilen tekrarlayan pnömotoraks atakları gelişti. Başlanan kemoterapi olumlu şekilde sonuçlandı. Nadir olmasına rağmen, çocukluk döneminin kistik görünümlü akciğer hastalıklarının ayırıcı tanısında pulmoner LCH tanısı akılda bulundurulmalıdır. Zamanında teşhis, uygun tedavi ve olası pnömotoraks atakları için yapılan hızlı girişimler hastanın prognozunda önemli yer tutmaktadır. *(Çocuk Enf Derg 2009; 3: 135-7)*

Anahtar kelimeler: Langerhans hücreli histiositoz, pulmoner tutulum

Introduction

Pulmonary Langerhans`-cell histiocytosis (LCH) forms part of a spectrum of diseases characterized by monoclonal proliferation and infiltration of organs by Langerhans` cells (1). Isolated type pulmonary disease occurs predominantly in adults, whereas this is rare in children (2). The adult predominance reflects the only consistent epidemiologic association; cigarette smoking is present in an overwhelming majority (1).

Spontaneous pneumothorax (PTX) occurs in approximately 10% of children with pulmonary LCH, and may show recurrence in adulthood (3). Although recurrent PTXs have a poor long-term outcome in adults, its prognostic significance is unclear in the pediatric age group because of the limited case number. Regarding the literature, the majority of subjects may have a fatal outcome despite being diagnosed and treated properly.

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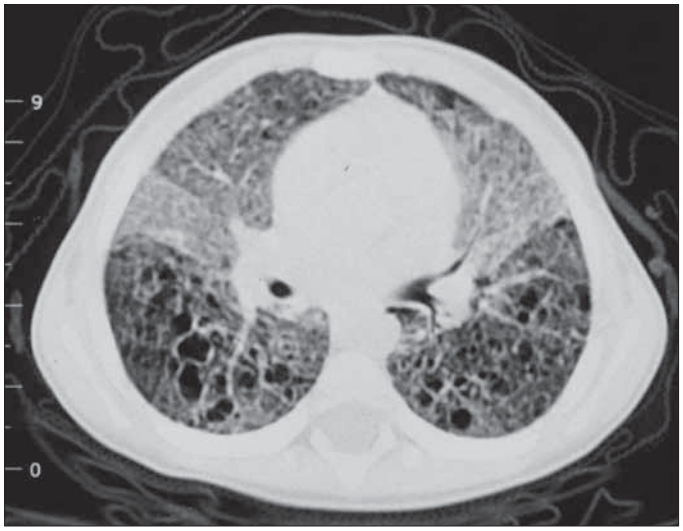

Figure 1. HRCT demonstrating peribronchial nodules and cystic changes

Case Report

A seventeen-month old female patient was admitted to our tertiary-care teaching hospital with the complaints of worsening malaise, fever and cough for the previous 2 months. Despite the use of wide-spectrum antibiotics for 3 weeks, her clinical picture had not improved at a local hospital. Appearance of reticulo-nodular image on the most recent chest X-ray (CXR) caused her transfer to our clinic with the presumptive diagnosis of miliary tuberculosis.

There was a reported pulmonary tuberculosis case in an adult relative who had occasionally visited the family. Hepatomegaly was the only pathologic finding on physical examination. The respiration rate, type and auscultation findings were regular. Her growth parameters were also within the normal range.

The hemogram, liver function tests, sweat chloride test and immune status showed normal results. Her PPD test provoked no response, and close contact screening of the family for tuberculosis was negative. Abdominal ultrasonography revealed diffuse hepatomegaly. We continued the four-drugs antituberculosis therapy which was ordered at the previous healthcare centre.

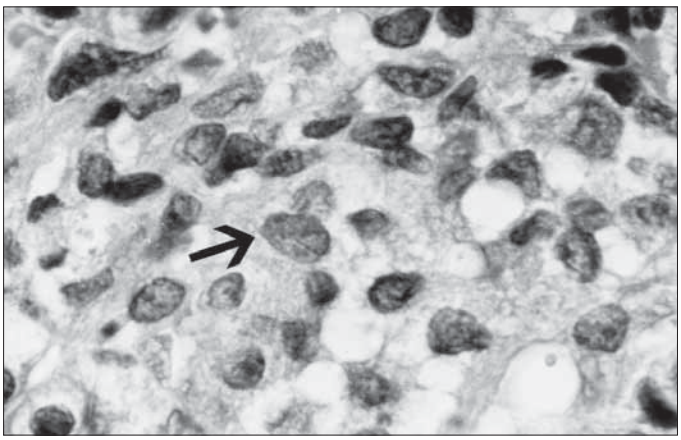

Figure 2. H-E stain morphology of histiocytes with abundant cytoplasm, and large nuclei with a coffee bean configuration characteristic of Langerhans' cells

Her follow-up CXRs showed not only a disseminating reticulo-nodular pattern but also a cystic appearance. High-resolution computed tomography (HRCT) of the thorax demonstrated peribronchial nodules and cystic changes which were less than 20 mm in diameter and typically had a thin wall (Fig. 1). Since the HRCT findings were not compatible for miliary tuberculosis, we performed open lung biopsy upon gradual development of cyanosis and dyspnea. Histology showed an infiltration composed of lymphocytes, plasma cells, eosinophils and histiocytes which had abundant cytoplasm, and large nuclei with a coffee bean configuration characteristic of Langerhans' cells (Fig. 2). Immunoperoxidase staining of the histiocytes revealed strong cytoplasmic positivity with S-100 protein antibody. In addition, immunohistochemistry showed dense infiltration of CD1a stained Langerhans' cells (Fig. 3).

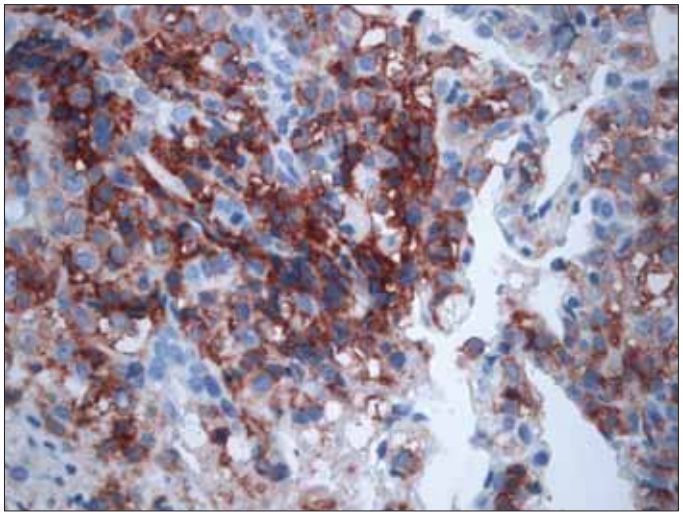

Figure 3. Langerhans' cells with CD1a stain

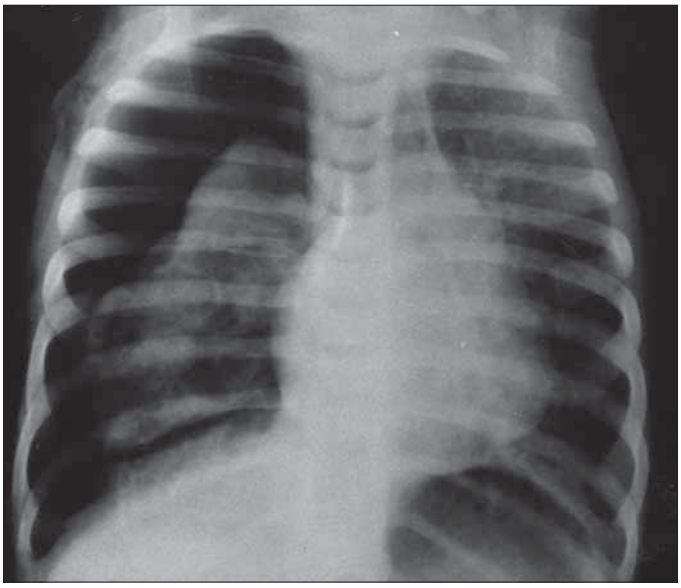

Figure 4. Pneumothorax in third episode

Concurrent radiological and scintigraphic evaluation of bones, bone marrow evaluation and cranial MRI showed no pathology.

She developed a right-sided PTX (Fig. 4) five days after operation which was successfully drained. However, the next 38 days saw an undulating clinical course due to recurrent bilateral PTXs (a total of four independent episodes). All the episodes were ameliorated by under-water sealed drainage and conservative interventions. Her initial chemotherapy for pulmonary LCH consisted of continuous methylprednisolone and mercaptopurine (6MP) tablets plus weekly etoposide and vinblastine injections. The patient responded well to this regimen, and was free of initial symptoms in her 12th month follow-up. However, mild to moderate pulmonary fibrosis developed which is an important mechanism of lung remodelling.

Discussion

The miliary pattern is a well-known chest radiographic pattern, consistent with the multiple nodules in the lung. A heterogeneous group of conditions comprising more than 80 entities may display this pattern (4). Random nodules are uniform and even in distribution which is the probable form in disseminated granulamatous infections such as tuberculosis or fungal disease (5).

Miliary tuberculosis refers to hematagenous dissemination of tubercle bacilli in primary and post-primary tuberculosis. The CXR plays an important role in the diagnosis but is limited by its low sensitivity (6), 60%. HRCT allows early specific diagnosis by showing multiple, well-defined nodules appearing in a random pattern. In addition, associated features such as a preexisting tuberculosis lesion, consolidation with or without cavitations, small pleural effusions and mediastinal lymph nodes may be visible (5). Therefore, thoracic HRCT must be evaluated in the differential diagnosis of a miliary pattern before initiating antituberculosis therapy, even in high-prevalence countries.

The most common presenting symptoms of pulmonary LCH are nonproductive cough and dyspnea. Weight loss, night sweats and anorexia occur in up to a third of patients (7) mimicking *M. tuberculosis* infection. The most common early radiographi c abnormalities are bilateral, symmetric, peribronchiolar, micronodular and interstitial infiltration with a predominance of middle and upper lobe involvement (6) as in *miliary tuberculosis*. Cystic changes are commonly superimposed on a background of reticulonodular pattern as they become more prominent in the later stages of disease. Typically thin walled lung cysts are less than 20 mm in diameter and necessitate thoracic HRCT for a probable diagnosis (8). Disease progression is accompanied by the consecutive development of bullae and subsequent fibrosis yielding a “honey-combing” appearance.

Spontaneous PTXs are thought to arise from the rupture of a thin-walled subpleural cystic lesion (9), a complication seen infrequently in childhood . PTX can occur at any time throughout the disease, but are occasionally seen as the initial manifestation. PTX has been previously described as a postoperative complication, just as in this case (3). It is likely that mechanical ventilation during the operation induces the development. If at all possible, this procedure should be postponed in order to avoid recurrent PTXs which were reported to carry a poor prognosis in adults and children. Instead of invasive procedures, a combination of classical thoracic HRCT findings and immunocytochemical investigations of bronchoalveolar lavage (BAL), using anti-CD1a antibodies (10), should be preferred for the definite diagnosis of isolated pulmonary LCH and this in turn will also diminish complications.

No specific recommendations are present in the literature for the management of PTXs in the course of pediatric pulmonary LCH. This case underwent only under-water sealed drainage since the timing and importance of pleurodesis and thoracotomy for recurrent PTXs have not yet been established. The small number of pediatric cases presenting at individual centers, and conflicting results pertaining to each technique prevent the formation of consensus. We would like to emphasize that drainage and effective conservative follow-up may be enough for the management of PTXs in pediatric pulmonary LCH even in recurrent episodes, and sophisticated procedures should be reserved for unresponsive cases.

As a result, the miliary pattern necessitates thoracic HRCT for the differential diagnosis. The combination of thoraxcic HRCT and immunocytochemical investigations of BAL may be sufficient to diagnose pulmonary LCH. Mechanical ventilation must be undertaken with caution in pulmonary LCH, and if possible avoided. PTXs, even when recurrent, do not always imply a poor prognosis in the pediatric population.

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