We herein report an extremely rare case of pulmonary Langerhans cell histiocytosis with a solitary enlarged inguinal lymph node. A 19-year-old man presented with a non-productive cough lasting for over a five-month period and an enlarged left inguinal lymph node that had persisted for four months. A histopathological study of the lymph node specimens found Langerhans cells coupled with eosinophils. Positive immunohistochemical staining for langerin, Cluster of Differentiation 1a, S100 in the Langerhans cells confirmed the diagnosis, and a mildly impaired ventilation function in addition to multiple peripheral pulmonary cystic lesions were detected. The patient was managed with prednisone (0.5 mg/kg daily), with slow tapering over several months.

Key words: pulmonary Langerhans cell histiocytosis, lymph node, immunohistochemistry, biopsy


Introduction

Langerhans cell histiocytosis (LCH) is a rare type of histiocytic syndrome characterized by the infiltration of tissues with specific Langerhans cells, dendritic cells, T-lymphocytes and other inflammatory cells (1, 2). LCH may affect single organs (SLCH, formerly termed eosinophilic granuloma), such as the bones, skin or lymph nodes, or may occur as a multisystemic illness involving several organs (MLCH, formerly termed Letterer-Siwe or Hand-Schuller-Christian disease). MLCH is further categorized into a high-risk group (involving one or more ‘risk organs,’ including the spleen, liver, lungs and bone marrow) and a low-risk group (without the involvement of risk organs). SLCH accounts for approximately one-third of cases of LCH. The estimated incidence of LCH is one to two cases per million in adults versus four to nine cases per million in children (1, 3-5). The occurrence of isolated pulmonary involvement in LCH (referred to as PLCH) is more rare in pediatric cases, although multisystemic LCH is more prevalent in children than that observed in the adult population.

To the best of our knowledge, extrapulmonary involvement is not present in the majority of patients. Although, if present, the pituitary gland (5-15% of patients), bone (4-15%) and skin (<5%) are the most common target sites. PLCH with extension restricted to the regional lymph nodes has only been rarely reported (6-9). We herein document a case of adult Langerhans cell PLCH accompanied by solitary inguinal lymphadenopathy.

We therefore share the clinical, histopathological and radiographic features of this rare case. The patient provided his written informed consent.

Case Report

A 19-year-old man noted a non-productive cough lasting for over a five-month period. He denied previous fever, weight loss, night sweats or bone pain. Four months prior to the current presentation, the patient detected an enlarged left inguinal lymph node, as large as an egg, the mass of which changed over time. He had been a mild smoker for less than one year, averaging 3-5 cigarettes a day. His medical and other history was otherwise unremarkable.

On a physical examination, the patient had a healthy general appearance and was afebrile, with a BMI of 20.5 kg/m². An examination of the ear, nose, throat and neck was unremarkable, with the exception of a 4x3-cm, solitary, mildly
mobile, nontender mass present in the left groin. Blood test results were within the normal limits, including a complete blood count and blood chemistry profile. High-resolution computed tomography (HRCT) enhanced scanning of the chest demonstrated multiple peripheral pulmonary cystic lesions without pulmonary nodules or enlarged mediastinal lymph nodes (Fig. 1, 2). Bronchoscopy showed no narrowing of any lobe bronchi, and cytology of the bronchoalveolar lavage fluid demonstrated no malignant or atypical malignant cells. The ratio of forced expiratory volume in 1 second (FEV₁) to forced vital capacity was 72%, while the ratio of FEV₁ to the predicted value was 68%. The diffusing capacity to carbon monoxide (DLco) was normal.

The patient underwent a lymph node biopsy, and hematoxylin and Eosin (H&E)-stained tissue sections revealed the proliferation of atypical cells with coffee bean-like nuclei, pink cytoplasm and focal nuclear grooving, coupled with eosinophilia. Nuclear pleomorphism was notable, characterized by prominent lobulation with indentation and twisting indentations of nuclei as well as occasional prominent nucleoli (Fig. 3A). Furthermore, slides stained for langerin, Cluster of Differentiation 1a (CD1a) and S100 for the immunohistochemical analysis were positive, as shown in Fig. 3B-D, respectively. Consequently, a series of cranial enhanced MRI scans, abdominal CT scans and a whole-body bone scan were performed, with no abnormal findings.

As a result, LCH of the lung and inguinal lymph nodes was diagnosed. The patient was managed with prednisone at a dose of 0.5 mg/kg daily, using slow tapering over several months and close monitoring. Pulmonary function tests were applied monthly, with no significant improvements noted two months later.

**Discussion**

The etiology of LCH remains unclear. Compelling evidence indicates that exposure to cigarette smoke is the most important factor associated with the development of PLCH, as over 90% of adult patients who develop PLCH are cigarette smokers or were previously subjected to substantial second-hand smoke (10). Previous trials have also demonstrated that cigarette smoke directly promotes pro-survival dendritic/Langerhans cell signal pathways (1). However, a perplexing and yet unresolved question arises regarding the phenomenon in which only a very small proportion of smokers develop PLCH, as observed in the present case; i.e., our patient had a very short and low-dose smoking history, possibly implying the role of endogenous host factors (genetic factors) or additional exogenous factors (viral infection).

PLCH is more common in adults than children, and the lungs may be the sole organ involved or the condition may occur as a component of multisystem disease (10). The characteristic feature of PLCH is the accumulation of Langerhans and other inflammatory cells in small airways, leading to the formation of nodular inflammatory lesions. Peribronchial lesions destroy the cellular and connective tissue components of the bronchiolar walls, thus resulting in progressive dilatation of the small airways, which are eventually surrounded by fibrous tissue (11). On chest HRCT, PLCH manifests as small nodules and thin- or thick-walled cysts, with a characteristic distribution in the upper and middle lung fields and relative sparing of the lung bases (12).

The onset of lymphadenopathy in cases of PLCH is rare, thus making the current patient’s clinical manifestation seven more rare than would normally be expected. After conducting a thorough literature review, we found only six documented cases of PLCH with regional lymphadenopathy (3, 6, 7, 13-15) (Table). Five of these cases involved enlarged mediastinal lymph nodes (two cases concomitant with submandibular or cervical lymph nodes, respectively) and the rest one was only cervical lymphadenopathy, of which only four cases had histologic evidence. To the best of our knowledge, there are no previously documented cases of
PLCH accompanied by isolated inguinal lymphadenopathy. The mechanism underlying the development of solitary lymph nodes in the setting of PLCH has not been thoroughly elucidated to date. Whether this condition occurs as part of the disease process or is the final phenotype requires more research.

A critical component of the management of adults with PLCH is smoking cessation. Pharmacotherapy with immunosuppressive medications should be considered for all adult patients with severe disease and those exhibiting a progressive decline in the lung function. Corticosteroids and other immunosuppressive agents, including chlorodeoxyadenosine (also known as cladribine or 2-CDA), cyclophosphamide and methotrexate, have been used to treat progressive disease (16, 17), and lung transplantation is a therapeutic option in a select number of patients who present with progressive disease despite receiving treatment with smoking cessation and immunosuppressive therapy. In the current case, because our patient had an impaired lung function, we selected prednisone therapy. However, to our disappointment, after two months of treatment, his pulmonary function showed no improvements. We will continue to evaluate the curative effect in the months ahead in order to determine whether this therapy is necessary.

PLCH affects both the mediastinal and peripheral lymph nodes, including the submandibular, cervical and inguinal lymph nodes.

The authors state that they have no Conflict of Interest (COI).
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References