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Case Report

A case of invasive Langerhans cell histiocytosis localizing only in the lung and diagnosed as pneumothorax in an adolescent female

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Abstract: In infants, Langerhans cell histiocytosis (LCH) is associated with poor clinical outcomes as Langerhans cells invade and damage multiple organs, a presentation that is different from that in adults. Here, we present a case of a 15-year-old female who visited ourclinic complaining of right chest pain and dyspnea. She was diagnosed with right pneumothorax by chest X-ray. Chest computed tomography showed multiple cystic changes in the bilateral lung. Additionally, bullous lesions occupying the upper lobe and multiple white tiny nodules on the surface of the lung were observed by thoracoscopy. These nodules comprised proliferating atypical CD1a/S-100-positive cells invading the pulmonary parenchyma, leading to the diagnosis of LCH. Because of the extensive invasion into the pulmonary parenchyma, chemotherapy was administered. This case of LCH was unique in that the age of onset was atypical and the tumor cells occupied a single organ, despite their malignant behavior.

Keywords: Langerhans cell, pneumothorax, young female, CD56

Introduction

Langerhans cell histiocytosis (LCH) is a very rare disease. Pulmonary Langerhans cell histiocytosis in adults is a benign disease and is usually caused by smoking; in such cases, LCH can be successfully treated by controlling the patient's smoking habits [1]. On the other hand, in children under 10 years of age, LCH represents a malignant blood disease invading multiple organs [2]. Herein, we introduce a case of LCH invading only the bilateral pulmonary parenchyma, thus causing pneumothorax in an adolescent female.

Case report

A 15-year-old female, who was a nonsmoker and previously healthy, visited our outpatient office complaining of dyspnea and right chest pain. She had no relevant medical or family history related to her symptoms. Chest X-ray revealed a right tension pneumothorax and bilateral bullous lesions at the lung apex. Chest computed tomography (CT) scan (**Figure 1A**) taken after chest drainage showed right pneumothorax and bilateral cystic changes in the lung parenchyma, predominantly in the bilateral upper lobes. Cystic walls were thickened compared with those in the pneumothorax of young adults. An operation was performed because of continuous air leakage for four days after chest drainage and the histological diagnosis of this uncommon cystic lung disease. Under thoracoscopic view, multiple bullous lesions were found to occupy most of the right upper lobe, and small white nodules of 2-3 mm in diameter were observed on the surface of the right middle lobe. The air leakage point was easily detected on the surface of one of the bullous lesions, and this leakage point was ligated. Some of the tiny nodular lesions and a small section of the bullous lesions were resected for histological diagnosis. The postoperative course was uneventful. Two months after surgery, the patient received chemotherapy according to the protocol JLSG-02, described by the Japan Langerhans

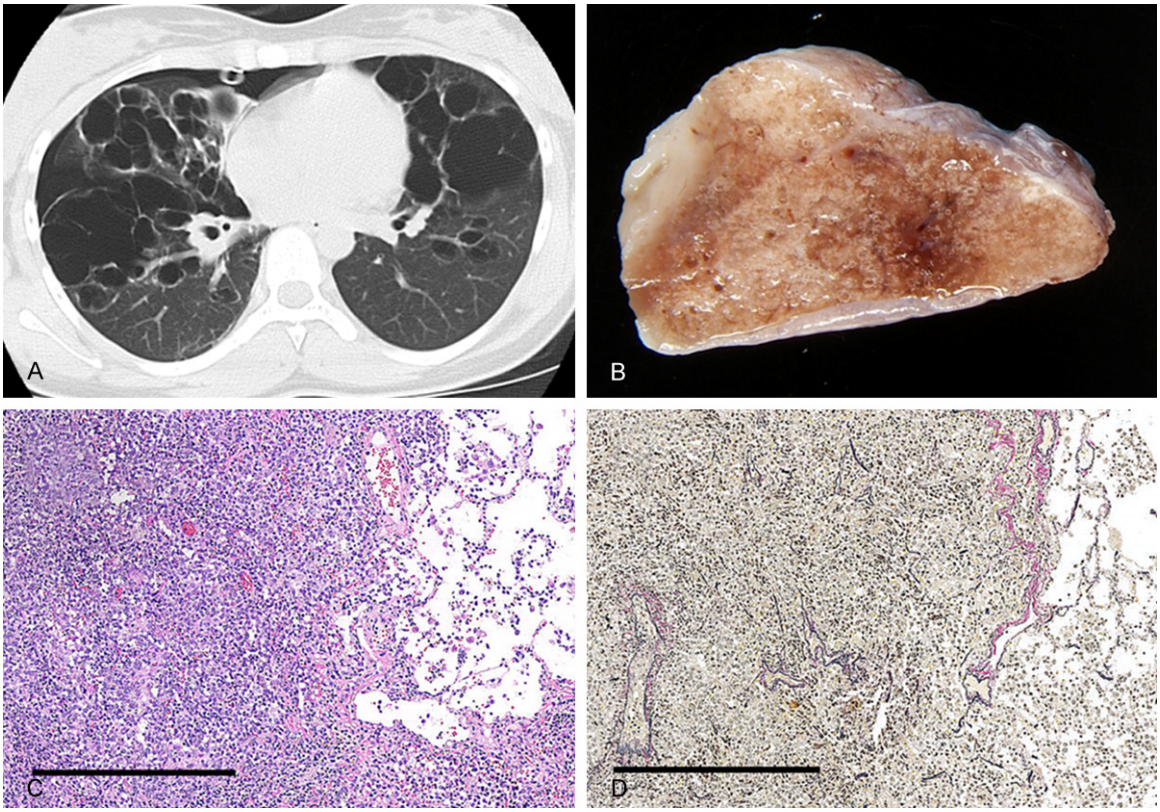

Figure 1. (A) Chest CT showed right pneumothorax and multiple cystic lesions in the bilateral lungs. (B) Macroscopically, excisional biopsy revealed tiny nodules approximately 2 mm meter in diameter and multiple subpleural cysts. Hematoxylin-eosin (HE) (C) and Elastica-van Gieson (EVG) (D) staining with low magnification imaging showed that the nodules were located around the bronchus and pulmonary artery, with destruction of elastic fibers of the alveoli and infiltration into the blood vessels. The bar is 400 μm.

Cell Histiocytosis Study Group. The patient has been receivingchemotherapy according to the JLSG02 protocol for 6 months. The current state of progression of the disease is not revealed.

Pathological findings

Macroscopically, excisional biopsy revealed a few tiny nodules and small cystic lesions (**Figure 1B**). Microscopically, lower magnification images showed some peribronchial nodules expanding into the surrounding alveolar septa and alveoli, as well as peripheral cystic enlargement of air spaces (**Figure 1C**). Higher magnification images revealed atypical cells with round, large nuclei and eosinophilic cytoplasms in the parabronchial nodules with little eosinophilic infiltration (**Figure 2A**). Elastica-van Gieson staining revealed that the tumor cells proliferated and expanded in stromal tissue, destroying the elastic fibers of the alveolar septa (**Figure 1D**). Infiltration into vessels was also observed. These atypical cells were immunohistochemically positive for CD1a, S-100, CD56, and CD4 and negative for alpha smooth muscle action (α-SMA), CD34, and AE1/AE3 (**Figure 2B-D**). Based on these findings, the final diagnosis was pulmonary LCH.

Additional evaluation

After pathological diagnosis, whole-body enhanced CT scan and positron emission tomography (PET)-CT was performed. CT scan showed no abnormal findings other than bilateral lung. Fluorodeoxy glucose (FDG) was also accumulated in the bilateral lungs, and no accumulation of any other agent was detected.

Discussion

LCH, which was identified by Lichtenstein in 1953, includes 3 types of diseases, eosinophilic granuloma (EG), Hand-Schuller-Christian disease (HSC), and Lettere-Siwe disease (LS). EG

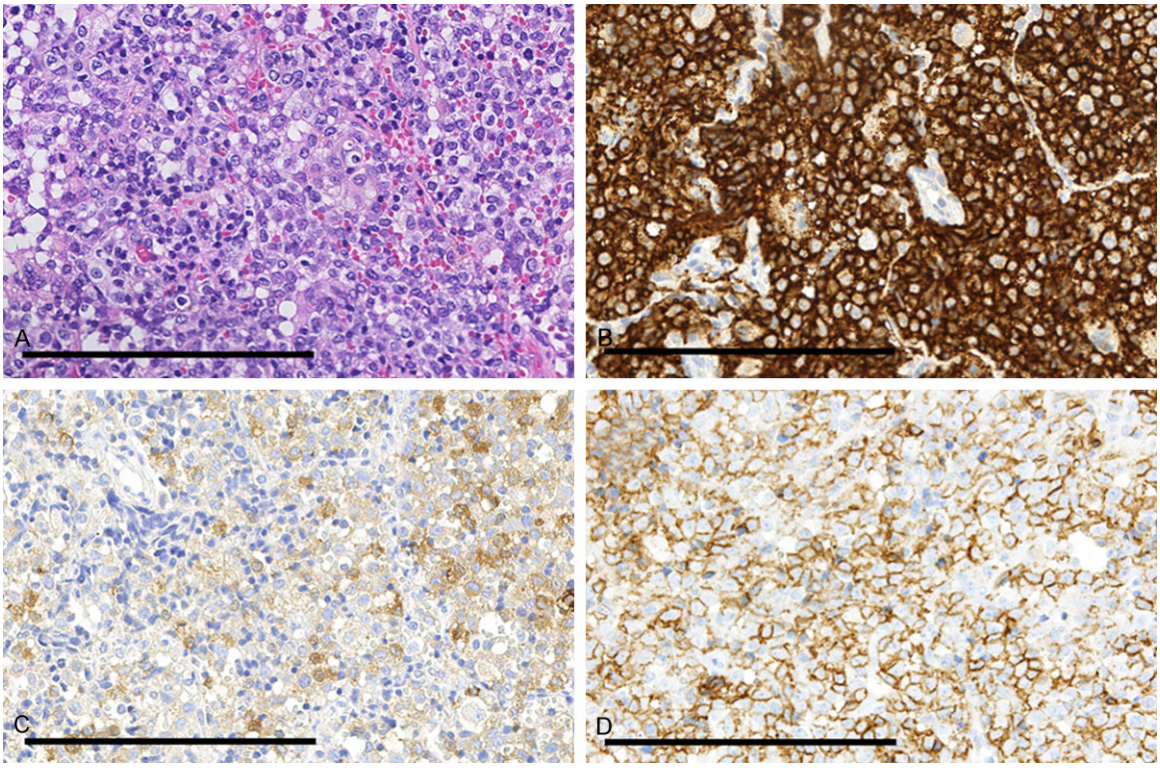

Figure 2. (A) High-magnification images showed that tumor nodules were composed of atypical cells with round, large nuclei and eosinophilic cytoplasms with lymphocytic and eosinophilic infiltration. Immunohistochemically, the tumor cells showed diffuse positive staining for CD1a (B) and CD56 (D) and focal staining for S-100 (C). The bar is 200 μm.

mostly occurs in patients over 20 years of age and is strongly associated with smoking. In 80% of EG patients, the only organ affected by Langerhans cells is the lung. Moreover, control of patients' smoking habits is highly effective for managing the disease and patients with EG generally have favorable prognoses. While most of adult LCH is EG, LCH in infants usually occurs as HSC. HSC spreads to multiple organs, but generally does not occur in life-supporting organs, such as the lung, heart, and liver, and exhibits slow progression. Exophthalmos, diabetes insipidus, and skull disorders are main symptoms of HSC. Finally, LS generally occurs in infants 3 years of age or younger and spreads to multiple organs, including life-supporting organs. In LS, the Langerhans cells themselves exhibit histological features common in malignant cells and destroy the parenchyma of targeted organs. Despite the use of chemotherapy in patients with LS, the prognosis is generally quite poor [3].

In LCH, Langerhans cells exhibit eosinophil-like cytoplasms and constricted nuclei, resembling fava beans. Immunohistochemically, Langerhans cells will be specifically stained by CD1a and S-100 [4], and among these CD1a/S-100-positive cells, CD56-positive cells are likely to invade and destroy the parenchyma of target organs [5]. In our case, the patient was 15 years old; no LCH classification includes patients of this age. Histologically, Langerhans cells possessed malignant features indicative of organ invasion and destruction and were cytologically CD56 positive. From a pathological perspective, the patient's disease was similar to LS. However, only the lungs were invaded by Langerhans cells. Therefore, we diagnosed this disease as malignant pulmonary Langerhans cell histiocytosis and started chemotherapy. The recommended chemotherapy for LCH is vinblastine, 6-mercaptopurine, and prednisone, according to the Histiocytosis Society [6]. In Japan, the Japan Langerhans Cell Histiocytosis Study Group (JLSG) recommends the JLSG-02 protocol for LCH [7]; we treated our patient with this protocol.

Intrathoracic ectopic endometriosis, lymphangioleiomyomatosis (LAM), pulmonary Langerhans cell histiocytosis (PLCH), Birt-Hogg-Dube

syndrome (BHD), lymphoid interstitial pneumonia (LIP), and amyloidosis are known causes of secondary pneumothorax in women [1, 8, 9]. Again, none of these diseases are thought to occur in adolescents of 15 years of age. Therefore, it was very difficult to make an accurate clinical diagnosis for this patient, who had pulmonary disease with pneumothorax. Thoracoscopic pulmonary biopsy played an important role in making the final diagnosis and initiating appropriate treatment for this very rare pulmonary disorder.

Disclosure of conflict of interest

None.

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