

CASE REPORT

Recurrent pulmonary infections as the first presentation of Letterer Siwe disease

Leen Jamel Doya^{1,*†}, Ghazal Dib¹ and Fouz Hassan²¹Department of Pediatrics, Faculty of Medicine, Tishreen University Hospital, Lattakia, Syria, ²Department of Dermatology, Faculty of Medicine, Tishreen University Hospital, Lattakia, Syria*Correspondence address. Department of Pediatrics, Tishreen University Hospital, Lattakia, Syria. Tel: +0963 992856983; E-mail: dr.leen.doya@gmail.com; leen.doya@tishreen.edu

Abstract

Langerhans cell histiocytosis (LCH) is a rare disease of unknown etiology that affects several organs. The fatal type of Langerhans cell histiocytosis is called Letterer Siwe disease (LSD) which is multisystem with a poor prognosis. Herein, we report a 20-month-old male who was admitted for recurrent pulmonary infections at the age of 10 months. Diagnostic workup revealed a Letterer-Siwe disease. The patient was treated with a good response.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare group of diseases characterized by accumulation and infiltration of histiocytes and dendritic cells driven by mutations in the mitogen-activated protein kinase pathway [1]. The estimated annual incidence of LCH is 1:500 000, mainly affecting males under 3 years old [2]. LCH may characterize as a single-system (unifocal or multifocal) and multifocal multi-system (Letterer-Siwe disease; LSD) [3]. The majority type of LCH is a single-system disease that may involve a limited number of organs, most common in skin and bone [4]. The multi-system disease affects multiple organs, most commonly skin, bone, lymph nodes, thymus, lungs, pituitary gland, liver, spleen, bone marrow and central nervous system, that cause organ dysfunction [3].

CASE REPORT

A 20-month-old boy was referred to the Pediatric clinic for recurrent pulmonary infections. He was the first child in the family, born at term weighing 4 kg, following a normal pregnancy. There were no concerns in the neonatal period. At 10 months old, he suffered from fever measured at (39.5–40)°C at a rate

of 2 to 3 times daily, partly controlled with antipyretic, associated with difficulty breathing. He was admitted to the pediatric department for 72 days. During admission, he had extensive subcutaneous emphysema of the neck and needed oxygen. He was diagnosed with staphylococcal pneumonia and treated with broad-spectrum antibiotic therapy. At 14 months old, he was admitted to the hospital for 2 weeks with a lung infection requiring an invasive ventilator for 1 week. There was not any other medical, surgical or family history. He was passive exposure to tobacco smoke. The child underwent all the compulsory immunizations recommended for his age. On physical examination, his body weight was 14 kg (90.32%), length was 85 cm (58.706%), temperature 39°C, oxygen Saturation 95%, arterial blood pressure was 90/55 mm Hg, he was vitally stable and generally well. The patient underwent multiple investigations that showed hypochromic microcytic anemia [Hb 10 g/dl, MCV 59 fl] with an inflammatory response [C-reactive protein (CRP) 52 mg/l, erythrocyte sedimentation rate (ESR) 84 mm at the end of 1st hour]. Other investigations including hepatic and renal function, blood glucose, and blood gas urinary investigations were normal. Chest X-Ray showed cloudy bilateral infiltrations (Fig. 1). Chest computed tomography (CT) showed bulging cysts, bronchiectasis with significant damage on the pulmonary tissue

[†]Leen Jamel Doya, <http://orcid.org/0000-0003-0814-5135>

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Figure 1: Chest-X-Ray demonstrating bilateral hazy infiltrates.

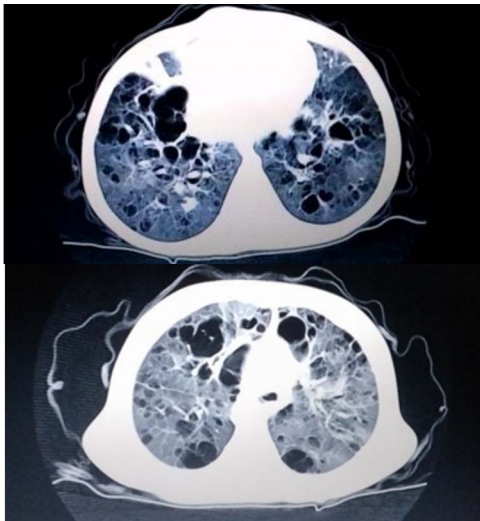


Figure 2: Chest computed tomography (CT) showed bulging cysts, bronchiectasis with significant damage on the pulmonary tissue.

(Fig. 2). Echocardiography, electrocardiogram (ECG), abdominal ultrasound, and direct investigation of *Bacillus Koch* in sputum on three-morning samples were performed that were normal. Pulmonary pressure was normal. Cystic fibrosis mutations, Immunoglobulin (IgG, IgA, IgE, IgM) and alpha 1 Antitrypsin were normal.

During the hospitalization, subcutaneous emphysema appeared in the neck (Fig. 3) with nearly confluent erythematous macules and papules like seborrhea dermatitis appeared throughout the scalp and expanded to the back and abdomen (Fig. 4). Histologic examination of a punch biopsy obtained which showed focal surface erosion with diffuse and nodular dermal infiltration by atypical relatively large cells, histiocytic like, with moderate eosinophilic or vacuolated cytoplasm and slightly irregular or grooved nuclei. Some areas of the tumor show significant mitotic activity. Most of the tumor cells are found to be positive for S100 protein, and numerous ones of tumor cells are positive for CD68 that would confirm the diagnosis for LCH. CT scan for pelvic and abdominal showed splenomegaly and hepatomegaly. X-Ray of the lower, upper limb and spine were normal.



Figure 3: CX-Ray showed subcutaneous emphysema in the neck.



Figure 4: nearly confluent erythematous macules and papules like seborrhea dermatitis appeared throughout the scalp.

Based on previous data, the patient was diagnosed with Histiocytosis X systemic type (LSD). The patient was treated with weekly Vp16 (150 mg/m²), vinblastine (6 mg/m²) and daily oral prednisone (2 mg/m²) for a total of 6 weeks. At this stage, the disease was in a regressive state and the patient proceeded to the second-line continuation chemotherapy consisting of three drugs (oral prednisone pulses, every three weeks vinblastine and etoposide [Vp16]). He completed the 52 weeks of the continuation phase, and recent imaging confirmed that he still has the non-active disease.

DISCUSSION

LCH is an unknown etiology, with several hypotheses that investigate whether it has a neoplastic or inflammatory origin, immunological, genetic or infectious (mainly viral) as triggering factor [5]. Historically, the first case of LSD was described by Letterer in 1924 and then defined the clinic pathological syndrome by Siwe in 1933 [6]. LSD usually appears within the first two years of life as cutaneous lesions in the scalp, face, thorax and perineum that are similar to seborrheic dermatitis. Many systemic symptoms may include ear drainage, anemia, fever, lymphadenopathy, osteolytic lesions, hepatosplenomegaly, and lung involvement [5]. Pulmonary LCH (PLCH) includes cough, tachypnea, cyanosis, clubbing, hemoptysis or it may be

asymptomatic. Pneumothorax and subcutaneous emphysema are lower incidences in infancy compared with adults [7].

In our case report, the pulmonary symptoms (recurrent pulmonary infections, subcutaneous emphysema) were the predominant symptoms, then the cutaneous lesions appeared and this considers rare in the literature. In the early stage of PLCH, chest X-ray reveals diffuse interstitial and alveolar infiltration, symmetric linear and nodular opacities that develop in the later stage to cystic, bullous formation and pneumothorax [8]. Although the condition is not chronic in our patient, damage to the pulmonary tissue was significant. The diagnosis is detected through the lung or other affected tissues biopsy that appears accumulation of Langerhans cells with variable numbers of eosinophils. Langerhans cells are immunohistochemically positive with antibodies to S-100 protein and CD1a [1]. Treatment of LSD depends on the number of organs affected. The treatment ranges from minimal therapy to intensive chemotherapy (Vinblastine and etoposide) associated with corticosteroids [9].

In summary, this was a rare case report of LSD with unusual clinical presentation. The diagnosis was based on histological examination and immunophenotyping of the biopsied tissue. The patient was treated with chemotherapy with full remission.

AVAILABILITY OF DATA AND MATERIAL

All data generated or analyzed during this study are included in this published article.

AUTHORS' CONTRIBUTIONS

All authors have read and approved the manuscript.

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COMPETING INTEREST STATEMENTS

All of the authors declare that they have no competing interests.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This case report did not require review by the Ethics Committee Tishreen university hospital, Lattakia, Syria.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor.

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