Langerhans Cell Histiocytosis in an Adult - a rare, life-threatening and not to be missed

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SUMMARY

Langerhans Cell Histiocytosis (LCH) is an uncommon neoplastic disorder characterized by accumulation of histiocytes in various tissues. The clinical manifestation is highly variable, ranging from an isolated skin rash or a single bony lesion, to fatal multi-organ failure. Due to its rarity and systemic involvement, the epidemiology of LCH is still not fully understood and most studies focus on the paediatric population. The extent of clinical involvement has important prognostic implications. Treatment options may be local or systemic depending on disease extent. Here we describe a rare case of adult onset LCH who presented with recurrent pneumothoraces, diabetes insipidus and papules and plaques over the scalp and forehead.

KEY WORDS:

Langerhans cell histiocytosis, Histiocytosis X, seborrhoeic dermatitis, diabetes insipidus, recurrent pneumothoraces

INTRODUCTION

Langerhan's cell histiocytosis (LCH), previously known as Histiocytosis X refers to a group of diseases resulting from the monoclonal infiltration of Langerhans cells in various organs[1]. The organs more frequently involved are skeleton (80% of cases), skin (33%) and the pituitary (25%)[2]. Other organs involved are the liver, spleen, the hematopoietic system and the lungs (15% each), lymph nodes (5-10%) and the central nervous system (CNS) excluding the pituitary (2-4%)[2]. The clinical course may vary from a self-limiting disease to a rapidly progressive one that might lead to mortality[2]. Between 30-40% of patients may develop permanent adverse sequelae[2]. It can occur at all ages but mainly affects children between 1-4 years; and the incidence of childhood LCH have been reported between 2.2-8.9/million/year[3]. LCH in adults is rarely reported. Hence, the management in adult patients is largely dependent on the primary presenting features and drawn from pediatric treatment protocols. Here, we describe a case of adult onset LCH with pulmonary, cutaneous and pituitary gland involvement.

CASE REPORT

A 24-year-old foreman presented with recurrent bilateral pneumothoraces requiring multiple chest drains. Soon after, in a clinical course that spanned several years, he developed polyuria, nocturia and multiple mildly pruritic, erythematous papules on his forehead, scalp and neck. There was absence of bone pain, gingival or bone swelling, fever, anorexia, weight loss and significant family history. He had a four-pack-year smoking history. He professed the faith of Jehovah Witness.

Clinically, he was tachypnoiec at rest with tracheal deviation to the left. The right lung was hyper-inflated with increased resonance on percussion and reduced breath sounds. There were no palpable lymph nodes, ascites or hepatosplenomegaly. Multiple erythematous papules were noted over the forehead, scalp and posterior neck without alopecia.

Spirometry revealed a restrictive pattern with reduced lung volume. The initial chest radiograph showed a left mediastinal shift with multiple lung cysts notably over the right lung with fine nodules over the right upper and left lung fields (Figure 1a). A high resolution CT thorax revealed multiple cystic lesions with septation in both lungs and honeycombing. Histopathology of lung biopsy from left thoracothomy only revealed lung bullae with fibrosis. Skeletal survey did not show lytic bony lesions and blood counts were normal. The urine osmolality (first morning sample) was 171mOsm/kg (Normal: 300-900mOsm/kg) while the plasma osmolality was high at 308mOsm/kg (Normal: 275-295mOsm/kg); consistent with diabetes insipidus. MRI of the brain showed thickening and enhancement of the pituitary stalk (Figure 1f). Connective tissue screening, serum immunoglobulin levels and serum α1 antitrypsin levels were normal. Biopsy from the scalp lesion showed dermal infiltrates of cells exhibiting irregularly cleaved vesicular nuclei with moderate amount of cytoplasm (Figure 1d) with positive immunohistochemistry staining of CD1α (Figure 1e) and S100.

Although the lung biopsy sample was inconclusive, the patient was diagnosed as adult onset of LCH with multisystem involvement of the lungs, skin, and diabetes insipidus due to central nervous system involvement. Right sided chemical pleurodesis was performed. Further cardiothoracic evaluation determined that the patient was unsuitable for lung transplant. Hence he was prescribed long term home oxygen therapy. He subsequently had recurrent

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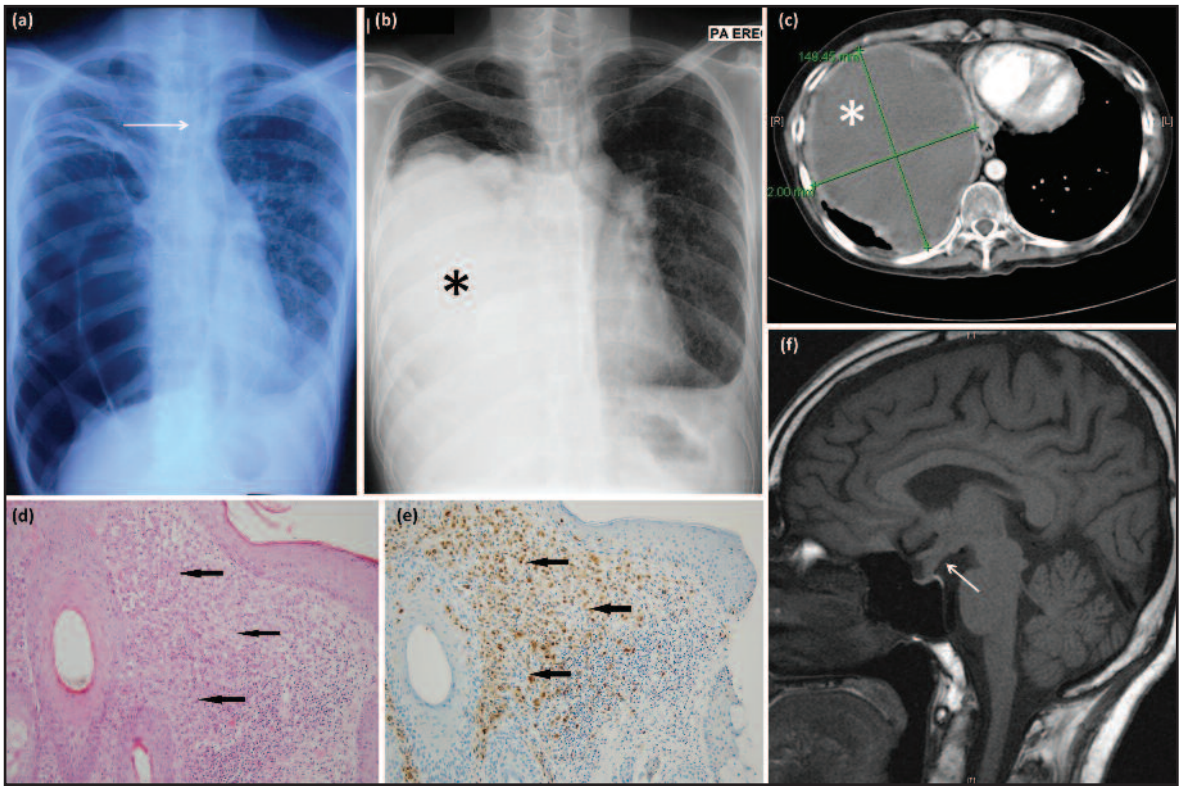

Fig. 1 : Figure 1(a) Left mediastinal shift (arrowed) and multiple cysts on the right with a fine nodular appearance over both lung parenchyma; 1(b) &(c) a large heterogenous pleural mass (*) visualized initially on the chest radiograph and then CT scan; 1(d) scalp biopsy (H&E stainings, x100) showed infiltrates of cells mainly in dermis. These cells had irregularly cleaved vesicular nuclei with a moderate amount of cytoplasm with 1(e) positive immunohistochemistry staining of CD1α (x100); 1(f) Thickening and enhancement (arrowed) of the pituitary stalk on MRI brain

chest infections and repeat chest radiographs and CT thorax revealed a large heterogenous right pleural mass (Figure 1b &c), thought to be a partially organized hematoma. However, he declined further investigations and a biopsy of the lesion was deemed unsafe in view of his views with regards to the transfusion of blood products.

The patient was then commenced on chemotherapy as suggested by Donadieu *et al*[4]. This protocol consisted of 6 weeks of intravenous vinblastine and oral prednisolone; followed by 3 weekly intravenous pulses of vinblastine. The skin lesions improved remarkably immediately after the initiation of chemotherapy. The nocturia also resolved. Unfortunately, the patient succumbed to a severe community acquired pneumonia complicated by upper gastrointestinal bleeding several weeks after completing his final course of vinblastine.

DISCUSSION

Most epidemiological studies described LCH in European paediatric populations. A recent analysis of 30 Asian patients with LCH similarly revealed higher incidence among children[3]. The only study that described LCH among adults was reported from the International Registry of the Histiocyte Society where 274 patients from 13 countries were studied[5].

In contrast to paediatric patients, LCH in adults is most often a multisystem disease[5]. About 70% of patients had multisystem disease while single-system LCH was found in 31.4% of patients[5]. The organs involved were most frequently bone followed by the lungs, pituitary gland, skin, lymph nodes, mucous membranes etc. Isolated pulmonary involvement was most frequently described in adults with single-system LCH. Patients with pulmonary LCH may present with non-productive cough, dyspnea, and chest pain associated with non-specific symptoms like fatigue, weight loss, night sweats and fever[6]. About 20% of patients present with acute symptoms of pneumothorax. The chest radiographs of patients with pulmonary LCH usually show a reticulo-micronodular pattern[6]. In more advanced cases, cysts may be seen within the infiltrates symmetrically in both lungs predominantly in the middle and upper lung fields[6]. Our patient presented with a predominantly pulmonary disease. The multiple cystic lesions caused recurrent pneumothoraces, resulting in a slow growing right pleural mass and consequently, advanced respiratory failure.

Although the skin lesions and diabetes insipidus occurred almost simultaneously with recurrent pneumothoraces, these features were not recognized as part of LCH in our patient. He was diagnosed with seborrheic dermatitis as the skin lesions were distributed over the scalp and forehead. In addition, the lesions partially responded to topical corticosteroids. The

symptoms of nocturia and polyuria were only documented and investigated later. It is important to note that the risk of diabetes insipidus among adults with LCH is probably equal to or even greater than that of children with LCH[5]. It was believed that LCH patients may have isolated diabetes insipidus or additional symptoms but may remain undiagnosed for extended periods of time leading to an underestimation of these sequelae[5].

As a Jehovah's Witness, the patient only consented to minimally invasive investigations i.e. skin biopsy, venepuncture and non-invasive radiological investigations. Recent data that suggests cladribine or cytarabine[6] might be more effective in cases with involvement of risk organs (hematopoietic system, spleen and/or liver) or tumorous cerebral involvement (pituitary stalk thickening, larger tumors in the hypothalamic-pituitary region; parenchymal, meningeal or choroid plexus lesions). However, this patient was treated with vinblastine and prednisolone based on older paediatric LCH treatment protocols, as vinca alkaloids are not myelo-suppressive and would not cause significant cytopenias (which might have necessitated blood product transfusions).

The overall survival of adult LCH at 5 years post-diagnosis was 92.3% with 100% for patients with single-system disease, 87.8% for isolated pulmonary disease and 91.7% for multisystem disease[5]. Our patient succumbed to severe pneumonia complicated by upper gastrointestinal bleeding while receiving chemotherapy, which was 7 years after his initial pulmonary symptoms.

In conclusion, we described a rare case of adult multisystem LCH. This disease requires a high index of suspicious among physicians to clinch the diagnosis. Careful multidisciplinary evaluation is essential and the diagnosis needs to be confirmed by correlation of the clinical presentation and histopathological examination of tissue samples.

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