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Case Report

Langerhans cell histiocytosis misdiagnosed as depression: a case report and literature review

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Abstract: Langerhans cell histiocytosis (LCH) is a rare hyperplastic disease of mononuclear-phagocytic system. But the early clinical manifestations of LCH are not typical with frequent misdiagnoses. We reported a 23-year old man of LCH initially misdiagnosed as depression accompanied by polydipsia and urorrhagia. This case suggests the possibility of LCH for young smoker men with unexplained psychological and behavioral abnormalities should be fully considered.

Keywords: Depression, langerhans cell histiocytosis, misdiagnosis

Introduction

Langerhans cell histiocytosis (LCH) is a rare hyperplastic disease of mononuclear-phagocytic system with a morbidity of below 1:200,000 [1]. Langerhans cell is a kind of dendritic cell distributed in skin squamous epithelium, lymph gland, thymus epithelia, bronchus mucous membrane, which exerts immune response by phagocytizing, presenting antigens and activating T-cells [2]. However, Langerhans cells in LCH are abnormally proliferated to form granuloma and thus infiltrate and damage organs. The diagnosis of LCH depends on finding characteristic Langerhans cell granuloma through histopathologic examination. But the early clinical manifestations of LCH are not typical with frequent misdiagnoses as bone tumour, dermatosis, lymphoma, leukemia, tuberculosis, lymphangioleiomyomatosis, external otitis, etc [3]. Here, we reported a LCH case initially misdiagnosed as depression accompanied by polydipsia and urorrhagia.

Case report

A young man of 23 years old with a 4-year smoking history (about 10 cigarettes per day) was admitted in West China Hospital suffering from unexplained poor concentration and uncommunicative status with polydipsia and urorrhagia for 2 years, and exertional dyspnea with dry cough for 1 year. Based on the clinical manifestations, diagnosis of depression for this patient was initially established two years ago by psychiatry department of West China Hospital and Efexor (75 mg qn) was prescribed for anti-depression for 2 years. However, the psychiatric symptoms were not significantly improved, and shortness of breath after movement was presented and aggravated with dry cough 1 year after treatment of depression.

On admission, vital signs were stable and moist crackles could be heard in both sides of the lung. Chest X-ray and CT showed both sides of the lung are suffused with cystic shadows of different size (**Figure 1A**, **1B**), but enhanced CT and MRI scan in head showed no significant abnormality (data not shown). Pulmonary function test demonstrated severe decline in both ventilation and diffusion. Arterial blood gases analysis indicated PaO_2 70 mmHg, $PaCO_2$ 42 mmHg and pH 7.40. Lung biopsy by thoracoscopy was performed and pathological report indicated nodular lesions were distributed in lung tissues (**Figure 1C**), mainly composed of S-100 (+) and CD1a (+) Langerhans cells (**Figure 1D**, **1E**) with scattered MPO (+) eosinophils (**Figure 1F**) and CD68 (+) multinucleate giant cells (**Figure 1G**). The Birbeck granule in Langerhans cells was clearly detected by elec-

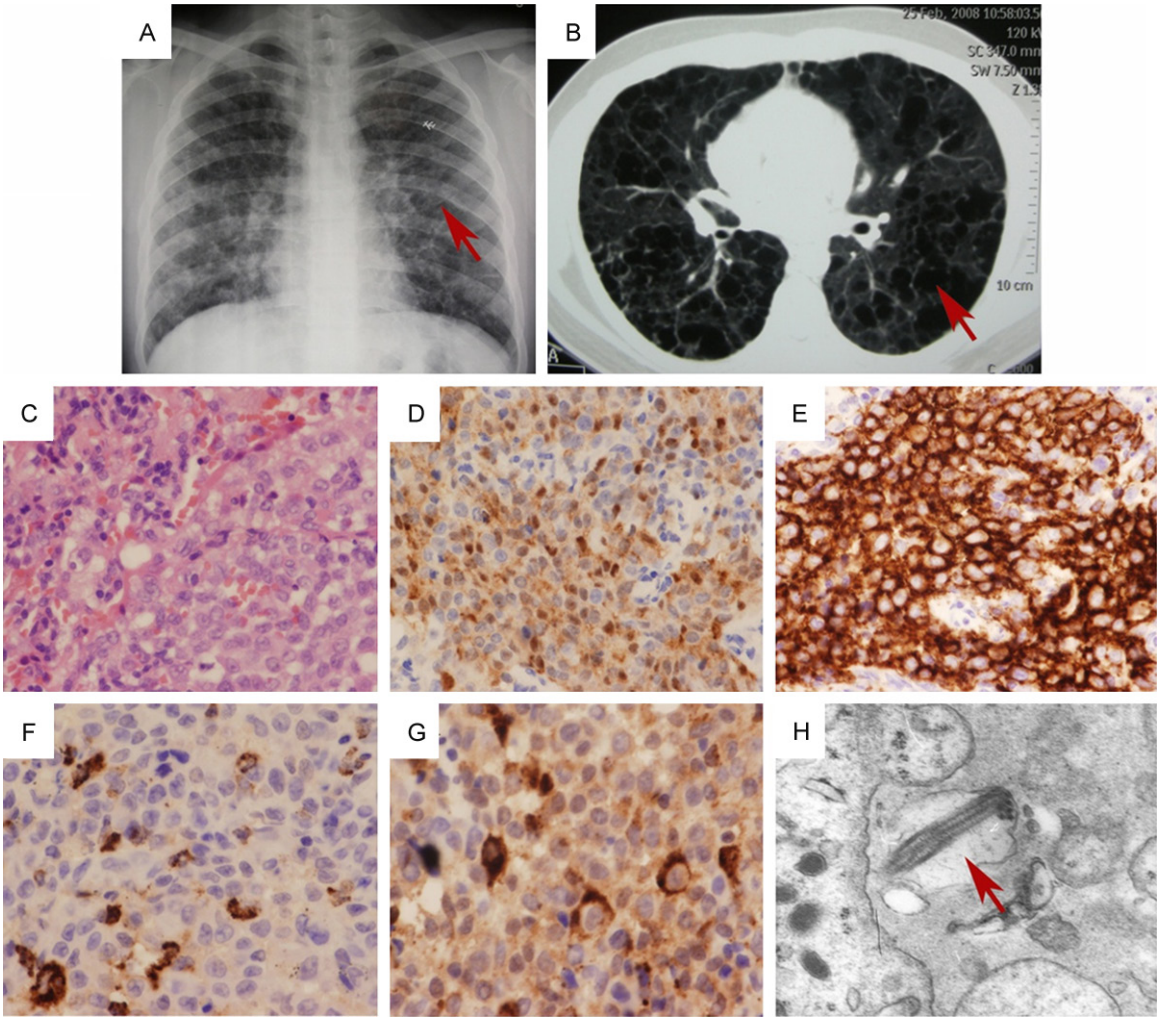

Figure 1. Clinical images of the case. A: Chest X-ray (arrow points the cystic changes in PLCH); B: Chest CT scan (arrow points the cystic changes in PLCH); C: Hematoxylin eosin staining, magnification ×200; D: S-100 immuno-staining langerhans cells (brown), magnification ×200 ; E: CD1a immuno-staining langerhans cells (brown), magnification ×200. F: MPO immuno-staining eosinophils (brown), magnification ×200; G: CD68 immuno-staining multinucleate giant cells (brown), magnification ×200; H: Electron microscope image (arrow points the Birbeck granule), magnification ×250,000.

tron microscope (**Figure 1H**). Overall, LCH was confirmed. Subsequently, the patient was treated with methylprednisolone (40 mg bid) for over 4 weeks, but the symptoms were deteriorated especially when pneumothorax repeatedly occurred in both sides of the lungs. Eventually, the patient died from severe respiratory failure on 42nd hospital day.

Discussion

Langerhans cell histiocytosis (LCH) is a rare histiocyte hyperplastic disease of unknown origin, which often occurs in low-aged population, mostly in children from 1 to 3 years old [1]. The manifestations of LCH are heterogeneous and nonspecific. LCH have been clinically classified into local and systemic forms. Local LCH often affects single organ with a good prognosis, and skeleton, skin and lung are mostly frequent impaired. Whereas systemic LCH affects more than one organ or tissue, especially liver, spleen and haematopoietic system are all “risk organs” for unfavourable prognosis [4]. Moreover, central nervous system (CNS) lesions are uncommon in LCH [5]. This case showed a systemic LCH involving lungs (pulmonary LCH, PLCH) and CNS.

PLCH is a common type of LCH, typically in young smoker adults [6]. Besides a neoplastic theory for PLCH [7, 8], the hypothesis of a reac-

tive response to cigarette smoke is supported by a large amount of evidence, although the underlying mechanisms have not been fully understood [6]. Cigarette smoke induces reactive changes in the epithelium of distal bronchioles and an accumulation of CD1a+ cells in smokers and murine models [9]. More importantly, cigarette smoke stimulates the production of local cytokines involved in the proliferation, differentiation and activation of dendritic cells in PLCH [10, 11]. Like this case, an accumulation of a large number of CD1a+ Langerhans cells in bronchiolocentric granulomas might significantly contribute to destruction and remodeling of surrounding lung parenchyma [10, 11]. However, CD1a+ Langerhans cells are unlikely to be the only cause of tissue damage. Several immune/inflammatory signals have been found in LCH granulomas might also be involved in parenchymal damage and tissue remodelling [12-14], which needs further investigations.

Alterations of CNS in LCH are rare and includes lesions of hypothalamic pituitary axis, choroid plexus, cerebrum, cerebellum, pons and basal ganglia, leading to diabetes insipidus, headache, convulsions, abnormal reflexes, ataxia, intellectual impairment and dysarthria [5, 15]. CNS lesions in LCH have an incidence of 5%~30% of polydipsia and urorrhagia [16]. Previous studies documented LCH could incorporate internalizing behaviors (such as depression), indicating in addition to CNS pathological changes, mental and behavior disorder was also implicated [17]. The sufferer in this case is a young man, who was initially misdiagnosed as depression and received anti-depression treatment for 2 years without improvement. Moreover, it should be worth noted that skull enhanced CT and MRI scan seldom displays characteristic pathological changes of LCH in CNS [18].

Overall, the possibility of LCH/PLCH for young smoker men with unexplained psychological and behavioral abnormalities should be fully considered, and it is very important in close monitoring to facilitate early diagnosis and treatment for LCH/PLCH.

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Disclosure of conflict of interest

None.

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