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A case of Langerhans' cell histiocytosis of the lung presenting with haemoptysis

伴隨咯血的肺部Langerhans細胞組織細胞增生症

Langerhans' cell histiocytosis of the lung can be part of a multisystem disorder or an isolated disorder. Ninety percent of adult patients with Langerhans' cell histiocytosis of the lung are smokers. This article reports a case of Langerhans' cell histiocytosis presenting with haemoptysis. The diagnostic signs on chest X-ray, high-resolution computed tomography, and histology are highlighted, followed by a short review of the literature.

肺部Langerhans細胞組織細胞增生症可以是系統多樣性紊亂的其中一種症狀，也可以是單獨出現的紊亂。該症九成患者為吸煙者。本文報告了Langerhans細胞組織細胞增生症患者伴有咯血的病例，重點提出此病症在胸腔X射線、高解像度電腦斷層照相術和組織學中的診斷結果，並對文獻作一簡短回顧。

Introduction

Patients with Langerhans' cell histiocytosis (LCH) of the lung can present with pneumothorax, cough, dyspnoea, chest pain, fatigue, weight loss, haemoptysis, and fever.¹ Langerhans' cell histiocytosis can also be an incidental finding on routine chest X-ray. It runs a clinical course distinct from multi-organ LCH. Ninety percent of adults with LCH of the lung are smokers.² Tobacco smoke has been postulated to induce non-clonal hyperplasia of LCH cells, in which occasional clones may emerge. These proliferations often regress, failing to progress to autonomous neoplastic disease.³ Recurrence of LCH after 4 years in a transplanted lung has been reported, despite the patient having ceased smoking after the operation.⁴ Chest X-ray appearances can vary from normal to reticulonodular shadowing and honeycomb fibrosis. Lung volume is normal, despite diffuse fibrosis. We report a case of LCH of the lung seen at the Tuberculosis and Chest Unit, Wong Tai Sin Hospital, Hong Kong.

Case report

A 41-year-old male patient was admitted to the hospital with haemoptysis. The patient was a lorry driver and smoked two packets of cigarettes a day. He reported good past health, and this was his first episode of haemoptysis. The patient reported coughing up a few mouthfuls of blood over the previous few days, and having mild chest discomfort. His appetite was normal, and there was no history of weight loss. Physical examination was normal. The patient was afebrile. Transcutaneous measurement showed oxygen saturation was 99% on room air.

Investigations

White blood cell count was 7.1×10^9 /L (reference range, $4.5-11.0 \times 10^9$ /L), and haemoglobin level 120 g/L (reference range, 140-175 g/L). Renal and liver function tests were normal. Electrocardiography showed sinus rhythm, with a heart rate of 52 beats per minute; there were no ST changes. Chest X-ray showed mild, diffuse fibrosis, with diffuse nodules evident, more prominent in the upper and mid-zones of the lungs (Fig 1). Lung volume was normal. Sputum analysis did not show any pyogenic organisms or acid-fast bacilli. There were no malignant cells evident. Skeletal survey showed only a lytic lesion over the right lunatae.

Key words:

Hemoptysis;
Histiocytosis, Langerhans-cell;
Lung

關鍵詞：

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Fig 1. Chest X-ray showing multiple small nodules (arrows)

Progress

In view of the diffuse, bilateral nature of the lesion and the presence of haemoptysis, a high-resolution computed tomography (CT) scan of the lung was completed. Centrilobular emphysema, probably smoking related, was seen in the upper zones of the lung. Numerous small nodules of 2 to 7 mm were spread diffusely throughout the upper and mid-zones. The lower zones were relatively spared. Some of the nodules showed cavitation (Fig 2a).

A video-assisted thoracoscopic biopsy of the lungs was completed. Histology showed nodular aggregates of Langerhans' cell histiocytes in sub-pleural lung parenchyma. The Langerhans' cell histiocytes had large, elongated nuclei, small nucleoli, and occasional nuclear grooves. Intermingled with these cells were a small number of eosinophils. The Langerhans' cell histiocytes were positive for S-100 protein and CD1a. Stellate, fibrous scars containing numerous, pigmented histiocytes were found in the remainder of the lung tissue specimen (Fig 2b).

The patient was referred to our smoking cessation clinic and was prescribed nicotine replacement therapy. Before further investigation was undertaken to determine the extent of the histiocytosis, the patient was lost to follow-up.

Discussion

The spectrum of LCH disease is wide. Single system disease can affect the skeletal system, skin, lung, or lymph nodes. Multisystem disease is associated with reticulo-endothelial system, liver or bone marrow dysfunction, and mortality can be as high as 50%.⁵ In the middle of the spectrum are those with multisystem disease but without organ dysfunction. The clinical entities of LCH include the following syndromes: Letterer-Siwe disease, Hand-Schüller-Christian disease, eosinophilic granuloma, and isolated LCH of the lung. Letterer-Siwe disease is a fulminant disease in children younger than 2 years, affecting the reticulo-endothelial system, bone, and lung. Hand-Schüller-Christian disease is a more indolent disorder, affecting bone and lung, and resulting in diabetes insipidus, exophthalmos, and osteolytic skull lesions. Eosinophilic granuloma is a localised form of the disease, affecting bone or lung. Isolated LCH of the lung is a rare disease. Most case series report less than 10 cases presenting over a decade, and many case series report a mixture of cases with isolated lung LCH disease and cases with multi-organ LCH disease. Service units probably encounter only two to three cases of LCH of the lung at most over 10 years.

Although LCH of lung is one of the few disease that present with normal lung volume despite diffuse fibrosis, it is difficult to make a diagnosis on the chest X-ray findings alone. Other conditions that present with similar chest X-ray findings include lymphangioleiomyomatosis, tuberous sclerosis, neurofibromatosis, stage III sarcoidosis, constrictive bronchiolitis, and any interstitial disease associated with emphysema. High-resolution CT scanning can provide a confident diagnosis in most cases, even in the terminal stages of the disease.⁶ It typically shows characteristic, small nodules (2-7 mm), diffusely distributed in the upper and mid-zones of the lung, and sparing the lower zones. There can be thin wall cysts alongside the nodules, and ground glass opacities, showing different stages of the disease in the same area. One characteristic feature of LCH of lung is cavitation within the tiny nodules.⁷ Lung function studies

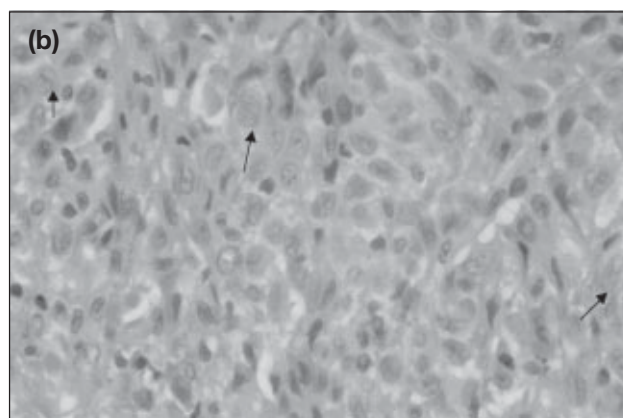
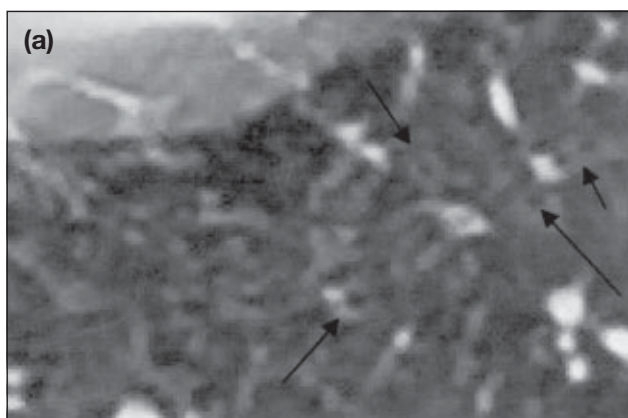


Fig 2. (a) High-resolution computed tomography scan showing cavitating nodules (arrows). (b) Histology slide showing Langerhans' cells with in-folding nuclear membrane and multiple nucleoli with eosinophils (H&E, x400)

may be normal, or show a restrictive, obstructive, or mixed pattern. There is usually a marked decrease in diffusion capacity of the lung.

Histologically, the Langerhans' cell is a pathologic cell type derived from the monocyte-macrophage line. Langerhans' cells are most commonly found in the dermis, the reticulo-endothelial system, the lung, and the pleura. The earliest lesions detected in LCH of the lung are interstitial accumulations of Langerhans' cells with eosinophils in the submucosa and interstitium of the bronchioles. This is also supportive of tobacco smoking as the aetiological cause. These lesions progress to discrete, symmetric nodules, usually with a fibrotic centre, with cellular peripheral interstitial tentacles. The characteristic Langerhans' cells are found in the periphery of the nodules. They can be stained with S100 and OKT6 (CD1) stain. The Langerhans' cell nucleus has a delicate nuclear membrane, which is often elongated and folded, with single or sometimes multiple small nucleoli. The peculiar rod-shaped organelles of Langerhans' cells are viewed on electron microscopy as Birbeck granules. Langerhans' cells have been found in cases of idiopathic lung fibrosis, extrinsic allergic alveolitis, sarcoidosis, and lung neoplasm, but proliferation of Langerhans' cells is only found in LCH. There is also an accumulation of intra-alveolar macrophages seen at the periphery of the lesions. Pulmonary vascular involvement is present in 80% of biopsy specimens.

The natural course of isolated LCH of the lung is variable. There have been reports of spontaneous regression of chest X-ray findings after smoking cessation.^{8,9} Corticosteroid therapy is indicated when there is progressive loss of lung function. Long-term steroid therapy in the early stages has been reported to prevent progression of the disease in the majority of cases. However, recurrence and transition to late stages has been observed.¹⁰⁻¹² A peculiarity of LCH of the lung is that features of the disease may change independently of each other, such as the resolution of radiographical signs despite the persistence of symptoms, and vice versa.

The prognosis for pulmonary LCH in multisystem histiocytosis X disease is dependent on the extent and severity of extra-pulmonary disease. Vassallo et al¹³ reported a median survival for patients with pulmonary LCH of 4 years, with 74% surviving 5 years, and 64% surviving 10 years. Pulmonary LCH has been reported to be associated with lung cancer, lymphoma, and carcinoid syndrome. However, when the confounding factor of smoking was adjusted for, there was no evidence of an association seen between LCH and lung cancer.¹⁴

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