PULMONARY LANGERHANS CELL HISTIOCYTOSIS - A RARE TYPE OF A RARE DISEASE

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ABSTRACT

INTRODUCTION: Langerhans cell histiocytosis is a rare disease (0.4 in 100,000) with a still highly debated aetiology - either a reactive or a neoplastic process. It is most commonly divided into single-system and multisystem disease. The pulmonary form is part of the former group and occurs mostly in adolescent and adult smokers (2nd through 4th decade of life).

AIM

The aim of this report is to provide more clinical data of one rarely documented disorder.

MATERIALS AND METHODS: We present a 42-year-old male patient with a respiration-associated pain of unknown origin. His physical examination was unremarkable. A CT scan was indicated, revealing multiple thin-walled cystic lesions and multiple small nodules in the pulmonary parenchyma, predominantly in the middle and upper lung segments, which was suggestive of pulmonary Langerhans cell histiocytosis. Through a video assisted thoracoscopy, several of the nodules were resected and sent for biopsy.

RESULTS: The patient was discharged on the day after the operation. The biopsy confirmed the diagnosis of Langerhans cell histiocytosis. Since systemic corticosteroids were contraindicated in this particular case, the patient was counseled to cease smoking. On the follow-up CT a tendency for a reversal of the condition was observed.

CONCLUSION: The pulmonary form of Langerhans cell histiocytosis is a rare disease, most commonly seen in relatively young smokers with non-specific presentation. The biopsy is the only definitive diagnostic procedure. The disease may resolve spontaneously or after smoking cessation. In more severe cases corticosteroids, chemotherapy or lung transplantation may be considered.

Keywords: *pulmonary langerhans cell histiocytosis, pulmonology, treatment, diagnosis*

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INTRODUCTION

Langerhans cell histiocytosis (LCH) is a term that describes a wide spectrum of rare disorders all of which are associated with the proliferation of immature dendritic cells in the epidermis - the Langerhans cells (1). The etiology of this disorder has been highly debated in the past. Previous data points out that LCH is a reactive process (2) that often brings about symptoms associated with inflammatory me-

diators, more notably IL-17A, which stimulates dendritic fusion (3). On the other hand, newer studies have proven the association of the BRAF V600E (1,4) and MAP2K1 (5) mutations with LCH, and tip the scales in favour of the neoplastic genesis of the disease. About 40% of the cases of pulmonary Langerhans cell histiocytosis (PLCH) are related to a BRAF mutation (1).

The most recent classification outlines a single-system disease (SS-LCH) and a multisystem disease (MS-LCH) on account of the organs involved (6). SS-LCH includes lesions confined to a single bone or a group of bones, the skin, the lungs, the posterior pituitary, etc (6). In MS-LCH more than one organ is involved (6). The hematopoietic system, liver and spleen are currently considered high-risk organs (6). This article will focus on PLCH.

MATERIALS AND METHODS

We are presenting a 42-year-old male who was admitted into the Clinic of Pulmonology and Phthisiatry at St. Marina University Hospital for the deterioration of respiration-associated pain. He had no other complaints and his physical examination was normal and unremarkable: his skin and mucosa were pink, his breathing was vesicular, his hearth sounds – clear, nothing was palpable in the abdomen and he had no peripheral edemas. His lab tests were as follows: bleeding time – 180 sec. HGB – 156; HCT – 0.489; PLT – 294; WBC – 11,32; GLU – 6,3; Cre – 56; INR – 1.12; PT – 14; FVC1 – 2.48; VC – 3.67; pO2 – 8.3; pCO2 – 5.3; pH – 7.44.

A high-resolution computed tomography (HRCT) revealed thin-walled cystic lesions, up to 20 mm in size, in the pulmonary parenchyma bilaterally. They had spread diffusely in both lungs, more

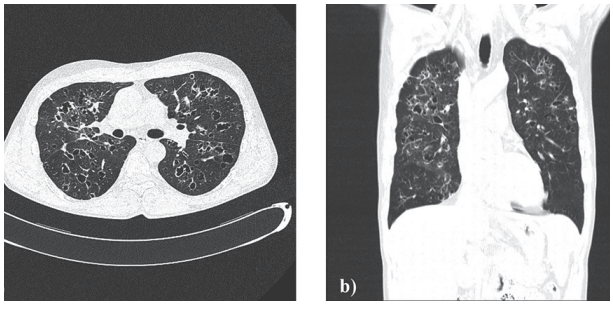

Figure 1

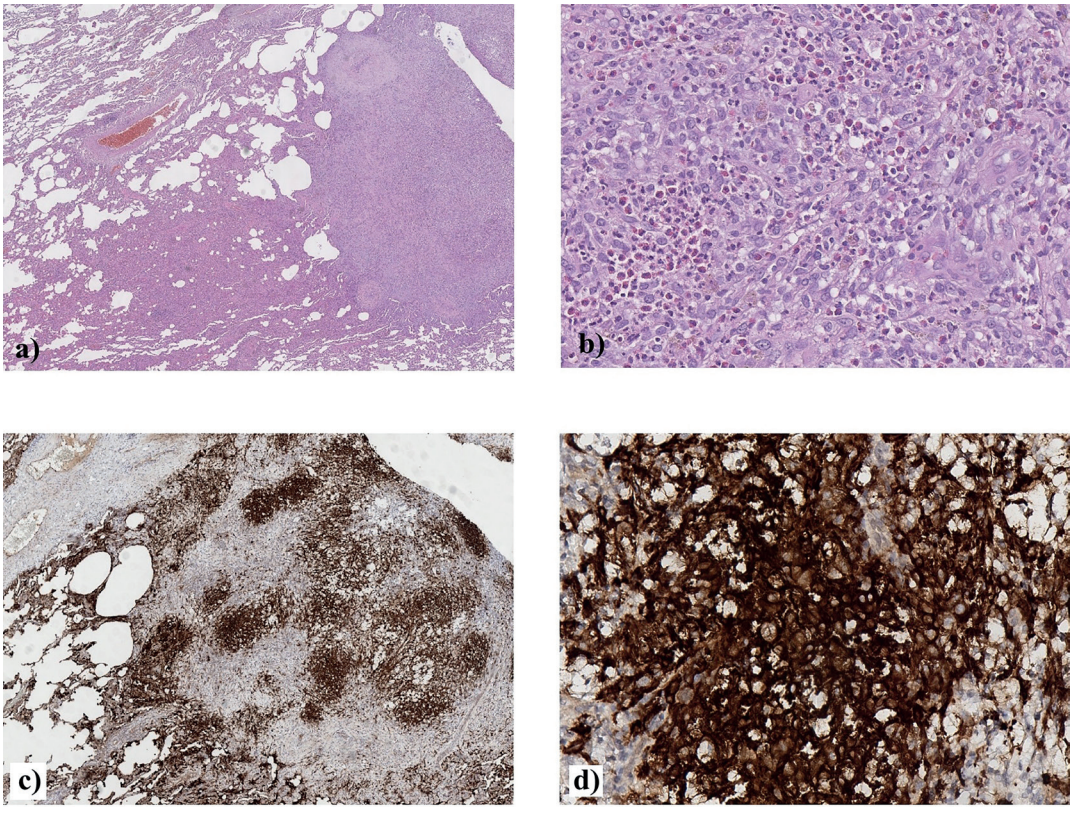

Figure 2

profusely in the middle and upper segments. Multiple subsolid nodules (up to 4 mm) were visualised predominantly in the upper pulmonary segments. A few (7-8) pretracheal lymph nodes with size up to 18/8 cm and intact structure were observed. The imaging of the lung was highly suspect of Langerhans cell hystiocytosis.

On the next day a video-assisted thoracoscopy (VATS) was performed in order to obtain biopsy material. During the procedure, fibrous plaques and multiple nodules were observed beneath the pleura in all three lobes of the right lung. A couple of the nodules were resected from the 2nd and 3rd segment. A thoracic drain was placed upon closure.

The histological materials showed pulmonary parenchyma with interstitial fibrosis, hemosiderosis, inflammation and multiple CD1a-positive large Langerhans cells. S100 protein was not expressed in these materials.

RESULTS

After the operation, the patient was medicated with bromhexin, metronidazole, metamizole and dexketoprofen and was subsequently discharged after two days. He was not indicated for systemic steroids, which are frequently prescribed (6), as he was also diagnosed with a gastric ulcer. However, the patient was encouraged to cease smoking as many cases of PLCH tend to have complete resolution after such actions (6).

During the follow-up, after one month, the patient confirmed smoking withdrawal. His CT images showed that the process in his lungs had a tendency for reversal, but still no complete resolution.

DISCUSSION

PLCH occurs most commonly in young smokers, with peak incidence during the 2nd through 4th decade of life (7). In a Japanese study, the incidence was calculated to be between 0.27 and 0.07 per 100,000 for men and women, respectively (8).

The pathogenesis of PLCH is still largely unclear in its mechanisms. It is very likely that tobacco smoking has a major role, since the majority of the patients have a history of smoking or exposure to cigarette smoke (9). Very few smokers, however, develop PLCH, despite the fact that all are exposed to the irritant and all of them have an increased macrophage numbers in their lungs (10). This hints that perhaps there are also endogenous factors involved. One such theory suggests that the migratory potential of the Langerhans cells is impaired and hence they persist in the tracheobronchial tree, where they can form inflammatory lesions.

The clinical presentation of PLCH can be very scarce. The patients can have cough or dyspnoea, which can normally be attributed to smoking. An abrupt chest pain can be more alarming and should indicate a search for a pneumothorax or rib involvement (11). Spontaneous pneumothorax can occur in 15-20% of the patients at any time of the treatment (7) and also tends to be recurrent (11). Constitutional syndromes may be seen in 10–20% of the patients (7). Very often the patients are asymptomatic (11).

Usually cysts and nodules seen on CT are considered the only diagnostically relevant image (6). The alteration areas are usually located in the upper and middle segments, sparing the lower ones, with centrilobular distribution and size <1cm in the early stages of the disease (12). The only definitive method of diagnosis is a biopsy stained with CD1a or S100 protein, with the latter being non-specific (11). The differential diagnosis usually includes sarcoidosis, silicosis, tuberculosis, metastatic disease, cavitated *Pneumocystis jirovecii* lesion, etc. (12).

The treatment in the ideal case involves smoking withdrawal as many patients' conditions resolve after that or at least improve drastically (6). Low-dose systemic corticosteroids are most commonly applied in patients with more progressive symptoms (6). Other, more potent immunosuppressive drugs can be used, like cladribine (2-cDa), which is reported to downregulate the histiocyte proliferation and has direct toxicity for monocytes and lymphocytes (7,14). However, the prophylaxis for lung infections in this case should be much greater and also cover *Pneumocystis jirovecii* and the herpes viruses (7). Trimethoprim/sulfamethoxazole and valaciclovir have been used in some of the cases (7,15). Vinblastine, despite being a first-line choice in chemotherapy in MS-LCH in children (6), has little effect in adult patients with PLCH (7,16). Lung transplantation has also been used in patients with end-stage PLCH (17). Despite the recurrence of the disease, in about 20% of the patients, it has a good posttrans-

plant survival rate (57.2% at 5 years) (17) and should be considered in patients who start to develop pulmonary hypertension (17).

CONCLUSION

PLCH is a rare disease, which often has an unremarkable clinical presentation. However, with diligent use of the current imaging modalities, and a mandatory biopsy of every nodular lesion, the diagnosis can be confirmed quickly. Very often the sole treatment is to remove the main pathogenic factor, i.e. the tobacco smoke, from the environment of the patient. This very often leads to a complete resolution. More aggressive treatments can be used under careful control in patients with systemic disease.

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