A case of pulmonary Langerhans cell histiocytosis in a young woman with coeliac disease

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Summary

Pulmonary Langerhans cells histiocytosis (pulmonary LCH) is an idiopathic unusual lung disease and its association with other systemic diseases has been rarely observed.

Here, we describe a young non-smoking woman with concomitant pulmonary LCH and coeliac disease that, despite therapy, suddenly deteriorated. To the best of the authors' knowledge, this is the first report in the medical literature describing an association of coeliac disease with pulmonary LCH. Considering the concomitant occurrence of both diseases in our patient and the severe course of pulmonary LCH observed, we hypothesise that coeliac disease and pulmonary LCH might be related by a common disturbance in immunity and the onset and/or the course of pulmonary LCH could be influenced or markedly worsened by the presence of coeliac disease.

Key words: pulmonary Langerhans cells histiocytosis; coeliac disease; interstitial lung diseases

Introduction

Pulmonary Langerhans cells histiocytosis (pulmonary LCH) is a rare lung disease usually observed in smokers. Less frequently it can be a manifestation of a systemic disorder. The prognosis of pulmonary LCH is quite variable with some patients experiencing spontaneous remission and others progressing to end-stage fibrotic lung disease. Association with other diseases is still uncommon. Here we report a case of pulmonary LCH in a non-smoker who also had coeliac disease.

Case report

A 20-year old woman was referred to our department because of progressive worsening dyspnoea. She presented a 2-year history of non-productive cough and mild dyspnoea on exertion. A diagnosis of coeliac disease was made 5 years before. The patient did not smoke nor had a history of smoking. Physical examination was normal except for the presence of scattered end-inspiratory crackles bilaterally. An increased erythrocyte sedimentation rate (ESR) (42 mm-h-^{1}) was observed. No other significant alterations in laboratory tests were found. A chest radiograph showed diffuse, bilateral, reticulo-nodular opacities. Examination of arterial blood gas at rest on air room was normal. Spirometry showed a combined obstructive and restrictive pattern. Carbon monoxide diffusing capacity was markedly reduced. The walking test showed a heavy desaturation after 3 min. The high resolution computed tomography of the chest demonstrated multiple thin-walled small nodules and irregular cysts, predominantly in the mild-upper zones (figure 1). Bronchoscopy and bronchoalveolar lavage yielded not diagnostic information. A surgical lung biopsy through video-assisted thoracoscopy was performed. The lung biopsies showed a patchy and nodular interstitial infiltrate in bronchocentric fashion composed of a mixture of histiocytes with reniform nuclei, eosinophils, lymphocytes, plasma cells and multinucleated giant cells. The immunohistochemical analysis was positive for S100 and CD1a, confirming the presence of clusters of Langerhans cells. The patient was treated with prednisone 1 mg/kg/day, progressively tapered to 0.25 mg/kg/day in eight months. Ten months later, our patient was admitted to our department for acute dyspnoea after a flu-like episode, pain in the right hip and headache. Diabetes insipidus was diagnosed and bony infiltration together with pituitary involvement was seen on RM. Therefore, pamidronate and desmopressin were added to the therapy. Later a progressive downhill course with rest hypoxaemia occurred. Therefore, we planned an intensive treatment and started a course of high dose prednisone (1 mg/kg/day) combined with vinblastine (5 mg/m^2/wk) followed by a slow tapering of prednisone to 0.5/mg/d. After 6 months of treatment, the patient reported a slight improvement of dyspnoea, but there were no major changes in HRCT of the chest and pulmonary function tests.

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Discussion

Pulmonary LCH is an uncommon interstitial lung disease with a peak incidence between 20 and 40 years of age [1]. The present case report shows some peculiarities: absence of cigarette smoking history, coexistence with the coeliac disease, severe course of the disease with an early uncontrolled multi-organ involvement and poor response to therapy.

Although the cause of pulmonary LCH is unknown, nearly all affected patients have a history of current or prior cigarette smoking, suggesting that smoking is causally related [2]. This hypothesis however does not explain the occurrence of the disease in children or, as in our patient, in the rare non-smoking patients. In these patients pulmonary LCH is often associated with extra-pulmonary localisation at the onset of the disease or, as occurred in this case, soon after the diagnosis. The diffuse disease appears to fit well with a systemic uncontrolled immune response to unknown antigen(s), initiated or propagated by Langerhans cells (LCs). LCs in LCH granulomas express surface markers, such as CD1a+/CD1c+, B7-1a and B7-1b, associated with an activated phenotype and show enhanced lymphostimulatory activity. Thus, abnormalities of the immune system may be responsible for deregulation and clonal proliferation of LCs, possibly induced by unknown antigens [3, 4].

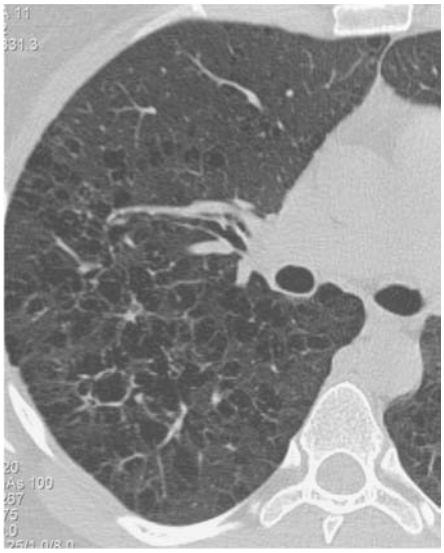

Figure 1

High-resolution computed tomographic scan of thorax showing multiple small nodules thin-walled and irregular cysts.

Multiple reports of various forms of interstitial lung diseases (ILDs) in patients with coeliac disease have been published [5–7]. However, to our knowledge, the present case is the first to report an association of coeliac disease with pulmonary LCH in the medical literature. The cause of a possible pathogenetic relation between pulmonary LCH and coeliac disease remains to be defined. Absorption of an extrinsic allergen or immune complexes through an abnormal gastrointestinal mucosa might induce pulmonary inflammatory responses triggering non-specific generalised activation of immune effector cells, and contribute to promote the initiation of antigen-specific immune-responses that lead to a reactive proliferation of LCs. An alternative hypothesis suggests that a common disturbance in immunity might underlie coeliac disease and pulmonary LCH as well as other ILDs. Coeliac disease has been associ-

List of abbreviations:

ILDs:	interstitial lung diseases
LCs:	Langerhans cells
pulmonary LCH:	pulmonary Langerhans cells histiocytosis

ated with HLA status and various autoimmune diseases [8]. Notably, recent studies raised the possibility that also pulmonary LCH might be associated with HLA haplotypes and inherited factors could promote emergence of clonal LCs [9]. Furthermore, reports of autoimmune diseases associated with LC histiocytosis have been described, reinforcing the concept that immunological dysfunction might play a role in LC histiocytosis pathogenesis [10].

In conclusion, both coeliac disease and pulmonary LCH are believed to be immunologically mediated and may share pathogenetic mechanisms. Although association of coeliac disease and ILDs, including pulmonary LCH, is not common, we think that these illnesses may be related by common immunological alterations and hypothesise that the onset and/or the course of pulmonary disorders could be influenced or markedly worsened by the presence of coeliac disease.

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