

Complete disappearance of lung abnormalities on high-resolution computed tomography: A case of histiocytosis X

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A case of pulmonary Langerhans cell histiocytosis, proved by both lung high-resolution computed tomography and lung biopsy, is described. Following smoking cessation, lung nodules and cysts gradually disappeared on serial computed tomography scans, with complete clearance of the lesions after 12 months. The role of tobacco smoking is discussed, in detail, against the background of the literature.

Key Words: *Cysts; Histiocytosis X; HRCT resolution; Smoking cessation*

Pulmonary Langerhans cell histiocytosis (PLCH) is an uncommon interstitial lung disease of unknown etiology. The natural history of the disease is not unknown but variable, ranging from reports of asymptomatic radiography to recurrent lung transplantations. It is usually present in young cigarette smokers, because more than 90% of patients have a history of tobacco use. We present a patient who had complete disappearance of lung abnormalities on high-resolution computed tomography (HRCT) following smoking cessation.

CASE PRESENTATION

A 50-year-old man was admitted to our Department of Pneumology, Belgium, because of a nonproductive cough that had lasted several months. The patient had a history of severe esophagitis and chronic gastritis. An appendectomy and a hemorrhoidectomy had been performed previously. There was no recent history of weight loss or recent medication intake. The patient had a 60 pack-year history of cigarette consumption, and was self-employed in a factory with no known occupational exposures.

A physical examination showed no lymphadenopathy or cutaneous abnormalities. Heart sounds were normal, and the lungs were clear. An abdominal examination was normal, and no organomegaly or masses were evident on palpation.

Chest radiography showed bilateral and symmetrical nodular opacification with a predominance of middle- and upper-lobe involvement. An HRCT confirmed the presence of multiple nodules, some having central cavitation, with a few irregularly shaped cysts (1 mm to 5 mm in diameter) and sparing of the costophrenic angles (Figure 1A). Functional lung

La disparition complète d'anomalies pulmonaires à la tomodensitométrie haute résolution : Un cas d'histiocytose X

On décrit un cas d'histiocytose pulmonaire de Langerhans, démontré à la fois par tomodensitométrie pulmonaire haute résolution et par biopsie pulmonaire. Lorsque le patient a cessé de fumer, les nodules et les kystes pulmonaires se sont graduellement dissipés aux tomodensitométries sérielles, et les lésions avaient complètement disparu au bout de 12 mois. On aborde longuement le rôle du tabagisme par rapport aux antécédents contenus dans les publications scientifiques.

tests showed a forced expiratory volume in 1 s of 4.00 L (105% of predicted), a forced vital capacity of 4.57 L (97% of predicted) and a forced expiratory volume in 1 s/forced vital capacity ratio of 87%, as well as a total lung capacity of 7.12 L (98% of predicted), a residual volume of 2.07 L (93% of predicted) and a diffusing capacity of the lung for carbon monoxide reduced to 64% predicted.

The results of enzymatic hepatic tests and the serum levels of urea, glucose, electrolytes, creatinine, total protein and albumin were normal. The complete blood count was normal, as well as antinuclear factor and antineutrophil cytoplasmic antibodies. The urine sample was unremarkable.

Bronchoscopy was noncontributory, and expectoration analysis and bronchial aspiration showed commensal flora. Both the Ziehl-Neelsen stain and the Lowenstein culture were negative. The bronchoalveolar lavage (BAL) total cell count was $980 \times 10^6/L$. The differential cell count was as follows: macrophages 91%, neutrophils 3%, lymphocytes 3% and eosinophils 3%. No CD1a Langerhans cells were found.

An open lung biopsy was undertaken. Macroscopic examination showed several well-defined gray nodules (0.5 cm in diameter). Histological examination showed granulomas composed of eosinophils, histiocytes and various amounts of collagen fibres. Many S-100- and CD1a-positive cells were present in the cellular nodules.

A bone scan and an abdominal CT scan showed no abnormalities suggestive of histiocytic infiltration.

Because these findings confirmed PLCH, the patient was advised to undertake a smoking cessation program. No other treatments were prescribed. The cough progressively decreased,

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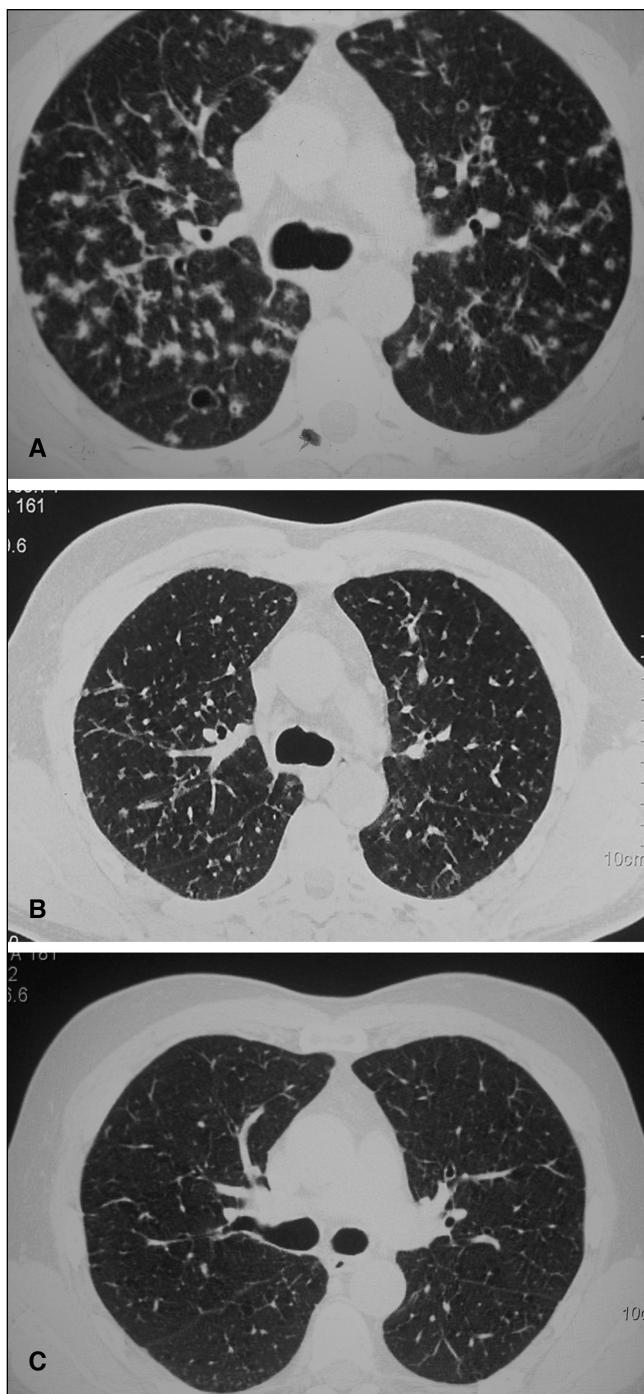


Figure 1) High-resolution computed tomography of the middle lung zones of nearly the same sections, at different times over the 12-month follow-up. **A** Bilateral nodular lesions with thick- and thin-walled cysts. **B** Reduction in size and number of nodules and cysts four months after smoking cessation. **C** Complete disappearance of abnormalities 12 months after smoking cessation, with evidence of centrilobular emphysema

and after three months of successful smoking cessation, the cough had completely disappeared. Four months after smoking cessation (Figure 1B), sequential lung HRCT was performed, which showed a dramatic decrease in parenchymal abnormalities. Twelve months after smoking cessation (Figure 1C), the abnormalities had completely disappeared, and the patient was

still asymptomatic. The functional lung tests were unchanged. At a three-year follow-up, no significant clinical, functional or radiological changes were noted.

DISCUSSION

PLCH is an uncommon disorder that is generally observed in young smokers. Its incidence and prevalence are unknown. Between 10% and 25% of patients are asymptomatic, the main symptoms being cough and dyspnea on exertion. Chest pain related to a pneumothorax is sometimes the initial symptom. Extrapulmonary symptoms (eg, cystic bone lesions and diabetes insipidus) are present in 5% to 10% of cases. The diagnosis is often suggested by radiological presentation and BAL studies. According to some clinical and radiological features, a few diseases should be considered in terms of differential diagnosis: chronic bronchitis (secondary to smoking and reflux-associated lung disease), sarcoidosis, tuberculosis, Wegener's disease, metastasis, respiratory bronchiolitis-associated interstitial lung disease and bronchiolitis obliterans with organizing pneumonia. In our patient, HRCT of the chest was very suggestive of PLCH, with parenchymal nodules and cysts distributed in both lungs and predominantly in the middle and upper lobes, sparing the costophrenic angles. The BAL analysis did not show the presence of elevated CD1a Langerhans cells, but the sensitivity of this analysis is reported to be less than 25% (1,2). Electron microscopy, which can demonstrate Langerhans cells with Birbeck's bodies allowing ultrastructural confirmation of histiocytosis X, was not performed. In our patient, the diagnosis was confirmed by the presence of nodules on surgical lung biopsies, including histiocytes positive for S-100 and CD1a.

Little is known about the causation and the natural history of PLCH in adults. The only consistent epidemiological association is with cigarette smoking, because the vast majority of patients have a history of smoking (3). Additional support for this association comes from a study by Zeid and Muller (4), which showed the development of an interstitial granulomatous inflammation in mice, similar to PLCH in humans, after exposure to tobacco smoke. To date, a number of hypotheses have been proposed to account for the association between cigarette smoking and PLCH, principally the immunostimulant effect of tobacco glycoprotein (5), the bombesin-like peptide secretion (6) from neuroendocrine cells in lung macrophages, the growth of lung fibroblasts and the bronchiolocentric distribution of the lesions.

Based on a comprehensive review of the literature, there have been reports of patients showing an improvement in chest radiographic findings after smoking cessation only (7-9). However, it is well known that chest radiographs are less accurate than HRCTs for detecting pulmonary abnormalities in patients with PLCH (10). To our knowledge, only two patients have been reported with a significant improvement based on HRCT findings following smoking cessation (11); the nodules of one of the two patients completely disappeared on HRCT. Another patient with complete resolution of coalescing air wall cysts on HRCT following smoking cessation was recently published in the Japanese literature (12). What is noteworthy in our patient is the disappearance of the HRCT abnormalities 12 months after beginning the smoking cessation program, despite numerous initial thick- and thin-walled cysts. Radiological resolution is, in fact, usually reported in patients with a recent onset of active disease

with mainly nodular lesions, with cysts usually being ascribed to airway luminal enlargement due to focal destruction of the alveolar walls. The initial normality of lung volumes in our patient, as in the two other reported cases (11) without any direct or indirect signs of radiological fibrosis, is intriguing, and may constitute a significant predictive factor for radiological resolution and a favourable outcome. The impressive disappearance of the lung lesions following smoking cessation adds to the growing evidence of the role of tobacco, but nonetheless, does not confirm a close link with the disease. For example, Tazi et al (8) have reported spontaneous resolution despite smoking persistence in two patients. The extent to which smoking cessation influences the progression and the long-term prognosis of the disease is yet to be established. Furthermore, there is a lack of data on the long-term natural history of PLCH.

In terms of treatment, smoking cessation should be considered before any other therapeutic modalities. In symptomatic patients, corticosteroids have been reported to be beneficial, but controlled trials of treatment are lacking. However, in terms of long-term benefit and relapse, no data on the role of smoking cessation or medication have been reported. The long-term prognosis of patients, especially those with normalization of the radiological findings, as is the case in our patient, has not yet been determined. Furthermore, the observation, reported by Davidson (13), of a patient who was symptom-free for six years with radiographic resolution and an abrupt symptomatic and radiographic exacerbation, suggests the need for a careful long-term follow-up of patients with PLCH. Against this background, the recent implementation of the trial, by the Histiocytosis Association of America (the LCH-A1), is encouraging (14).

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