Rare disease

An unusual radiological presentation of pulmonary Langerhans' cell histiocytosis

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Summary

Langerhans' cell histiocytosis is a proliferative disease of the dendritic cell lineage. It usually has a characteristic radiological presentation of apical nodules and small cysts occurring predominantly in young adult smokers. Here we report a case of multisystem Langerhans cell histiocytosis in a 75-year-old woman with unusual chest radiology.

BACKGROUND

Langerhans' cell histiocytosis (LCH) is a proliferative disease of the dendritic cell lineage.¹ It is classified into two broad clinical groups (single system and multisystem) dependent on the number of sites involved (commonly lung, skin and bone).²

Pulmonary LCH is a rare interstitial lung disease (ILD) accounting for approximately 5% of all ILD.² It most commonly affects young adults between the ages of 20 and 40 years.³ Over 90% are current or former smokers, although smoking is less prevalent in those with associated multisystem disease.³

The clinical presentation of pulmonary LCH is often non-specific (cough and dyspnoea being most prevalent³), with up to 25% being asymptomatic,⁴ and a further 10% presenting with pneumothorax.³

Chest x-ray (CXR) classically demonstrates small nodules or reticulonodular opacities, cysts and honeycombing with costophrenic sparing.⁵ High-resolution computerised tomography scanning most commonly demonstrates nodules and cysts in an apical distribution³; however, atypical findings include pleural effusions, mediastinal lymphadenopathy,⁶ solitary pulmonary nodules and solitary bulla.³ The atypical findings are more common in multisystem disease.

Here we present a case of LCH of the lung and skin with an unusual radiological presentation.

CASE PRESENTATION

The patient is a 75-year-old woman who presented to hospital in October 2011 with a 6-week history of lethargy, weight loss (6 kg), dyspnoea and a non-productive cough. She had a background history of stable myelodysplasia, diagnosed 8 years before, not requiring transfusion. She was on no regular medication, but had trialled

Figure 1 Submammary skin rash.

Figure 2 Chest x-ray on presentation.

Figure 3 CT thorax demonstrating peripheral septal thickening and ground glass opacification.

fluticasone/salmeterol and salbutamol for the dyspnoea, with no effect. She had no other significant medical or respiratory history. She had never smoked. In April 2011, she developed an itchy erythematous eruption on the submammary skin, which did not resolve with topical clotrimazole and hydrocortisone. In September 2011, the rash extended rapidly and presented as a crusted finely papular eruption in the submammary, inguinal and postauricular flexures with extension to the lateral neck. There were widespread crusted papules on the back. The skin rash had become more prominent prior to her hospital presentation (see figure 1).

Other than the rash she had clinical evidence of bilateral pleural effusions. There were no features of right heart failure.

INVESTIGATIONS

Full blood count was significant for a marked monocytosis (3.74×10^9 per litre) and mild anaemia (Hb 99 g/l). Biochemistry revealed low sodium of 122 mmol/l. Serum brain natriuretic peptide was normal. C-reactive protein was 62 mg/l. A repeat bone marrow biopsy was consistent with myelodysplasia without evidence for infiltration or blast transformation. CXR (see figure 2) revealed bilateral

Figure 4 Skin biopsy: within the skin biopsy from submammary chest wall, there was an upper dermal and epidermotropic infiltrate of relatively uniform large cells disposed loosely and in aggregates. They displayed abundant eosinophilic cytoplasm and infolded or bean-shaped vesicular nuclei sometimes with longitudinal grooves. Positive immunohistochemical staining with S100, CD1a and langerin (CD207) demonstrated these to be differentiated Langerhans cells. The histiocytic marker CD68 was negative. The more specific MelanA and HMB45 melanoma markers were negative, and CK7 was negative for Paget's disease. Admixtures of lymphocytes and scattered eosinophils were also present within the dermis.

Figure 5 Open lung biopsy. 1—high-power H&E showing the septa containing a mixed infiltrate, including histiocytes. 2—high-power of CD1a stain showing the Langerhan cell histiocytes.

pleural effusions and an increase in interstitial markings, predominantly in a perihilar distribution. Echocardiogram was normal. Respiratory function testing demonstrated a restrictive abnormality with a moderate reduction in gas transfer (FEV_1/FVC 72%, FEV_1 2.03 (82%), FVC 1.46 (72%), TLC 3.90 (76%), RV 1.87 (84%), haemoglobin corrected (HC) D_{LCO} 9.5 (45%), (HC) Kco 2.92 (70%).

A CT chest revealed bilateral pleural effusions, unusual interlobular septal thickening with associated, predominantly peripheral, ground glass opacification (see figure 3). There were neither nodules nor cysts present.

She underwent a skin and thoracoscopic lung biopsy, which both demonstrated a Langerhan cell infiltrate with CD1a and langerin positivity consistent with LCH (see figures 4 and 5).

TREATMENT

She was started on cytarabine 100 mg/m² daily for 3 days and has thus far tolerated treatment well.

OUTCOME AND FOLLOW-UP

There has been some regression of the skin rash; however, chest radiology has remained unchanged to date (figure 6).

DISCUSSION

LCH is currently thought to represent a cell proliferation disorder, secondary to an activating mutation of the BRAF oncogene.¹ Disease is variably reported as polyclonal or monoclonal. In pulmonary LCH the trigger for cell proliferation is likely to be cigarette smoke or another inflammatory stimulus.^{1–3} The characteristic progression of pulmonary LCH starts with bronchiolocentric, stellate nodules that progressively undergo necrosis. Small cysts and interstitial fibrosis occur with advancing disease. This is typically in an apical distribution.³

The clinical course of pulmonary LCH is quite variable. A significant proportion may spontaneously resolve, but overall survival is shorter when compared with the general population, with approximately 50% of the death rate attributed to progressive respiratory failure.⁴ A low diffusing capacity for carbon monoxide is one of the most useful predictors of a poor outcome.⁴

In single system pulmonary disease the radiological presentation is characteristic in young active smokers, with the diagnosis often made without histology.⁷ Treatment involves smoking cessation. Glucocorticoids may be useful in treating pulmonary nodular disease and in those with progressive decline in respiratory function.³

Figure 6 CT thorax 6 months following commencement of therapy.

In multisystem LCH, organs involved include the skin, bone, lung and sometimes brain with associated referable clinical presentations. Whether systemic disease represents a distinct clinical entity from pulmonary LCH is unclear. There are no trials to guide treatment, although many authors advocate a regimen of cytotoxic agents.³ Treatment outcomes have been variable and inconsistent.

In this case, the presence of a skin rash with an unexpected diagnosis of LCH and evidence of an ILD prompted a lung biopsy confirming pulmonary involvement. The case is notable for the very atypical radiological presentation and increases knowledge of the variability in chest radiology appearances in multisystem LCH.

Learning points

- Pulmonary Langerhans' cell histiocytosis (LCH) classically presents with apical cystic lesions in smokers.
- Multisystem LCH can present in a number of different systems including skin and bone.
- In cases where the diagnosis is unclear, surgical biopsy, if safe to do so, is essential.

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Competing interests None.

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