CASE REPORT

Pulmonary Langerhans Cell Histiocytosis in pre-existing chronic myelomonocytic leukaemia: a rare association

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Learning points for clinicians

The association of PLCH in a patient with established CMML is rare. Both conditions are associated with disordered cellular proliferation of monocyte progenitor cell derivatives and chromosome 7 aberrations. The association between LCH and CMML will require further study. Cladribine offers a treatment option for single system PLCH in ex-smokers.

Case history

A 72-year-old lady with a 58 pack year smoking history presented with a 2 week history of dyspnoea, lethargy, night sweats and abdominal pain. Past medical history was significant for rheumatoid arthritis, chronic myelomonocytic leukaemia (CMML), diabetes mellitus and previous breast cancer. She was not on any immunosuppression or pneumotoxic drugs. Examination revealed oxygen saturations of 96% on air and signs of her previous breast surgery but was otherwise non-contributory. Blood tests were notable for an elevated white cell count of $21 \times 10^9/l$ (neutrophils $12.5 \times 10^9/l$, lymphocytes $4.2 \times 10^9/l$, monocytes $3.4 \times 10^9/l$) and calcium of 2.9 mmol/l. A chest radiograph (CXR) showed diffuse nodularity bilaterally (see Figure 1). A CXR 10 months earlier had been unremarkable. Pulmonary function tests showed a restrictive ventilatory defect with reduced gas transfer. High resolution computed tomography (HRCT) of the chest revealed florid centrilobular ground glass nodularity throughout both lungs with multiple small areas of cavitation (see Figure 1a) with sparing of both lung bases (not shown).

There was a neutrophilic alveolitis (60%) on bronchoalveolar lavage. Due to the diffuse and atypical nature of the HRCT appearances and the need for a definitive diagnosis, a video-assisted thoracoscopic surgery (VATS) lung biopsy was undertaken. This revealed a nodular area in a bronchocentric distribution with lymphocytes, histiocytes and eosinophils and notable CD1a staining consistent with Langerhans Cell Histiocytosis (LCH) (see Figure 1b).

The patient significantly reduced her smoking consumption and required long-term oxygen therapy given the extent of parenchymal lung disease. She underwent pulmonary rehabilitation and remained symptomatically stable 6 months later but with declining lung function: forced vital capacity now 69% predicted, transfer factor now 25% predicted. She is being considered for cladribine treatment if she manages to completely stop smoking.

Discussion

LCH is a rare granulomatous disease and can affect multiple organ systems or one system. The condition is characterized by uncontrolled proliferation of reticulohistiocytic structures, polynuclear eosinophils, neutrophils, lymphocytes, plasma cells, multinucleate giant cells and Langerhans cells which may infiltrate any organ and cause granuloma formation. Whilst no cause of the disease has been identified, isolated Pulmonary LCH (PLCH) has a strong association with cigarette smoking. LCH may affect either sex and occur at any age, 5 year survival

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for PLCH is estimated to be 74%. It may present in a variety of ways including serendipitously as an incidental CXR finding. Indeed, 23% of PLCH patients were asymptomatic and diagnosed incidentally in one series although it most commonly presents with respiratory symptoms (72%) including cough (50%) and dyspnoea as in this case (35%) which is often exertional. Radiological features of LCH are variable but characteristic features are bilateral nodules (which may be cavitating) and/or cysts with sparing of the lung bases.

Smoking cessation can lead to radiological resolution and is the cornerstone of therapy for PLCH. Therapy is usually directed to those with multi-system LCH or those with progressive single system disease. Prednisolone and vinblastine are first line options for induction and continuation therapy for multisystem disease but are of no proven benefit in isolated PLCH. Single-agent chemotherapy with cladribine may be a promising treatment for isolated PLCH for those with progressive disease that have failed to respond to smoking cessation.

LCH is rarely associated with haematological disorders and malignancy including CMML (cutaneous LCH), with a suggestion of shared abnormalities of chromosome 7 in bone marrow cells and are possibly originated from the bipotent progenitor cells. To date, there are no reports of PLCH and CMML. We speculate similar shared mechanisms may be responsible here and we believe this association is worthy of further study.

Conflict of interest: None declared.

References