Case report

Reversible cerebellar signs due to sarcoid-related severe hypercalcaemia

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Learning Points for Clinicians

1. Severe and symptomatic hypercalcaemia can occur in sarcoidosis but remains uncommon, <5% of cases (malignancy should remain top of the list in unexplained cases). If rehydration and steroids are unsuccessful, other options are ketoconazole and chloroquine in this context.

2. It is imperative to know the serum calcium level (amongst other electrolytes) in patients with abnormal mentation and neurological signs before undertaking cross-sectional neuroimaging. In this particular case, the computed tomography (CT) brain scan could have been avoided.

3. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) should be favoured as a diagnostic tool (especially if neck ultrasound core biopsy is not an option), avoiding the need for more invasive procedures requiring general anaesthesia, such as mediastinoscopy.

Case history

A 58-year-old Caucasian man presented on the acute medical take with a week-long history of impaired cognition, abnormal gait and constitutional symptoms (weight loss and anorexia). Past medical history was significant for insulin controlled type 2 diabetes mellitus. There were no relevant occupational or travel factors.

Examination findings were significant for centripetal adiposity (weight: 149 kg, body mass index: 48), horizontal nystagmus, dysdiadochokinesis and an ataxic broad-based gait. Other general and neurological examination was normal.

Significant blood tests revealed severe hypercalcaemia (corrected calcium of 4.4 mmol/l) and renal impairment (creatinine 190 mmol/l, baseline 100 mmol/l 2 months earlier). Parathyroid hormone was suppressed (0.3 ng/l), and full blood count was normal (eosinophil count of <0.04). Serum electrophoresis showed no monoclonal bands.

Chest radiography showed bilateral reticulonodular shadowing but no mass lesion. A CT scan of head was normal (performed before the calcium result had been available). Contrast CT of the thorax, abdomen and pelvis illustrated widespread perilymphatic nodularity (see Figure 1a), hilar, mediastinal and abdominal lymphadenopathy. Radiologically, this was suggestive of sarcoidosis supported an elevated serum angiotensin converting enzyme level of 190 U/ml (normal range: 20–70 U/l) although the differential remained lymphoma. There was no evidence of malignancy or other organ involvement.

His cerebellar symptoms and signs had already promptly resolved with treatment of his hypercalcaemia with rehydration obviating the need for...
further neuroimaging. An ultrasound-guided core biopsy of the supraclavicular node (noted on CT) was unsuccessful. The patient went on to have an EBUS-TBNA under conscious sedation with a 21G needle, otherwise as previously described1 to sample the hilar lymph nodes. EBUS-TBNA core biopsies confirmed the presence of non-necrotizing granulomatous inflammation with Schaumann bodies (see Figure 1b) and the diagnosis of sarcoidosis (endobronchially the mucosa was normal). Prednisolone was commenced with good effect on serum calcium and symptoms and the patient discharged home shortly thereafter with early followup in the chest clinic.

Discussion

Sarcoidosis is a multisystem disease characterized by tissue infiltration with non-caseating granulomas. Hypercalcaemia is a recognized feature but in the case of severe hypercalcaemia, malignancy must remain high in the differential. Presentation with symptomatic hypercalcaemia in sarcoidosis is relatively rare and typically affects <5%2,3 of cases. Patients typically present with constitutional symptoms related to systemic inflammation or symptoms related to particular organ involvement. Acute renal impairment occurs more commonly due to toxic effects of high calcium on the kidney rather than glomerulonephritides related to sarcoid. A return to baseline creatinine and resolution of neurology with hydration in our patient negated the need for renal biopsy and more extensive neuroimaging.

In terms of diagnosis when considerable mediastinal lymphadenopathy is present, neck ultrasound core biopsy and EBUS-TBNA offer non-invasive alternatives to mediastinoscopy. If there is significant parenchymal disease, transbronchial biopsy is an alternative via conventional bronchoscopy but can cause pneumothorax and bleeding. Endobronchial biopsies are also helpful especially when the mucosa is nodular. In this case, given the patient’s adiposity, transbronchial biopsy was avoided.

Glucocorticoids remain the mainstay of treatment for pulmonary sarcoid but careful consideration must be given to alternatives, especially in the context of diabetes and adiposity or other relevant comorbidities. Alternative agents should be considered when there are intolerable side effects (uncontrolled diabetes, excessive weight gain or osteoporosis), disease progression despite adequate therapy (0.5 mg/kg/day for 4 weeks, and then reduced to a maintenance dose to control symptoms and disease progression4) or a need for prolonged therapy with steroid-related complications. When steroids are contraindicated or not tolerated, ketoconazole or chloroquine (the latter used less because of the potential retinal effects) has been used as alternative agents for sarcoid-related hypercalcaemia via inhibition of 1α-hydroxylase.2–3 Evidence for the commonly used second line agents for sarcoidosis is largely observational5,6 and must be weighed against risks of immunosuppression. Agents typically used include mainly methotrexate, azathioprine and leflunomide with the greatest evidence to date for methotrexate.

Conflict of interest: None declared.

References

1. Medford AR, Agrawal S, Free CM, Bennett JA. A performance and cost analysis of endobronchial ultrasound-guided

Figure 1. (a) CT scan (lung windows) showing perilymphatic nodules. (b) EBUS-TBNA biopsy showing non-caseating granulomata and Schaumann bodies.
transbronchial needle aspiration in a UK tertiary respiratory centre. QJM 2009; 102:859–64.


