Unusual association of diseases/symptoms

Diabetes insipidus secondary to sarcoidosis presenting with caseating granuloma

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Summary

Diabetes insipidus is a rare complication of sarcoid infiltration of the hypothalamic-pituitary region. Non-caseating granuloma formation is typical of sarcoidosis. Anterior and posterior pituitary function may be affected. MRI coupled with endocrinology assessment is the usual method of investigation. A 25-year-old Caucasian male with no significant medical history presented with polyuria and polydipsia. Water deprivation test confirmed diabetes insipidus. CT scanning of the chest confirmed lymphadenopathy. Lymph node biopsy revealed caseating granuloma. Extensive investigation for tuberculosis was negative. The patient was started on intranasal desmopressin and steroids with marked improvement in symptoms. This is the first reported case of neurosarcoidosis with diabetes insipidus and caseation on histology that we are aware of. Differentiating between caseation due to sarcoidosis and tuberculosis on histology is possible by the use of special stains. Return of normal endocrine function is unusual and the patient is likely to require desmopressin therapy for life.

BACKGROUND

Sarcoidosis is a multi-system granulomatous disease of unknown aetiology.¹ Although endocrine complications of sarcoidosis are rare, diabetes insipidus appears to be one of the more frequently observed disorders.² Histological change of non-caseating granuloma is typically seen with sarcoidosis. We describe an unusual case of sarcoidosis presenting with diabetes insipidus associated with histological evidence of caseating granuloma on lymph node biopsy. As far as we are aware, this is the first reported case of this combination of features. We have used this opportunity to review the available literature relating to both diabetes insipidus secondary to sarcoidosis and histological changes seen with sarcoidosis.

CASE PRESENTATION

A 25-year-old Caucasian male with no significant medical history presented with a 3-month history of increasing polyuria and polydipsia with urine output of approximately 7 l/day. Weight and appetite were stable with no night sweats reported. There were no risk factors for tuberculosis (TB). Examination revealed the patient to be clinically dry with palpable cervical lymph nodes, but was otherwise normal.

INVESTIGATIONS

A diagnosis of diabetes insipidus was confirmed by water deprivation test, with weight loss of more than 3% body weight within the first 3 h of testing. MRI with gadolinium of the head failed to show any evidence of pituitary or hypothalamic infiltration. Anterior pituitary function assessment proved normal.

CT imaging of the chest to investigate palpable cervical lymph nodes showed patchy parenchymal change at the right apex (figure 1) along with extensive cervical and hilar lymphadenopathy. Lymph node biopsy was

performed with histology showing caseating granuloma formation. The patient went on to have bronchoscopy with bronchio-alveolar lavage which proved unremarkable with no acid-fast bacilli seen on fluid analysis. Serum angiotensin converting enzyme and QuantiFERON-TB Gold were normal. PCR of lymph node tissue was negative for *Mycobacterium tuberculosis*. Ophthalmology assessment showed no evidence of anterior or posterior uveitis.

OUTCOME AND FOLLOW-UP

The patient was started on desmopressin intranasally, with almost complete resolution of symptoms within 2 weeks. Extended culture of lymph node tissue for TB proved negative. A diagnosis of diabetes insipidus secondary to sarcoidosis was made and the patient started on steroid therapy. He remains well and continues on desmopressin and steroid therapy for now.

DISCUSSION

Approximately, 4000 new cases of sarcoidosis are diagnosed each year in the UK. More than 90% of these primarily involve the respiratory system, with neurological involvement being relatively rare with rates of 5–16% reported.¹ Where there is infiltration of the hypothalamic-pituitary region, studies show that the posterior pituitary is highly likely to be involved with clinical manifestations of diabetes insipidus and galactorrhoea. Anterior pituitary involvement can vary from isolated hormonal deficits to panhypopituitarism with loss of thermal and thirst regulation. Deficiencies of growth hormone, follicular stimulating hormone and leutinising hormone are the most frequently observed anterior pituitary disorders.² Rarely, direct involvement of thyroid and adrenal glands can lead to functional deficiency. Pancreatic involvement has been reported but does not appear to lead to diabetes mellitus.³

Figure 1 CT chest showing right upper lobe parenchymal changes. Although sarcoidosis typically affects the upper lobes, the most common feature seen with lung involvement is bilateral hilar lymphadenopathy. Upper lobe parenchymal changes may also be seen in tuberculosis.

MRI with gadolinium is the recommended modality for initial assessment of granulomatous infiltration of neural tissue.⁴ Studies have also shown the usefulness of MRI in adjusting treatment for neurosarcoidosis based on changes in lesion number and character.^{5 6} There is currently no convincing evidence to support the routine use of PET-CT scanning. It may however be beneficial in certain cases where there are no obvious superficial biopsy sites and deeper lymph node group involvement needs to be determined.⁷

Common MRI findings may include infundibular involvement, pituitary stalk thickening or pituitary gland enlargement as well as lesions situated in other areas of the brain. There is also evidence to suggest that loss of hyperintense signal from the posterior pituitary on T1 weighted images is indicative of an infiltrative process.⁸

The presence of caseating granuloma in our patient caused significant diagnostic and management difficulties. There were no risk factors for TB or fungal infection and the clinical picture was more consistent with sarcoidosis. All investigations for infectious causes proved negative. Examining the literature, there are numerous case reports of sarcoidosis associated with caseating granuloma.⁹ Typically, the necrosis in sarcoidosis is focal, very small in

size and is located centrally in relation to the granuloma. Histological distinction between sarcoidosis and TB can be achieved by using special stains such as Van Gieson stain.^{10 11} This will highlight the predominantly collagenous material of sarcoidosis from the frank caseation of TB. Use of Gomori's stain will help in excluding fungal causes.

The mainstay of treatment of sarcoidosis remains steroid therapy. Alternative agents including methotrexate, cyclophosphamide, hydroxychloroquine and infliximab are used in resistant cases or where glucocorticoids are not tolerated.⁵ Unlike pulmonary disease where treatment need not be initiated depending on the stage of disease, neurological involvement is regarded as an absolute indication to start therapy.

The prognosis for recovery of normal endocrine function remains poor despite treatment. Studies show that despite radiological evidence of regression with steroid therapy, return of endocrine function remains unlikely.^{12 13} There are case reports supporting recovery in patients started on steroid therapy within 1 month of onset of symptoms, although it is difficult to establish whether this is related to rapid institution of treatment or an atypical disease course.^{14 15} Unfortunately due to the insidious

onset of symptoms, most patients have already passed this point at the time of presentation. Our patient presented with a 3-month history of polyuria and polydipsia and as such he will most likely require lifelong desmopressin therapy. Steroid treatment will continue for now to prevent further neurological complications from new lesions.

Learning points

- ▶ Diabetes insipidus secondary to neurosarcoidosis is a rare but serious disorder.
- ▶ It may be accompanied by anterior pituitary dysfunction as well as loss of temperature and thirst regulation.
- ▶ Endocrine assessment coupled with MRI is the standard route of investigation.
- ▶ Although direct biopsy of pituitary lesions is difficult, PET-CT can be used to identify lymph node involvement and thus suggest an alternative biopsy site.
- ▶ Treatment with steroids is unlikely to restore normal endocrine function.
- ▶ Caseation may be seen with sarcoidosis but is usually focal, small and centrally located within the granuloma.
- ▶ The use of Van Gieson and Gomori's stains can help distinguish caseation secondary to sarcoidosis from that due to TB or fungal infection.

Competing interests None.

Patient consent Obtained.

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