The Confused Sarcoid Patient

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Abstract

We present the case of a 67 year old lady with confusion, hypercalcaemia, acute kidney injury and weight loss. She denied any respiratory symptoms. CT Thorax, Abdomen and Pelvis showed lymphadenopathy and US guided biopsy a lymph node confirmed a non-caseating granuloma. Patient was started on steroid and her renal profile and calcium level improved.

Keywords: Sarcoidosis; Hypercalcaemia; Acute Kidney Injury

Abbreviations

AKI: Acute Kidney Injury; LDH: Lactate Dehydrogenase; CT TAP: Computer Tomography of Thorax, Abdomen and Pelvis; PTH: Parathyroid Hormone; ESRD: End Stage Renal Disease

Introduction

Renal disease occurs in approximately 35 to 50 percent of patients with sarcoidosis, though is commonly undetected [1]. The classic renal lesion is noncaseating granulomatous interstitial nephritis, but this lesion rarely causes clinically significant renal disease.

Case Report

This is the case of a 67 year old lady who was referred to A&E because of a concern about confusion and hallucinations. Her family described a fluctuating confusion associated with dizziness, visual hallucinations and constipation. She had a past medical history including hypercholesterolaemia, chronic lower back pain, peptic ulcer disease, depression, mild cognitive impairment, previous alcohol dependency and recent history of use of valerian root to self-medicate for difficulty sleeping. Her regular medications included desunin, esomeprazole, venlafaxine, colpermin. She was living alone without a home care package and mobilised independently. She denied any recent alcohol use and her children monitored her home for evidence of same. She smokes 10 cigarettes a day.

She had a slow deterioration of cognition over a period of 3 weeks. Her deteriorating cognition seemed to be fluctuating and was associated with vivid visual hallucinations for three weeks. She had always had difficulty sleeping but over the 3-week period she was suffering from sleep-wake inversion. Her general practitioner had recently weaned her off of her regular zopiclone. Instead of weaning slowly the patient had stopped it suddenly. She started taking over the counter valerian root in its place. Valerian root can cause mental dullness, fatigue, abdominal pains, chest tightness, tremor and insomnia. On presentation she complained of thirst, polyuria, abdominal pain, constipation, lower back pain and brain fog. Her family felt that her mobility had deteriorated and did not allow her to mobilise unaided.
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On examination her vitals were within normal limits. There was no postural hypotension. Her cardiac, respiratory and abdominal examinations were normal. Her gait could not be assessed secondary to presumed ataxia. She was however moving all 4 limbs with generalised weakness. Her blood results revealed a severe AKI with a creatinine of 289 umol/L and urea of 10.6 mmol/L. 3 years previously her creatinine had been normal. Her calcium was strikingly high at 3.4 mmol/L (adjusted). Urine dipstick was negative for blood and protein. Her chest and abdominal X-ray were normal. At this point the differential diagnoses included AKI secondary to dehydration, hypercalcaemia secondary to vitamin D toxicity, side effects of valerian root, multiple myeloma, primary hyperparathyroidism, solid organ malignancy.

Initially hypercalcaemia was treated with intravenous fluids and then IV furosemide was added. This intervention although it brought calcium down to 2.9 mmol/L, it failed to bring it to normal levels and had no impact on creatinine. However, her confusion did resolve over the first week of admission along with her difficulty mobilising. Endocrinology advice was sought. PTH levels were mildly suppressed at 1.5 pmol/L. It was felt that this was unlikely to be primary hyperparathyroidism and that malignancy was more likely. Cinacalcet was commenced along with vitamin D; which was found to be low. Multiple myeloma screen and LDH was normal. Breast examination was normal. Renal ultrasound was carried out to investigate the unresolving acute kidney injury despite IV fluids. This was normal.

A CT TAP was carried out which revealed multiple pathologically enlarged lymph nodes within the thorax measuring up to 1.6 cm (Figure 1), 4 mm nodule in the right middle lobe, multiple enlarged coeliac lymph nodes (Figure 2) measuring up to 1.3 cm, 1.1 cm right external iliac node, 1.2 cm right inguinal node. No lytic or blastic osseous lesions. Non-contrast CT Brain revealed chronic ischaemic changes. An ultrasound guided biopsy was carried out on the right inguinal node (Figure 3). This core of tissue contained multiple non-caseating granulomas.

A diagnosis of sarcoidosis was made. Prednisolone 20 mg once per day was initially commenced. Her calcium continued to be uncontrolled on this dose and it was increased a few days later to 40 mg per day. In 1 week her calcium had normalised and her creatinine had halved. A tapering dose of 5 mg/week was commenced and patient will be followed up as an outpatient.

**Discussion**

Hypercalciuria and hypercalcemia are most often responsible for clinically significant renal disease [2-5]. Glomerular disease, obstructive uropathy, and end-stage renal disease (ESRD) may also occur but are uncommon.

Hypercalcemia and/or hypercalciuria, resulting from hyperabsorption of ingested calcium due to increased production of calcitriol by activated mononuclear cells [6-9].

Patients with sarcoidosis interstitial nephritis present with an elevated serum creatinine that is detected on routine screening or as part of their initial evaluation for sarcoidosis. Most patients have clear evidence of diffuse active sarcoidosis elsewhere.

Hypercalcemia has been described in patients with granulomatous disorders, most commonly sarcoidosis and tuberculosis.

Hypercalcemia in sarcoidosis and other granulomatous diseases is due to parathyroid hormone (PTH)-independent extrarenal production of calcitriol from calcidiol by activated mononuclear cells (particularly macrophages) in the lung and lymph nodes.

Treatment of the hypercalcemia or hypercalciuria in granulomatous disorders is aimed at treatment of the underlying disorder. In addition, treatment of hypercalcemia or hypercalciuria includes reducing intestinal calcium absorption and calcitriol synthesis [6-9].

Reducing calcium intake (no more than 400 mg/day) may improve hypercalcemia and hypercalciuria.

Moderate-dose glucocorticoid therapy (10 to 30 mg/day of prednisone) is typically used to treat sarcoidosis. The serum calcium concentration begins to fall in two days, but the full hypocalcemic response may take 7 to 10 days depending upon the prednisone dose [6-9].
End-stage renal disease (ESRD) requiring some form of renal replacement therapy is uncommon. When it occurs, ESRD is most often due to hypercalcaemic nephropathy rather than granulomatous nephritis or a glomerulonephropathy.

In the largest observational study, among 46 patients with sarcoidosis-related interstitial nephritis, only two progressed to ESRD (at 15 and 2 years after presentation) [1].

**Conclusion**

Reflecting back on this case sarcoidosis was not on the list of differentials at presentation. The patient's main concern was difficulty sleeping. It is important to keep sarcoidosis in mind in a patient with deteriorating renal function and hypercalcaemia.

**Bibliography**


