Refractory hypercalcaemia in the context of osseous sarcoidosis

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Case Report:

A 64-year-old female presented with myalgia, arthralgia and delirium with three recent admissions with recurrent hypercalcaemia, managed with IV fluids and bisphosphonates. Despite treatment, calcium remained consistently elevated at 2.8-3.0mmol/L. Past medical history included chronic kidney disease and type 2 diabetes treated with insulin. The choice of treatment in this patient was challenging due to steroids influencing diabetic control and steroid sparing agents affecting eGFR. This was a diagnostic challenge given distracting possible alternative diagnoses including multiple over the counter supplements being used. Serum ACE was not initially available. Whilst actively looking for underlying malignancy, a diagnosis of sarcoidosis was reached.

Investigations:

- **Serum calcium** 3.73mmol/L (2.05-2.55mmol/L)
- **Serum ACE** 80 U/L (20 - 70 U/L). Elevation in serum ACE is seen in 75% of sarcoid patients (1)
- **24 hour urinary calcium** 7.7 mmol/24 hours (2.5-7.5mmol/24 hours)
- **Vitamin D** 76 (within normal range)
- **Parathyroid hormone** 1.0 (1.6-6.9pmol/L)
- **Myeloma** and bone marrow aspirate screen negative.
- **CT Abdomen pelvis** showed no malignancy.
- **PET scan** Extensive lymphadenopathy, multiple sites of bone involvement and avid splenomegaly.
- **Inguinal node biopsy** non-caseating granulomatous lymphadenitis, pathognomonic of granulomatous disease.
- Elevated calcium, raised serum ACE and histopathological findings were consistent with sarcoidosis.
- Baseline eGFR 30mL/min/1.73m*2. Peri-diagnosis eGFR 17. Post treatment eGFR 35. This suggests possible renal sarcoid. Renal biopsy was too high risk as she was unable to accept blood products.

Figure 1:

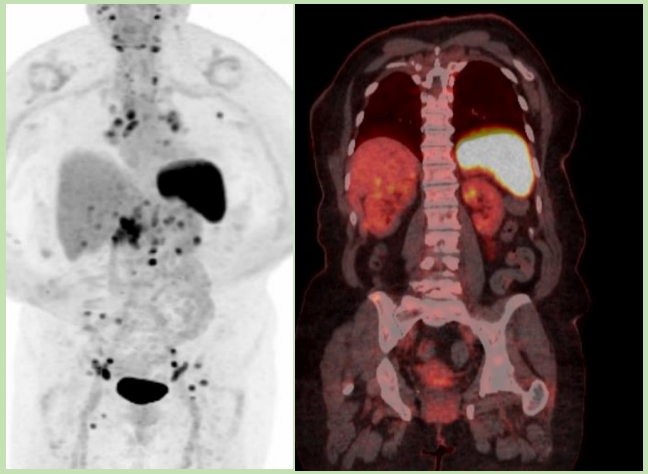

Figure 1 shows coronal images from PET scan, demonstrating extensive lymphadenopathy, multiple sites of bone involvement and avid splenomegaly.

Figure 2:

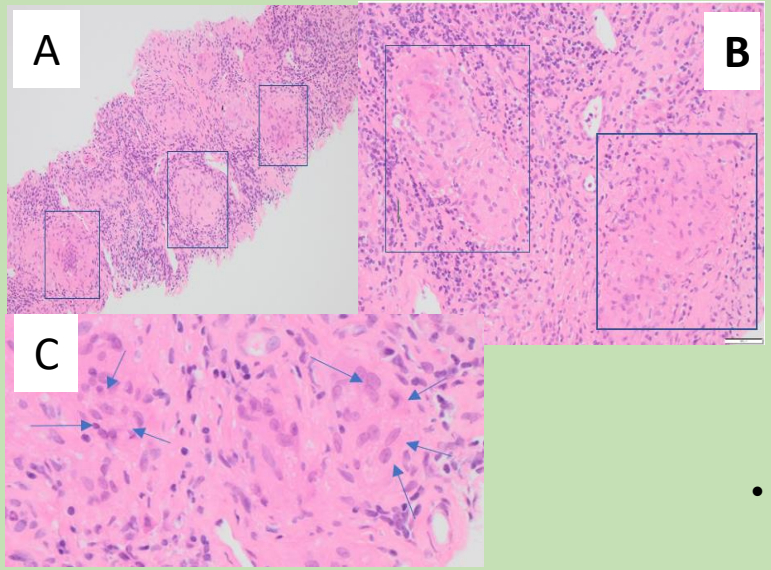

Figure 2 demonstrates aggregations of histiocytes (A), forming granulomas (B, C). These granulomas do not show evidence of a necrotising core ; indicating granulomatous lymphadenitis, for which there are multiple differential diagnoses. The well-defined borders, collection of epithelioid histiocytes in a syncytial arrangement (C), and lack of a necrotising centre are suggestive of sarcoid like granuloma (4). Histopathologic-clinical correlation together supported the diagnosis of sarcoidosis.

Management:

- IV fluids to accelerate renal excretion of calcium.
- Prednisolone to supress the inflammatory response from active macrophages. The pathophysiology of sarcoid hypercalcaemia is complex.
- The choice of steroid sparing agents was a challenge in a patient with CKD.
- Hydroxychloroquine was trialled but hel due to intolerance (rash).
- Azathioprine was used at low dose as TPMT was lower than normal levels (65mU/L).

Learning Points:

- Sarcoid is a rare but recognised cause of treatment resistant hypercalcemia , which can be challenging to diagnose, requiring multidisciplinary input.
- PET scan and biopsy were helpful in changing the suspicion of malignancy to sarcoidosis.
- Steroid sparing agents have a key role given her diabetes.
- Osseous sarcoidosis is a rare cause of hypercalcaemia, with only 3% of sarcoid patients presenting with symptomatic high calcium.
- So osseous sarcoid is often undiagnosed.

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