1. Aims
To increase awareness of sarcoidosis as a cause of hypercalcaemia through example of a case study, and highlight the diagnostic challenge of sarcoidosis.

2. Case Study
A 63 year old Caucasian female presented with a three month history of malaise and weight loss. She had previously been treated for a left breast carcinoma and was otherwise well. Examination was unremarkable. Chest x-ray was normal. Blood tests revealed an acute kidney injury on a background of previously normal renal function (Figure 1A). Serum calcium was critically elevated at 3.93mmol/L and parathyroid hormone (PTH) suppressed (Figure 1A). The initial diagnosis was of hypercalcaemia secondary to malignancy.

Intravenous normal saline and pamidronate disodium were given to lower the serum calcium. Treatment response was marginal, and a trial of corticosteroids was initiated to poor effect (Figure 2). A malignancy work-up revealed right axillary lymphadenopathy on breast ultrasound. CT of the chest, abdomen and pelvis highlighted mediastinal, paraaortic, axillary and pelvic lymph nodes, but no evidence of metastases (Figure 1B). Bone scintigraphy was normal.

Histological lymph node analysis reported non-necrotising granulomatous inflammation, negative for acid fast bacilli. A serum angiotensin converting enzyme (ACE) level was elevated at 142IU/L (normal range 8-65), supporting a diagnosis of sarcoidosis.

3. Outcome
Oral corticosteroid therapy (prednisolone 30mg once daily) was initiated for the treatment of hypercalcaemia secondary to systemic sarcoidosis. The patient displayed an excellent symptomatic and calcium lowering response (Figure 2). Renal function normalised concomitantly.

4. Discussion
- Severe hypercalcaemia (corrected calcium > 3.5mmol/l), as in our case, is a medical emergency with risk of arrhythmia, coma and death. 90% of cases of hypercalcaemia are secondary to malignancy and hyperparathyroidism (Figure 3) [1]. A previous history of breast carcinoma and non-elevated level of PTH was suggestive of malignancy. This diagnosis was challenged by the lack of calcium response to fluid, bisphosphonate and calcitoning therapy, which suggested the hypercalcaemia did not result from a state of increased bone turnover.

- In granulomatous disease and specifically sarcoidosis - many clinical features can overlap with malignancy, including symptoms of weight loss, anorexia, malaise, lethargy and fever. The diagnosis of sarcoidosis is therefore often challenging.

- Sarcoidosis is characterised by non-caseating granuloma formation. Sarcoidal granulomas (Figure 4), which can affect multiple sites, produce angiotensin-converting enzyme (ACE). However, the value of serum ACE as a diagnostic tool is limited, with elevated levels in only 60% of cases [2,3].

- Sarcoidosis-induced hypercalcaemia is subsequent to macrophage overproduction of calcitriol (1,25-dihydroxyvitamin D) in an immunoregulatory response to granuloma formation, which occurs via the enzyme 1α-hydroxylase [4]. Corticosteroids act to inhibit 1α-hydroxylase [5], and are the first-line treatment for hypercalcaemia secondary to sarcoidosis.

5. Consent
Written informed consent was obtained prior to the publication and presentation of this case report, and any accompanying images.

6. References