

Inadvertent Haemodialysis in a Pulmonary Tuberculosis Patient with Hypercalcaemia

Dear Editor,

Malaysia is a country with an intermediate burden of tuberculosis (TB) with a prevalence of 121 cases per 100,000 population per year.¹ TB usually presents with fever, chronic cough, weight loss and lack of appetite, dyspnoea and night sweats. Hypercalcaemia is a well known but rare complication of TB. The prevalence of hypercalcaemia in patients with untreated TB varies widely between countries. In Malaysia, the rate is in the range of 2.3% to 27.5%.^{2,3}

The development of hypercalcaemia depends on the total intake of calcium and vitamin D, the amount of sun exposure, degree of renal impairment and extra renal production of vitamin D by the alveolar T-lymphocytes and macrophages.⁴ The intensity of each of these factors play a role as not all patients with similar factors will go on to develop hypercalcaemia. The production of vitamin D is also related to the degree of immune and inflammatory response of the host.⁴

Despite being a nation with an intermediate disease burden of TB; surprisingly, misdiagnosis or delayed diagnosis of TB still occurs. We describe a patient who presented with hypercalcaemia and renal failure who underwent haemodialysis. Unfortunately although the hypercalcaemia was the clue to the diagnosis of pulmonary TB, this link was missed.

Case Report

A 61-year-old Malay man was referred to our centre for the further management of end-stage renal failure and hypercalcaemia after presenting to 2 separate medical centres. He had a background of type 2 diabetes complicated with nephropathy. He complained of intermittent cough with fever for the past 2 years. He also admitted to having marked loss of weight and loss of appetite.

When he presented to the first medical centre, he was investigated for pyrexia of unknown origin. He was not informed of the results of tests performed, except the bone marrow and trephine biopsy (BMAT), which showed monoclonal gammopathy of undetermined significance (MGUS). However, the result traced by us was not consistent with MGUS as there were only 2% plasma cell in the marrow, and no monoclonal increase of gammaglobulin.

A year later, he presented to the second centre with upper gastrointestinal bleeding. During that admission he was found incidentally to have renal failure and hypercalcaemia. He was diagnosed with end-stage renal

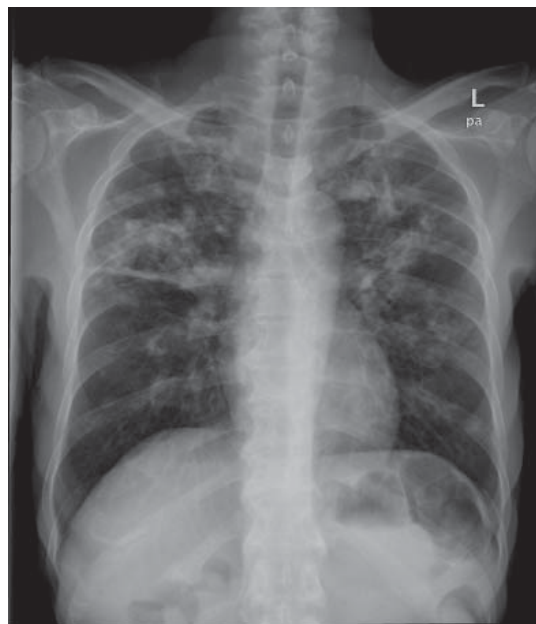


Fig. 1. Chest X-ray of the patient showing bilateral upper zone consolidation and cavitation.

failure and haemodialysis was initiated. The cause of the hypercalcaemia was attributed to the end-stage renal failure (tertiary hyperparathyroidism). He was referred to our centre for further management of hypercalcaemia as it failed to respond to therapy. The symptoms of intermittent cough and fever remained.

On examination, the patient appeared cachectic with bilateral upper zone crepitations with bronchial breath sound. Examination of the other systems was unremarkable. The chest radiograph showed bilateral upper zone consolidation and cavitation, in keeping with pulmonary TB. The sputum smear was positive for acid fast bacilli. The investigation showed a calcium level of 3.20 mmol/L, phosphate 1.20 mmol/L, urea 7.0 mmol/L, creatinine 281 μ mol/L, albumin 28 g/L, total protein 81 g/L, total bilirubin 6 μ mol/L, alanine aminotransferase (ALT) 11 U/L and alkaline phosphatase (ALP) 74 U/L. The thyroid function test was normal. The serum parathyroid hormone was suppressed (<0.31 pmol/L). Repeated bone marrow and trephine biopsy confirmed no evidence of multiple myeloma or MGUS. None of the tumour markers (prostate specific antigen, carcinoembryonic antigen, alpha-fetoprotein and CA19-9) were raised. Serum angiotensin converting enzyme

was not performed in this patient. Anti-TB treatment was commenced with ethambutol, isoniazid, pyrazinamide and rifampicin. The hypercalcaemia resolved and haemodialysis was withdrawn. His creatinine level remained around 250 to 270 $\mu\text{mol/L}$.

Discussion

The delay in the diagnosis and initiation of treatment of TB is a serious health problem. This can lead to progression of the disease and even to a patient's demise. There are numerous causes of delay in the diagnosis and treatment of TB. These can be classified broadly into patient delay, and doctor delay.⁵ Patient delay is the time interval from the manifestation of the first symptom of the disease to the time it is brought to medical attention. A doctor delay is the time interval from the date of first medical consultation to initiation of anti-TB treatment. It is clear in our case that the delay in treatment was due to doctor delay. Although the existence of the association between hypercalcaemia and TB has been reported in the literature, the doctors still failed to identify the possible link between a high calcium level and pulmonary TB. The low level of clinical suspicion and failure to perform further basic and proper investigations and referral to government hospital are the major contributing factors of doctor delay.⁵

We often encounter hypercalcaemia in the clinical wards. The more common causes of hypercalcaemia are hyperparathyroidism and malignancy. Symptomatic hypercalcaemia can occur in patients with TB during the active phase. In Malaysia, only 12% of TB patients with hypercalcaemia develop symptomatic hypercalcaemia.³ However, the occurrence of the disease may not correlate with the level of calcium. This is because the level also depends on calcium intake, level of vitamin D, amount of sun exposure and degree of renal impairment. Liam et al³ have shown us that the incidence of hypercalcaemia is higher in equatorial countries due to the frequent exposure to the sun leading to abundant vitamin D production and increased gut

calcium absorption. The resolution of the hypercalcaemia in pre-treatment TB depends on the resolution of TB with anti-TB. It is also noted that rifampicin and isoniazid also cause a decrease in serum vitamin D.

TB is easily diagnosed when the classical symptoms and signs are present. However, we should not forget that TB can involve any organ and mimic other diseases. It should have been considered in this patient with a long history of fever and chronic cough. Our case illustrates the importance of a good history taking, a thorough physical examination and appropriate laboratory work-up tailored to the patient's presentation. We suggest that clinicians be more vigilant and consider uncommon presentations of TB to avoid unnecessary delay in initiating treatment.

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