Hypercalcaemia - A Rare Manifestation of Tuberculosis - A Case Report

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INTRODUCTION

Hypercalcaemia is defined as a serum calcium level of more than 10.50 mg/dl. Although there are several causative factors for hypercalcaemia, primary hyperparathyroidism and malignancy are the two most common causes encountered in clinical practice. Other causes include vitamin D intoxication, granulomatous diseases like sarcoidosis, tuberculosis and some fungal infections, thyrotoxicosis, Addison’s disease, milk-alkali syndrome, vitamin A intoxication, therapy with thiazide diuretics and lithium, familial hypocalciuric hypercalcaemia and prolonged immobilization. All these account for fewer than 10% of all causes of hypercalcaemia. These rare causes of hypercalcaemia are important to consider in certain clinical situations when the underlying cause of hypercalcaemia cannot be attributed to primary hyperparathyroidism or overt malignancy.[1]

PRESENTATION OF CASE

A 27-year-old married female presented to the emergency department of Gauhati Medical College and Hospital with the chief complaints of amenorrhea for 9 months, low-grade fever, cough, abdominal pain and distention, decreased appetite, weight loss from 5 months and constipation from 1 month. She was married for 7 years with a history of infertility. During this period, she was evaluated in a local hospital several times and on evaluation, most of the investigations were normal except for the presence of hypercalcaemia on more than one occasion. On examination, the patient was normotensive with the presence of pallor. Examination of the abdomen revealed a doughy consistency on palpation, with the presence of distention and tenderness. Shifting dullness was present and on auscultation, bowel sounds were absent. There were no palpable lymph nodes. Neurological, cardiovascular and respiratory system examinations were within normal limits. A gynaecological examination was done which revealed an abdominopelvic mass per vaginal examination.
On routine investigations, her total leucocyte count was 14.52 × 10^3 /μL with absolute neutrophilia, haemoglobin was 8.8 g/dL with the predominantly normocytic normochromic picture, creatinine was normal, albumin was 3.4 g/dL, serum bilirubin and liver enzymes were normal. Serum amylase was 676 U/L and serum lipase was 4063 U/L. Her albumin corrected serum calcium level was 16.98 mg/dL. Ultrasonography of the abdomen showed coarse hepatic echotexture, mild ascites, bilateral renal medullary nephrocalcinosis, and oedematous small bowel loops.

On further workup, serum TSH was normal (2.42 μIU/L). Parathyroid hormone level was slightly low (0.127 Pmol/L), serum phosphate level was normal (3.2 mg/dl), Vitamin D₃ level (25 hydroxycholecalciferol) was low (19.71 ng/ml), whereas 1,25 dihydroxyvitamin D₃ level was high (108 pg/ml).

Diagnostic ultrasound-guided paracentesis revealed exudative tap with high ascitic fluid protein (5.2 g/dl), low sugar (50 mg/dl), leucocyte count of 30 cells/mm² with 80 % lymphocytes. Ascitic fluid cytology for malignant cells was negative. Contrast-enhanced computed tomography scan of thorax and abdomen showed gross ascites with enhancing peritoneal thickening, omental caking, omental smudging with prominent abdominal lymph nodes suggestive of tubercular peritonitis, discrete to confluent nodules few in the tree in bud pattern in bilateral lung fields suggestive of active infective aetiology. Attempts for ultrasound-guided fine-needle aspiration cytology of peritoneum failed. Serum protein electrophoresis for the myeloma band was negative. Contrast-enhanced MRI of abdomen and pelvis revealed endometrial hyperplasia with endometriomas in bilateral ovaries.

Hypercalcemia is known to occur in granulomatous diseases most commonly sarcoidosis and tuberculosis.[2,3] Hypercalcemia, although occurs infrequently, is a well-recognized complication of active tuberculosis, the incidence varying between 2 % and 25 % depending on the geographical area where the study is conducted, intake of calcium, serum vitamin D levels, and exposure to the sun.[4-6,7] In this patient, the diagnosis of tuberculosis was made based on her chief complaints, clinical examination and computed tomography findings, and improvement with anti-tubercular therapy. A study done by Ramanathan, et al. reported a case of abdominal tuberculosis presenting with the hypercalcemic crisis.[8] Our finding of hypercalcemia with rapid response to anti-tubercular treatment is also consistent with the case reported by Tan, et al.[9] and Soofi, et al. who showed improvements in serum calcium levels within 4 weeks and 3 weeks of starting ATT respectively.

Mild hypercalcemia (11.11-15.5 mg/dl) is usually asymptomatic. Some patients may complain of vague neuropsychiatric manifestations like difficulty in concentration, personality changes or depression. Severe hypercalcemia (> 12-13 mg/dl) may result in lethargy, stupor, coma, as well as gastrointestinal manifestations like nausea, anorexia, constipation, and pancreatitis. These gastrointestinal symptoms were present in this patient. Hypercalcemia reduces renal concentrating ability, thus causing polyuria and polydipsia. Also, hypercalcemia may cause significant electrocardiographic changes like bradycardia, AV block, and short QT interval. However, none of these findings was present in this patient.

In tuberculosis and other granulomatous diseases, there is extra-renal production of 1,25 dihydroxyvitamin D₃ by alveolar macrophages and T lymphocytes possibly CCB T lymphocytes.[9] The alveolar macrophages have 1-alpha hydroxylase activity which converts 25 hydroxyvitamin D to 1,25 dihydroxyvitamin D₃ at an increased rate. Moreover, activated vitamin D also plays an important role in the regulation of granulomatous inflammation and influences the cell-mediated immunity to tuberculosis. If produced in large amounts, there may be spillage into the systemic circulation causing severe hypercalcemia.[10] In this patient, 25 hydroxyvitamin D level was low whereas 1,25 dihydroxy vitamin D₃ level was high, which is consistent with the mechanism of hypercalcemia in tuberculosis.

The patient was treated with aggressive fluid resuscitation and analgesics for the management of pancreatitis and hypercalcemia. Her abdominal pain resolved and bowel sounds returned after 3 days, she also started passing stool normally. On the basis of her CT findings, she was started on anti-tubercular therapy with isoniazid 300 mg, rifampicin 450 mg, pyrazinamide 1500 mg and ethambutol 1200 mg once daily. During this period as well, intravenous fluids were continued together with enteral feeding. Her serum calcium levels were regularly monitored and from day 3 of starting ATT, her serum calcium levels started to decline and on day 7 it decreased to 12.8 mg/dl. On day 16, after starting ATT, most of her symptoms resolved and her calcium levels were 102 mg/dl. She was discharged with the advice to continue anti-tubercular therapy and maintain proper hydration and diet. She was asked to follow up in Medicine OPD and in gynaecology for further workup of her infertility.
She came for follow up in medicine OPD after 3 months of starting ATT. The serum calcium levels were normal, she was feeding well and she gained weight of about 6 kilograms in these 3 months.

**FINAL DIAGNOSIS**

One should always think about tuberculosis as a possible cause of severe hypercalcemia, especially in India where tuberculosis is quite prevalent. Thus, can it be concluded with the bottom line, “cause somewhere, cause nowhere, tuberculosis everywhere”?

**REFERENCES**


