Case Report

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Acute Kidney Injury Secondary to Abdominal Tuberculosis: A Diagnostic Dilemma - A Case Report

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Abstract

Tuberculosis is a serious public health issue in developing countries. Hypercalcemia, though reported in granulomatous disease, is mild and asymptomatic in tuberculosis. A 16 year old girl female presented with significant weight loss, loss of appetite and on examination hepatosplenomegaly. Ultrasound abdomen (USG) showed mesenteric and retroperitoneal lymphadenopathy with hepatosplenomegaly with mild ascites. We report an unusual case of hypercalcemia with renal injury due to abdominal tuberculosis in an immunocompetent female.

Introduction

Tuberculosis is a serious public health issue in developing countries. Hypercalcemia, though reported in granulomatous disease is atypical in tuberculosis. It is an immune-mediated response by the macrophages present in the granulomata which causes an increase in reabsorption of calcium from bones and intestine and suppression of the parathyroid gland leading to decrease PTH release.[1] This leads to an increase in calcium levels in the blood. Hypercalcemia can further cause renal injury. We report an unusual case of hypercalcemia with renal injury due to abdominal tuberculosis in an immunocompetent female.

Case report

A 16 year old girl female presented to our OPD with generalized weakness, loss of appetite and weight loss (10 kgs) for three months with no history of fever, cough, diarrhea. Her vitals were stable and physical examination did not reveal any abnormality except mild pallor. There was mild hepato-splenomegaly with no tenderness or fullness in the abdomen. On being investigated, hemoglobin was 10 gm / dl with a normal total leucocyte count. Her liver function tests were normal. Ultrasound abdomen (USG) showed mesenteric and retroperitoneal lymphadenopathy with hepatosplenomegaly with mild ascites. Chest radiograph and Mantoux test were negative. The rest of the tuberculosis workup was normal.

After one week of initiation of therapy, she was readmitted with complaints of frequent falls. She had stopped taking anti tubercular therapy after two days due to nausea and vomiting. On admission her vitals were stable and had no new findings on general and systemic examination. The investigations revealed a normal hemogram except hemoglobin of 10 gm / dl with a microcytic hypochromic picture. ESR was 75 mm and serum calcium level was 15 mg / dl with a corrected calcium of 15.9 mg/dl. Her phosphorous was 3.87 mg / dl, serum albumin 2.9 g/dl and globulin 3.6 g / dl with normal liver function tests. However, blood urea was 80 mg / dl and serum creatinine 2.5 mg / dl. Urine routine microscopy examination was normal. PTH level was 6.18 pg / ml (12 - 72 pg/ml) and Vitamin D was 79.1 ng / ml which ruled out hypervitaminosis D. Serum angiotensin converting enzyme level

was (60.7 U/L) which was within normal limits. The Myeloma panel showed no evidence of monoclonal gammopathy. 24-hour urinary calcium level and urinary calcium creatinine ratio were also normal. Whole body positron emission tomography CT (PET CT) showed a lesion with high fluorodeoxyglucose uptake in the terminal ileum. [Fig 1] A diagnostic laparoscopy with biopsy was done. [Fig 2] Microscopically, the lesion showed granuloma. It consisted mainly in the recruitment at the infectious stage of macrophages, highly differentiated cells such as multinucleated giant cells, epithelioid cells, and foamy cells, all these cells being surrounded by a rim of lymphocytes and caseous necrosis in the center [Fig 3]. Gene Xpert (Cepheid, made in USA) from the biopsy sample was positive. Hence a diagnosis of abdominal tuberculosis causing hypercalcemia and acute kidney injury was made. The patient was rehydrated with isotonic saline. Bisphosphonates and corticosteroids – Prednisolone 40 mg daily for two weeks, tapered 5 mg weekly was also given. The patient improved symptomatically as her serum calcium and creatinine levels decreased and was given anti tubercular therapy for six months with regular follow-ups. After two months, her general condition and lab parameters improved.

Figure 1. Showing a PET CT image of the abdomen suggestive of high FDG uptake in the terminal ileum

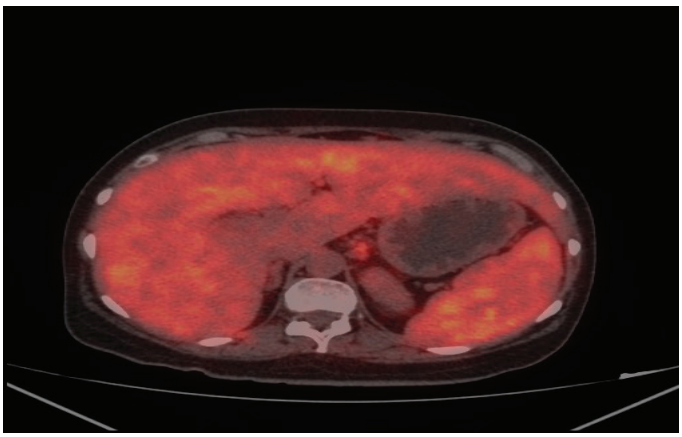


Figure 2. Showing diagnostic laparoscopy and biopsy: Small whitish tubercles over visceral and parietal peritoneum, inflammatory adhesions on the visceral and peritoneal surface, thickening, hyperemia, and retractions of the greater omentum.

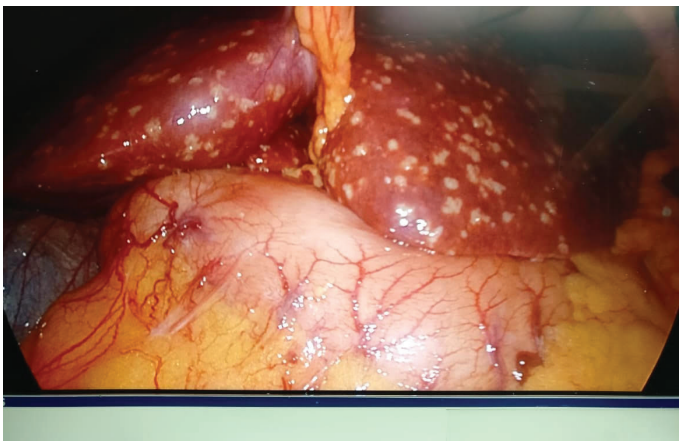
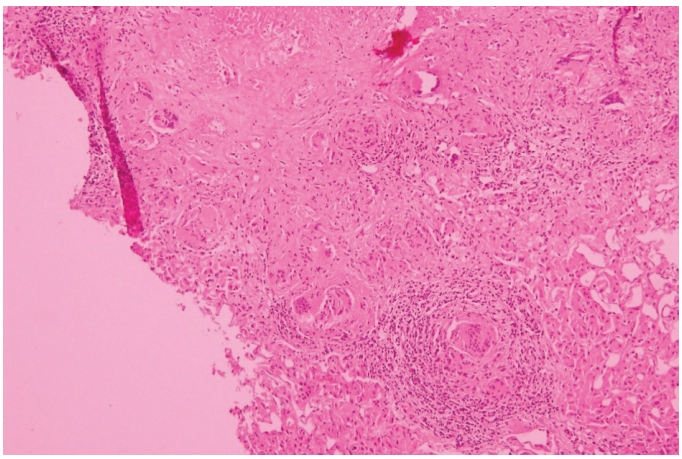


Figure 3. Shows histopathology of the specimen: showing granuloma with multinucleated giant cells, epithelioid cells, and Foamy cells, surrounded by a rim of lymphocytes and caseous necrosis in the center



Discussion

Worldwide 1% to 3% gastrointestinal (GI) tuberculosis (TB) cases are present.[2] The ileocecal region is the most commonly involved region but it can involve any part of the gastrointestinal tract.[3,4] Diagnosis is difficult because of its non-specific presentation.

GI TB responds well to standard antituberculous drugs. Surgery is only needed in cases that develop complications such as strictures or obstruction, or do not respond to medical therapy. High clinical suspicion, early introduction of anti-tubercular therapy, and involvement of an interprofessional team are necessary for reducing morbidity and mortality.

The first step in the evaluation of a patient with hypercalcemia is to assess whether it is parathyroid dependent or independent. A normal or low parathyroid hormone level would mean a parathyroid independent pathology. Common granulomatous disorders like tuberculosis and sarcoidosis are commonly associated with hypercalcemia but they are rarely symptomatic.[5] Various studies have noted the incidence of hypercalcemia in tuberculosis to be between 2.3% and 28%.[6,7] The manifestations of hypercalcemia include polyuria, polydipsia, vomiting, dehydration, constipation, and reduced level of alertness in absence of neurological disease. ECG findings suggested shortened QT interval.

The pathophysiology of hypercalcemia in tuberculosis and sarcoidosis is due to the extrarenal conversion of 25 hydroxyvitamin D_3 to the active form 1, 25 dihydroxy vitamin D_3 by the activated macrophages in the granuloma.[8] This occurs due to the increased production of 1 hydroxylase which is independent of PTH. The active form of Vitamin D results in increased reabsorption of calcium from bone and intestine leading to hypercalcemia. The renal injury associated with hypercalcemia occurs due to various mechanisms. It may be due to vomiting and dehydration or hypercalciuria can itself give rise to nephrocalcinosis and nephrolithiasis. Direct renal vasoconstriction can also reduce the GFR. These patients are managed with isotonic saline with loop diuretics followed by calcitonin. Dietary modifications are also required which include low calcium, low oxalate, and elimination

of vitamin D supplements. Bisphosphonates and glucocorticoids are the mainstay of treatment. They induce osteoclast apoptosis directly and reduce osteoclastic bone resorption. Bisphosphonates affect proliferation and differentiation of osteoblasts and prevent their apoptosis, whereas they also neutralize the RANKL-mediated stimulation of osteoclasts.[9] Steroids decrease 1 hydroxylase activity thereby reducing the level of 1,25 dihydroxy Vitamin D_3 levels. This leads to reduced calcium absorption.

It has also been observed that ketoconazole a general inhibitor of P450 enzymes decreases calcitriol production hence decreasing calcium levels. An antimalarial drug such as chloroquine, or hydroxychloroquine can also be used as it decreases the inflammatory activity of the disease. [10]

Conclusions

Symptomatic hypercalcemia with acute kidney injury is rarely a presenting complaint in granulomatous disorders like tuberculosis. It should be promptly managed with isotonic saline, loop diuretics, and corticosteroids. The incidence of hypercalcemia due to tuberculosis is between 2.3% and 28%.

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