Case Report

Pyogenic liver abscesses and symptomatic hypercalcemia: The report of an unusual association

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ABSTRACT

Hypercalcemia is usually caused by primary hyperparathyroidism or malignancy, a number of other conditions can be important to consider. Of the infectious causes of hypercalcemia described in the literature *Staphylococcus aureus* leading to hypercalcemia has not been reported so far. The clinical scenario of a 53-year-old female is discussed in this report who presented with fever and drowsiness. On evaluation was found to have hypercalcemia and pyogenic liver abscesses. No known cause of hypercalcemia could be identified in this patient after a thorough evaluation. The blood cultures were suggestive of S. aureus and following successful treatment with antibiotics, her liver abscesses improved and she was discharged with normal serum calcium levels, connoting the cause and effect relationship.

KEY WORDS: Staphylococcus Sepsis; Pyogenic Abscesses; Hypercalcemia

INTRODUCTION

Hypercalcemia is often an important clue to the underlying illness which could range from underlying malignancy to hyperparathyroidism in the majority of cases. However, the other causes of hypercalcemia described in the literature are Vitamin D intoxication, sarcoidosis, tuberculosis, some fungal infections, and thyrotoxicosis, The list goes on increasing as more and more insights in calcium homeostasis get unraveled. Hypercalcemia has been observed in Addison's disease, milk-alkali syndrome related to the prescription of absorbable alkali and calcium, Vitamin A intoxication, therapy with thiazide diuretics or lithium carbonate, familial hypocalciuric hypercalcemia, prolonged immobilization in patients with high skeletal turnover, and the recovery phase of rhabdomyolysis-associated acute renal failure. However, all such conditions amount to less than about 10% of all causes of hypercalcemia.[1] Various infections leading to hypercalcemia have been described in the literature, and the central point in most of such infections is the granuloma formation and overproduction of 1,25 dihydroxy Vitamin D, leading to excessive calcium in the body. It is always prudent to rule out pseudohypercalcemia and exclude the condition before embarking on the management of symptomatic hypercalcemia.

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CASE REPORT

A 53-year-old female was brought to Emergency Department of Sheri Kashmir Institute of Medical Sciences with a history of fatigue and drowsiness of 1 day duration following low-grade fever in the preceding week. The patient was drowsy but was responding to verbal commands. The patient was a known case of type 2 diabetes mellitus for the past 5 years and was on oral hypoglycemic agents, and she had no history of acute or chronic complications of the diabetes. Apart from hypoglycemic agents she had no other drug history. She denied any animal contact, raw milk ingestion,

trauma, or long travel. Fever had been low grade with no diurnal variation associated with occasional chills. The examination of the patient revealed mild scleral icterus, mild pedal edema. The pulse was 74 beats/min regular, blood pressure was 130/80 mm of mercury, and JVP was normal. The temperature documented in the hospital was 38°C. The abdominal examination showed soft hepatomegaly 3 cm below costal margin. There was mild splenomegaly, but no free fluid could be appreciated on abdominal examination. Chest examination showed few crackles at bases, and there was no wheeze. The cardiovascular examination was normal. The neurological examination was also normal. The septic screen was sent soon after the admission and the laboratory reports in the evening as shown in Table 1 were suggestive of hypercalcemia 14.5 md/dl (Normal range - 8.7–10.4 mg/dL) Keeping in view fever, pending the culture reports, broad-spectrum antibiotics were started. After fluid therapy at 150ml/hr the patient was given injection calcitonin 8 IU/kg SC q 12 h and serum calcium levels were monitored. The etiology of hypercalcemia was further evaluated with differential diagnosis of multiple myeloma (MM), hyperparathyroidism ect. The limited skeletal survey did not reveal any lytic lesions. Her serum and urine electrophoresis were not suggestive of MM. The X-ray chest showed prominent bronchovascular markings and no consolidation or pleural fluid was noted. The echocardiography was unremarkable. Keeping in view high liver enzymes and predominantly direct hyper-bilirubinemia viral markers (hepatitis A virus, hepatitis B virus surface antigen, anti-hepatitis C virus, and immunoglobulin M hepatitis E virus) and HIV serology were sent which turned turned out to be negative days later. An ultrasound of the abdomen showed hepatosplenomegaly and normal intra-hepatic biliary radicles, and there were multiple hypoechoic lesions. The portal vein and hepatic veins were normal. Her amoebic serology was negative. Computed tomography scan of the abdomen was done [Figure 1] which showed multiple liver abscesses, no intrahepatic biliary duct dilatation. The portal vein was normal. An impression of pyogenic abscesses was made. The blood culture report was suggestive of *Staphylococcus aureus* sensitive to Vancomycin.

The antibiotics were continued for 4 weeks intravenously. Later antibiotics were switched to orals and continued for another 3 weeks. She was discharged in stable condition with an advice for follow-up. Patients investigations at the time of discharge were all normal.

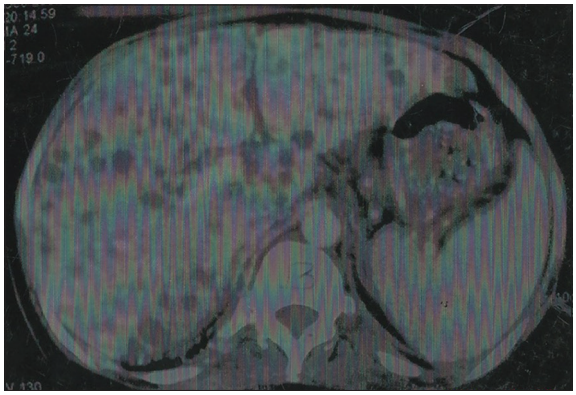

Figure 1: Computed tomography scan showing liver abscesses

Table 1: Investigation on presentation and discharge

Test	Result pre-treatment (on presentation)	Result post-treatment (on discharge)	Normal range
Hemoglobin	12.5	12.3	12.2–15.3 g/dl
White blood cell	15.2	5.6	6–16×109/l
Platelet	150×109/l	150×109/l	150–450×109/l
Total bilirubin	2.2	1.0	0.8–1 mg/dl
Direct bilirubin	1.3	0.8	0.0–0.6 μmol/L
AST	335	30	5–30 U/L
ALT	257	29	5–30 U/L
ALP	182	100	50–100 U/L
GTT	497	65	7–30 IU/l
Albumin	2.9	39	38–54 g/l
Total proteins	5.2	4.5	3.5–5.6 mg/dl
INR	1.1	1.1	0.8–1.2
Urea	38	40	30–40 mg/dl
Creatinine	1.2	1.0	0.8–1 mg/dl
Na/K	131/3.8	142/3.6	
Serum glucose	120	102	65–110 mg/dl
Serum calcium	14.5 mg/dl	8.5 mg/dl	8.7–10.4 mg/dL
Parathyroid hormone	5 mol/L	5 mol/L	2–6 mol/L

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Glutamyl transpedtidase

DISCUSSION

The successful management of hypercalcemia usually depends on determining its etiology. In most of the patients, the cause is obvious from the clinical setting, and the results of serum assays of parathyroid hormone PTH, parathyroid hormone-related protein, and Vitamin D metabolites often clinch the diagnosis. The index case had normal serum albumin, normal platelets and thus pseudohypercalcemia was ruled out and since she was symptomatic hypercalcemia was aggressively managed while investigating the cause of her high serum calcium levels in the hospital. She proved to have multiple pyogenic liver abscesses, and with antibiotic treatment, her serum calcium levels normalized Possibly *Staphylococcus aureus* producing multiple liver abscesses was the cause of her hypercalcemia. The liver lesion leading to hypercalcemia described in the literature is hepatic granulomatosis in chronic dialysis patient,[2] and pyogenic liver abscess as a cause of hypercalcemia has not been reported. It is quite possible that endogenous production of 1,25-dihydroxyvitamin D might have led to the hypercalcemia as the patient's 1,25-dihydroxyvitaminz D levels were elevated. Hypercalcemia due to endogenous production of 1,25-dihydroxyvitamin D has been described in Crohn's disease, and it has been postulated that granulomatous lesions secrete 1,25-dihydroxyvitamin D leading to hypercalcemia.[3] Elevated and other causes of hypercalcemia associated with elevated 1,25-dihydroxyvitamin D include Wegener's granulomatosis, Acute granulomatous pneumonia Talc granulomatosis, Silicone granulomatosis, BCG, and Calmette-Guérin bacillus.[1] The patient proved to have an infectious cause of hypercalcemia. Various infections known to cause hypercalcemia include cytomegalic virus infection in AIDS, Nocardia asteroides pericarditis, and Brucellosis. There is a report of an 18-year-old male twins with cat scratch fever, hypercalcemia and hypercalciuria with elevated 1,25-dihydroxyvitamin D levels. In their patient, serum and urinary calcium concentrations returned to normal when the bacterial infection was successfully treated.[4] The index case also responded to antibiotic therapy and her serum calcium levels normalized. Apart from antibiotic therapy steroids are known to lower serum calcium levels as in acute granulomatous pneumonitis, a rare complication of methotrexate therapy has been reported in association with hypercalcemia and inappropriately elevated levels of 1,25-dihydroxyvitamin D. Glucocorticoid therapy reduces the 1,25-dihydroxyvitamin D levels.[5] The patients have been described with rare and usually poorly understood causes of hypercalcemia as the index case.

CONCLUSION

This case highlights our incomplete understanding of calcium metabolism in humans and suggests hitherto undiscovered areas in which clinical investigation might improve our knowledge of the normal homeostasis of calcium.

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