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Neuropsychiatric Presentation Following Teriparatide Treatment Causing Altered Sensorium

ABSTRACT

Aim: The aim of this study was to neuropsychiatric presentation following teriparatide treatment causing altered sensorium. **Background:** Patient with a history of osteoporosis on injection teriparatide daily for the last 2 months was recently operated for minimally invasive L3-L4 decompression and L3-L5 percutaneous fixation with L4 vertebroplasty. **Case Description:** A 63-year-old postmenopausal female women, who presented with dizziness, increased thirst, constipation, and persistent drowsiness. The patient was found to have hypercalcemia (13.5 mg%). Magnetic resonance imaging brain and cerebrospinal fluid examination were inconclusive. Positron emission tomography scan was performed to rule out multiple myeloma and any underlying malignancies. Serum protein electrophoresis was normal. **Conclusion:** As the patient was on regular teriparatide, it was considered the cause of her raised calcium levels. The patient responded to bisphosphonate therapy, hydration, and calcitonin. After 48 h of treatment, the patient's serum calcium levels returned to normal and the patient improved. **Clinical Significance:** Patients who are on regular treatment of teriparatide should be closely monitored for hypercalcemia and evaluated for the symptoms related to it.

Key words: Bisphosphonate, Calcitonin, Hypercalcemia, Magnetic resonance imaging spine, Positron emission tomography-computed tomography

INTRODUCTION

Calcium homeostasis is controlled by the parathyroid hormone (PTH), calcitonin, and Vitamin D, which controls calcium levels in the body. The normal serum calcium varies from 8.5 mg/dL to 10.5 mg/dL. Hypercalcemia can be further divided as mild 10.5–11.9 mg/dL (2.5–3 mmoL/L), moderate 12–13.9 mg/dL (3–3.5 mmoL/L), and severe >14 mg/dL (>3.5 mmoL/L). It could be due to many different causes such as dehydration, drugs, and infections.

Hypercalcemia is mainly seen in patients with primary hyperparathyroidism and various types of cancer.[1] Hypercalcemia is observed in the advanced stage of cancer. Hypercalcemia of malignancy is suggestive of poor prognosis. The most common malignancies seen with hypercalcemia are multiple myeloma, lung cancer, multiple metastases in bone, renal cell carcinoma, and carcinoma of the breast.[2] Other cancers, include lymphoma, rhabdomyosarcoma, etc., can cause hypercalcemia.[1]

Among primary hyperparathyroidism, parathyroid adenoma is reported in most cases. Other reasons for hypercalcemia include pulmonary diseases such as sarcoidosis and tuberculosis, thyrotoxicosis, kidney failure, Paget's disease of the bone, prolonged period immobilization, and medicines which are administered like lithium, thiazides, vitamin D, and calcium supplements.

Patients with an acute rise in serum calcium into the moderate-to-severe range are often symptomatic, with neurologic symptoms, musculoskeletal, gastrointestinal, and renal which can be seen as neuropsychiatric ("Psychiatric moans") presentation includes difficulty with concentration, drowsiness, confusion, psychosis, and coma. Renal manifestations such as renal stones, nephrogenic diabetes insipidus, distal renal tubular acidosis, and even renal failure in cases which are not treated. Gastrointestinal symptoms such as anorexia, nausea, vomiting, pancreatitis, and cholelithiasis.[1]

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CASE REPORT

A 63-year-old female who had recently been operated for Minimally invasive surgery L3-L4 decompression and L3-L5 percutaneous fixation with L4 vertebroplasty due to her history of osteoporotic fracture in L4. She presented with

the complaints of generalized weakness, dizziness, increased thirst, constipation, and increasing drowsiness. She was hemodynamically stable and physical examination did not reveal any abnormalities apart from pain in the operating site. She has a background history of hypertension for 20 years diabetes mellitus for 20 years and hypothyroidism for many years. All comorbid diseases were well under controlled with medications. She was on regular injection teriparatide 20 mcg S.C. per day for the last 2 months for osteoporosis.

Her hemoglobin was 9.3 g%, total leukocyte count of 13,010/mm^{3}f, platelets of 422,000, sodium 136 mEq/L, potassium of 3.91, and chloride of 96.6, creatinine-0.54, liver function test includes total bilirubin-0.69, serum glutamic-oxaloacetic transaminase-38, serum glutamic pyruvic transaminase-31, gamma-glutamyl transpeptidase-167, ALPO4-137, total protein-6.93 g%, albumin-3.6, globulin-3.4, prothrombin-12.1, International Normalized Ratio-1.13, erythrocyte sedimentation rate-72, lactate dehydrogenase-337, C-reactive protein-4.31, procalcitonin-0.117, Triple H (human immunodeficiency virus and hepatitis B surface antigen, hepatitis C virus)- negative, and chest X-ray was normal. Magnetic resonance imaging (MRI) of the lumbar spine was s/o post-operative changes and nothing abnormal. Parathyroid-12.2 (normal 10–65 pg/mL), calcium-13.5 mg/dL (N-8.5–10.5 mg/dL) was detected incidentally, Vitamin D3-45 (N-30–100 ng/mL), ammonia-41.8 mcg/dL (N-15–45 mcg/dL).

She deteriorated clinically and became stuporous, MRI brain with contrast was done to rule out any structural abnormality which was not showing any abnormalities. Her routine cerebrospinal fluid (CSF) examination along with meningoencephalitis bio fire with culture was performed which did not reveal any abnormalities, since the patient was recently operated for the spine, joint infection panel bio fire was sent which was found to be sterile. Serum protein electrophoresis did not show any abnormalities like multiple myeloma. Positron emission tomography (PET) scan did not reveal any malignancy and other conditions which cause extra-renal production of 1,25(OH)D such as lymphoma as well as sarcoidosis, other causes like multiple myeloma, skeletal metastases and PTHrP.

She was then treated with injection zolendronic acid 5 mg intravenous (IV), Inj. hydrocortisone 100 mg IV TDS for 1 day, injection calcitonin 100 mcg S.C 8 hourly for 1 day. Moreover, rehydration with intravenous fluids and 0.9% normal saline was administered. After which the patient started to show signs of improvement in her conscious level and became fully conscious and oriented. Her serum calcium levels came down to 9.24 after 3 days [Figure 1]. She was vitally and hemodynamically stable and was discharged after 3 days of treatment.

DISCUSSION

Teriparatide, a recombinant human PTH for the treatment of severe osteoporosis (T score > −2.5) is used in high-risk patients with vertebral and nonvertebral fractures, as well as including glucocorticoid-induced osteoporosis. Generally, the main side effects of teriparatide include nausea, vomiting, dizziness, hypertension, and allergic reactions. Mild transient hypercalcemia occurs in up to 3%.[3] Whereas, delayed hypercalcemia that is when it exceeds 24 h after administering teriparatide has been rarely reported with unclear predisposing risk factors.[4]

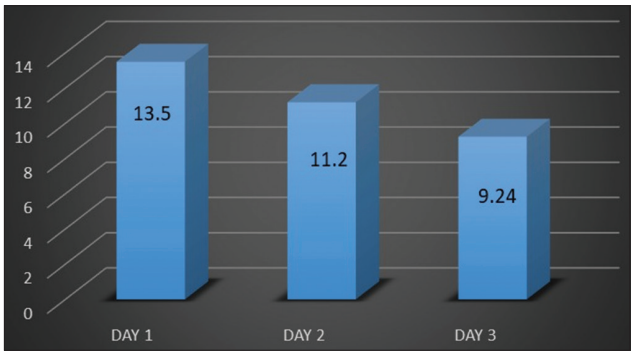

Figure 1: Serum calcium lever over 3 days

Teriparatide is quickly absorbed and eliminated and has a short half-life of 1 h. In cases of teriparatide-induced hypercalcemia, most of them resolve within a few days after omitting the drug. As the pathophysiology is still not fully understood, the cause of hypercalcemia may be due to the association with raised resorption seen in the bone.

There is a transient rise in serum calcium levels with teriparatide which is seen maximally after approximately 4.2 h and then a fall to the preexisting levels of calcium is seen before the following dose of teriparatide which is administered after 24 h.[5] In our patient, after ruling out structural and metabolic causes of altered sensorium, hypercalcemia was detected and managed immediately. Since the patient was taking injection teriparatide regularly, hypercalcemia due to injection teriparatide induced was considered and treated accordingly.

CONCLUSION

Altered sensorium can occur due to metabolic encephalopathy. However structural etiology should be ruled out by various investigations such as MRI brain, CSF examination, and PET scan. Hypercalcemia is a rare presentation which should be considered in patient with old age, immobilization, and osteoporotic fractures. Teriparatide, an osteoanabolic drug is approved for osteoporosis in postmenopausal middle age females thus preventing fractures and increases the bone marrow density of the patient. Teriparatide has substantial benefits in improving bone marrow density it has the potential to cause life-threatening hypercalcemia. Delayed moderate to severe hypercalcemia which is seen after 24 h of stopping the drug is rarely observed which is seen in this case. In the acute phase of bone fractures, especially in immobilized patients have a greater risk of development of hypercalcemia.

Patients who are on regular treatment of teriparatide that they should be closely monitored for hypercalcemia and evaluated for the symptoms related to it.

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