Case report

Hypervitaminosis D induced hypercalcemia leading to coma: A case report

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(Received: October 2022 Revised: May 2023 Accepted: June 2023)

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ABSTRACT

An elderly female presented with abdominal pain, vomiting and easy fatigability. Her sensorium gradually declined and became comatose. She was on Methotrexate, folic acid and prednisolone for her rheumatoid arthritis. The neurological examination and neuroimaging did not contribute in making the diagnosis. It is challenging to diagnose a metabolic cause of coma. Once diagnosis is established, the management becomes easier. On detailed investigation, she was found to have severe hypercalcemia with corrected serum calcium level being 18.2 mg%. Serum vitamin D level was also high, 150 ng/ml. On probing for detailed history, it was revealed that she had been taking a weekly dose of 60,000 IU of vitamin D for nearly 5 years. In recent times, association of various diseases has been reported with vitamin D deficiency. Vitamin D supplementation seems justified in this patient considering her age and the fact that she had rheumatoid arthritis; she was also taking corticosteroid. The recommended dose of vitamin D has been 400–800 IU/day. However, it is often prescribed at a dose of 60,000 IU/week, and sometimes patients self-medicate. There are no guidelines available for prescribing vitamin D at such a strength. Though safety of vitamin D has been established, vitamin D toxicity can occur sporadically with serious consequences. This was managed with intravenous fluids and diuretics. The patient also required subcutaneous calcitonin and low dose of corticosteroid, in addition to a session of haemodialysis for her hypercalcemia. The patient's sensorium gradually improved as her calcium level returned to normalcy.

Keywords: Hypercalcemia; hypervitaminosis D; coma.

INTRODUCTION

Hypercalcemia (serum calcium>10.4 mg/dl) presents variable symptoms, depending on its severity. As per serum calcium levels, hypercalcemia is classified into mild, moderate and severe. Sometimes the level of serum calcium may not match with the severity of the patient's symptoms. But generally the patient may have nausea, vomiting, trouble concentrating, personality changes, or depression, peptic ulcer disease, nephrolithiasis. In case of severe hypercalcemia, a stupor or coma may develop. Hypercalcemia, clinically, is seen more commonly in case of malignancies or hyperparathyroidism, milk-alkali syndrome, etc., Hypervitaminosis D is often overlooked as a cause of hypercalcemia.

Case Report

A 70-year-old female presented with chief complaints of vomiting, epigastric pain, generalised weakness and easy fatigability for about one-and-a-half months. This was associated with shortness of breath on exertion. She had a known case of rheumatoid arthritis for 10 years on tablet Prednisolone 5 mg/day, tablet Methotrexate 15 mg/week and tablet Folic acid. She had hypertension for 10 years but was on irregular medication. She was noted to be anaemic, pulse rate 86/minute regular, blood pressure 142/90 mmHg. There was no lymphadenopathy. The cardiovascular examination revealed a systolic murmur, which was considered to be of functional origin due to anaemia. The respiratory system and abdominal examination were unremarkable.

Patient was investigated. Her haemoglobin was 7.6 g%, liver function tests were within normal limits, creatinine of 2.83 mg/dl and urea of 37 mg/dl. The patient was given one unit of packed red blood cells and haematinics. Further on, the patient's sensorium began to deteriorate and neurological examination was unremarkable. Magnetic resonance imaging of the brain did not show any abnormality. Serum calcium level however was raised, which subsequently started following an upward trend with a maximum calcium level of 16.4 mg/dl. Since her serum albumin was low(1.8 g %), the corrected calcium was calculated to be 18.2 mg/dl. She was further evaluated for hypercalcemia. The parathyroid hormone level was 82.7 picograms per millilitre (with normal range 12-88 pg/ml).There was no clinical evidence of malignancy. Thyroid hormones were also within normal limits and no signs of any granulomatous disease. However, her vitamin D level was significantly elevated with a value of 150 nanogram/ml. On further probing, attendants revealed that the patient had been taking vitamin D 60,000 international units once every week for the past five years or so. The patient was then treated with intravenous fluids and diuretics to manage hypercalcaemia, but did not show significant improvement. She was started on calcitonin injection 200 international units subcutaneously twice daily and also underwent a session of haemodialysis. The patient

was started on a low dose of glucocorticoids. Post these interventions, the patient started to improve clinically along with calcium levels falling back to its normal limit. The patient was then discharged from hospital after resolution of her symptoms. She is being regularly followed up as an outpatient. Her condition has remained stable.

DISCUSSION

Calcium plays a very important role in several functions of the body (1). Besides parathyroid hormone and calcitonin, Vitamin D (Vit. D) plays a significant role in calcium homeostasis (2). The active and passive absorption of calcium from the intestine is dependent on Vit D and increase in Vit D may lead to hypercalcemia (3). The Institute of Medicine recommends 4000 IU of Vit D/day. However, toxicity can occur if taken at higher doses for longer duration (4).

Although most of the patients are asymptomatic or mildly symptomatic, some patients with hypercalcemia may present with impaired sensorium or coma (5). Hypervitaminosis D may be considered when serum Vit D level is more than 100 ng/ml (6). The index case had Vit D level of 150 ng/ml. Once hypervitaminosis D is ascertained as the cause of hypercalcemia, cessation of Vitamin D is necessary, along with other measures to decrease calcium levels. It includes use of intravenous fluids in people who have adequate renal function with or without the use of loop diuretics. Glucocorticoids are effective in reducing calcium absorption from the intestine and decreasing 1,25-dihydroxy vitamin D production. Calcitonin lowers calcium levels by inhibiting bone resorption and decreasing tubular reabsorption of calcium (7). Calcium-free haemodialysis may also help in rapidly correcting hypercalcemia.

Vitamin D deficiency/insufficiency has been linked to various disease states. This patient had rheumatoid arthritis and low intake of Vitamin D has been linked to higher disease activity. Vitamin D is currently being prescribed as a supplement to treat several disease conditions and with good reason. In a study conducted on the use of sodium-glucose cotransporter 2 inhibitors, it was found that Vit. D supplementation had a therapeutic effect on diabetic neuropathy (8). In another study conducted on the prevalence of Vitamin D deficiency in Covid 19 patients, it was concluded that vitamin-D deficiency and insufficiency are quite prevalent among COVID-19 patients and there is a role of Vitamin D supplementation in Covid 19 management (9). The index patient had several reasons why she should be taking Vit. D supplementation. These indications could be old age for osteoporosis, rheumatoid arthritis and steroid therapy. In recent times, Vit. D at a dose of 60,000 International Units once a week is often prescribed probably for ease of administration, but there are no guidelines available about uses at such strengths. It is often advised to be given for a "limited" period. This patient was taking this once a week for about 5 years. She had developed a coma due to hypercalcemia. Her sensorium had improved as the calcium levels declined towards normalcy.

CONCLUSION

To conclude non-neurological causes of poor sensorium are often difficult to approach and diagnose and a suspicion of hypercalcemia within applicable clinical scenarios should be considered. Furthermore, hypervitaminosis D particularly Iatrogenic is often overlooked as a cause of hypercalcemia.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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