Case Report:

Iatrogenic hypercalcaemia in an elderly lady

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ABSTRACT

An 83-year-old lady known to have type 2 diabetes mellitus, hypertension and primary hypothyroidism presented with the complaints of increased thirst of one month duration, diffuse abdominal pain, constipation and mild nausea of one week duration. She was found to have hypercalcaemia. Review of her treatment records revealed that she had received a high dose of vitamin D (average dose of 63,000 IU/day) over two months. Serum vitamin D was 347 ng/mL. Patient was advised to withhold all calcium and vitamin D preparations and further managed with intravenous 0.9% saline, diuretics and zoledronic acid. She improved clinically; her serum calcium levels became normal and she was subsequently discharged in stable condition. This case illustrates that inappropriate therapy with grossly excessive doses of vitamin D can result in intoxication leading on to hypercalcaemia.

Key words: *Hypercalcaemia, Vitamin D intoxication, Unmonitored use of Vitamin D*

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INTRODUCTION

Vitamin D intoxication is rarely observed in clinical practice. It occurs due to inappropriate use of high doses of vitamin D, which leads to hypercalcemia. Identification of vitamin D intoxication initially may be difficult, as the clinical manifestations are non-specific[1]. Awareness of this entity and thorough clinical history taking, with particular attention to the medication details and dosing schedule will help in the diagnosis and timely management of vitamin D intoxication.

CASE REPORT

An 83-year-old lady presented with chief complaints of increased thirst for the preceding one month, constipation and diffuse abdominal pain of one week duration. She also gave a history of mild nausea, general weakness and giddiness. She was known to have type 2 diabetes mellitus, hypertension and primary hypothyroidism, all of which were well controlled. On examination she had features of mild dehydration. In view of her age and the recent change in bowel habits, the possibility of an intrabdominal lesion, possibly a gastrointestinal malignancy was considered.

Laboratory evaluation (Table 1) revealed elevated serum calcium and serum 25-hydroxy vitamin D3 [25(OH)D3] levels. Initial serum creatinine was also mildly elevated. Serial electrocardiograms were found to be normal. Ultrasonography of the abdomen was normal.

On detailed questioning she reported intake of large doses of both oral and parenteral vitamin D preparations. She had received 6 lakhs IU intramuscular of vitamin D six times over a period of 5 weeks followed by three doses of

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Table 1: Laboratory investigations at the time of initial prsentation

Laboratory Investigations	Patient Values	Normal range
Serum calcium (mg/dL)	12	8-10.5
Serum phosphorous (mg/dL)	3.7	3.5-5
Serum albumin (g/dL)	3.7	3-5.5
Serum 25 (OH) vitamin D3 (ng/mL)	347	30-100
Serum PTH (pg/mL)	70	12-88
Serum alkaline phosphatase (IU/L)	37	90-120
Serum alanine transaminase (IU/L)	14	10-35
Serum aspartate transaminase (IU/L)	26	10-40
Spot urine calcium/creatinine ratio	0.54	<0.2
Serum creatinine (mg/dL)	1.42	0.3-1.3
Serum sodium (mmol/L)	133	135-145
Serum potassium (mmol/L)	4.23.	5-4.5
Haemoglobin (g/dL)	10.2	12-16
Serum TSH (mIU/L)	2.2	0.5-5
Fasting plasma glucose (mg/dL)	90	<100
HbA_{1C} (%)	5.9	<5.7

TSH = thyroid stimulating hormone; PTH = parathyroid hormone;
HbA_{1C} = glycosylated haemoglobin

60,000 IU each over the subsequent three weeks. This translated to a total dose of 37,80,000 IU administration over two months, equivalent to 63,000 IU/day.

A diagnosis of vitamin D intoxication was made. All calcium and vitamin D supplements were stopped. Patient was managed with 0.9% saline and zoledronic acid (4 mg intravenously). Serial serum calcium values showed a decreasing trend (Figure 1). Patient serum creatinine decreased from 1.42 mg/dL to 1.2 mg/dL. Patient was discharged after normalization of serum calcium and is doing well on follow-up. Her serum vitamin D levels on last follow-up were normal (60ng/mL).

DISCUSSION

Vitamin D intoxication is one of the important causes of hypercalcaemia.[1] It has been reported in both children and adults.[2-4] Excess intake of vitamin D due to misunderstanding of dose schedule/preparations or unmonitored use of vitamin D may be responsible for vitamin D intoxication. [4,5]

The Endocrine Society's Clinical Practice Guidelines on Vitamin D deficiency states that the safe upper limit of vitamin D intake for adults is 4000 IU/day.[6] Chronic intake of 40-100 times (i.e., 40,000-1,00,000 IU/day) of normal physiologic requirements may result in vitamin D intoxication.[1,7]

Our patient had serum vitamin D levels of 347ng/mL, which indicates a toxic level of vitamin D (i.e., >150 ng/mL).[7] She had taken Vitamin D in very high doses approximately 63000 IU/day for 2 months by means of injections and oral preparation. These patients usually present with features of hypercalcaemia such as increased frequency of urination, increased thirst, abdominal pain, nausea, vomiting, constipation, headache, fatigue, altered sensorium and coma (in severe cases).[1]

However, in our patient, the symptoms were very non-specific and therefore the presence of hypercalcaemia was not clinically suspected. Only on routine laboratory testing, the elevated serum calcium was noted. This emphasizes the

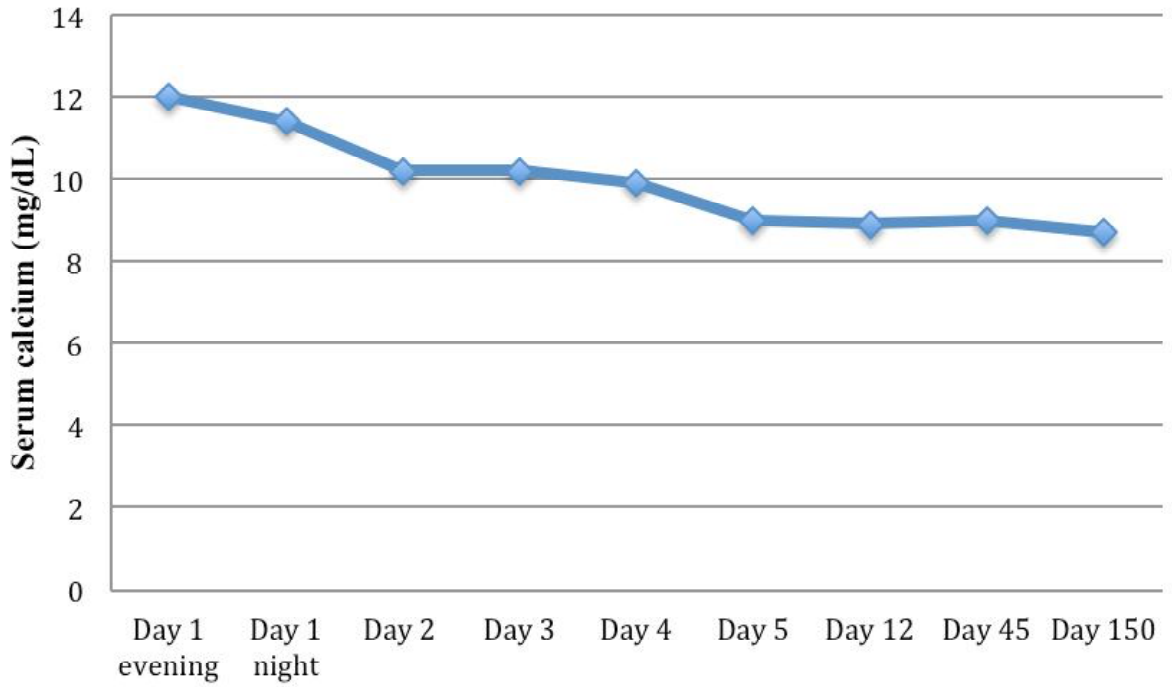

Figure 1: Trends in serum calcium levels with treatment

importance of considering hypercalcaemia as a differential diagnosis in patients presenting with predominantly abdominal complaints like nausea, vomiting, abdominal pain and constipation.

In our patient spot calcium to creatinine ratio was 0.54 (>0.20) which is clearly indicative of hypercalciuria (normal reference interval <0.14).[8] Serum parathyroid hormone levels (PTH) were normal in this patient, as it was done on next day of admission and by that time serum calcium became 10.2 mg/dL. This may explain normal PTH rather than suppressed PTH as expected.

She was managed by withholding all calcium and vitamin D preparations along with IV 0.9% saline, diuretics and zolendronic acid. The hypercalcaemia in vitamin D intoxication is both due to enhanced absorbtion of calcium from the gut as well as due to increased resorption of bone.[9] Contrary to common belief, the direct action of vitamin D on the bone is resorptive.[9] The contribution of bone resorption to hypercalcemia can be addressed by use of bisphosphonates (e.g., zoledronic acid), which are known to inhibit osteoclast function.[10] On follow-up also patient maintained normal vitamin D and calcium levels (Figure 1) and all her symptoms were resolved.

In individuals who are receiving vitamin D preparations, it is better to check serum calcium and phosphorous periodically as estimation of serum 25 (OH) D3 is costly to prevent iatrogenic hypercalcemia.

It is very important for the treating physician to have knowledge of the various preparations and appropriate dosing schedule of vitamin D replacement according to standard guidelines. Prompt recognition and early initiation of appropriate treatment in vitamin D toxicity is very gratifying.

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