Acute Kidney Injury Secondary to Vitamin D Toxicity: Report of Two Cases

Khurshid A. Banday, M.D., Mohammad Ashraf Bhat, M.D., Nazir A. Palla, M.D., Tufail Ahmad, M.D., Abdul Rashid Reshi, M.D., Mohammad Saleem Najar, M.D.

Department of Nephrology, Sher-i-Kashmir Institute of Medical Sciences Srinagar, Kashmir (J&K)

ABSTRACT

We present two patients with hypercalcemia and acute kidney injury from intentional overdose of injectable vitamin D supplement. The patients presented to the nephrology department with varied clinical manifestations. Both had received a cumulative dose of vitamin D in millions of units. Both made a complete clinical recovery after hydration and low dose steroids. These cases highlight the need for caution when using unregulated injectable form of vitamin D. JMS 2011;14(2):63-65

Key words: Vitamin D, acute kidney injury, hypercalcemia

Vitamin D toxicity is a known cause of hypercalcemia and acute kidney injury.^{1,2} It can be due to accidental ingestion, faulty food fortification, self medication and malpractice related excessive administration.³⁻⁷ Its incidence has been on the up in Kashmir valley and more cases are reporting to hospitals with complications.⁸ We report here 2 cases of malpractice-related vitamin D intoxication who presented with hypercalcemia, acute kidney injury and mental obtundation.

Case 1

A 70 year old male, hypertensive for 10 years (on amlodipine), hypothyroid (on 75µg thyroxine) was admitted with altered sensorium, polyuria and constipation. There was no history of vomiting, fever, weakness of any part of body. There was history of multiple injections of Vitamin D₃ (2 injections of Arachitol 6 lac units / week for 2 months), for

arthralgias and generalized debility, a cumulative dose in millions of units. Examination revealed patient in grade 2 encephalopathy, grossly dehydrated, pulse of 52 beats/min, regular, B P of 160/100mmHg with a normal chest, abdominal examination. Cardiovascular examination revealed bradycardia and CNS examination showed no neck rigidity, grade 2 encephalopathy with no focal neurodeficit. Routine chemistry revealed- Hb 10.5 g/dL, TLC 8.9×10^9 /L, DLC: N 64 %, L 24%, platelet 150×10^9 /L, ESR 12, urea 117 mg/dL, creatinine 2.5 mg/dL (0-1.5 mg/dL), glucose 99 mg/dL, serum calcium 14.2 mg/dL (9.5-11.5 mg/dL), serum phosphorus 3.6 mg/dL (3.5-5.5 mg/dL), uric acid 6.6 mg/dL, LDH 330 U/L, total protein 6.6 g/dL, albumin 4.0 g/dL, bilirubin 0.75 mg/dL, SGOT 35 U/L, SGPT 40 U/L, ALP 210 U/L. Urine examination was normal, 24 h urinary proteins 0.15 g/day, the 24 h urinary calcium 350 mg. Serum PSA was normal and his serum electrophoresis was normal, chest X-ray revealed cardiomegaly with prominent aortic knuckle, electrocardiography revealed sinus bradycardia with a QT interval of 0.40 sec. An abdominal and a neck ultrasound were normal. A non contrast CT scan of head was normal. Serum PTH was 13.5pg/ml (15-68pg/ml), Vitamin D (25 OH) was 375nmol/ml (intoxication level >250). The patient was managed for hypertension, hypothyroidism (under treated) and Vitamin D induced

Correspondence and Reprint requests to:

Dr Khurshid A Banday

Additional Professor,

Department of Nephrology,

Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K.

kabanday@gmail.com

hypercalcemia with acute kidney injury. Patient was given antihypertensive, intravenous fluids, low dose steroids, proton pump inhibitors and his thyroxine dose was increased. The level of serum calcium on the 5th day of treatment was 10.2 mg/dL, that of phosphorus was 3.94 mg/dL, and the creatinine level stabilized at 1.5 mg/dL. Hypercalcemia improved, patient became conscious, dehydration got corrected and creatinine showed a downward trend. Patient was discharged in a stable condition and is on follow up with normal calcium and renal functions.

Case 2

A 38 year old female, normotensive, presented with generalized weakness of six months duration and recent onset intermittent vomiting. She was referred with azotemia & proteinuria. She denied any history of fever, pain abdomen, loose stools, arthralgias and rash. She gave history of taking multiple injections of Protobol (anabolic steroid) & Vitamin D (6 lac units) once in a fortnight for past 2 years. On examination she had a lean built, was conscious, oriented, dehydrated, no pallor, no lymphadenopathy. Her chest, CVS, abdominal and neurological examination was normal. Laboratory investigations showed a Hb 12.5 g/dL, TLC 8.0×10^9 /L, DLC: N 75 %, L 20%, platelet 120×10^9 /L, ESR 08/1st hour, urea 88 mg/dL, creatinine 3.5 mg/dL (0-1.5 mg/dL), glucose 99 mg/dL, serum calcium 13.2 mg/dL (9.5-11.5 mg/dL), serum phosphorus 4.5 mg/dL (3.5-5.5 mg/dL), uric acid 6.6 mg/dL, LDH 320 U/L, total protein 6.5 g/dL, albumin 3.8 g/dL, bilirubin 0.8 mg/dL, SGOT 28 U/L, SGPT 30 U/L, ALP 220 U/L. Urine showed 2+ proteins, no RBC's, no WBC's, and her 24 hour urinary proteins was 1.2 grams, the 24 h urinary calcium 320 mg. Her serum electrophoresis was normal as was her chest X-ray and electrocardiography. An abdominal and a neck ultrasound were normal. Serum PTH was 6 pg/ml (15-68pg/ml), Vitamin D (25 OH) 375nmol/ml. The patient was managed with antihypertensive, intravenous fluids, steroids, and proton pump inhibitors. She was discharged with a creatinine of 2.4mg/dl and her calcium decreased to 10.2mg/dl. In three months of her follow up she has shown a decline in her serum creatinine to 1.8mg/dl and her serum calcium is within normal limits.

Discussion

Vitamin D deficiency is not uncommon in "sunny" India.⁹⁻¹¹ The daily requirement of vitamin D is about 200-600 IU and it is mainly produced in the skin after total body exposure to UV light. Sunlight exposure from November through February in north India is insufficient to produce significant vitamin D in the skin.^{10,11} The season, the geographic latitude, the time of day, cloud cover, smog, and sunscreen affect UV exposure and vitamin D synthesis.¹²⁻¹⁴ Most of northern India, including Kashmir has been established as a vitamin D deficient zone.¹⁵⁻²⁰ In the Kashmir valley, the prevalence of vitamin D deficiency is quite high, 69.6% in

individuals exposed to the outdoors to 100% in those confined indoors, reflecting the lower mean weekly exposure to sunlight.²¹ The prevalence of vitamin D deficiency among elderly people can be estimated to be at least 50%, whereas it has been reported in 80% of "veiled" pregnant women.

The clinical spectrum ranges from subclinical to frank deficiency with serum 25-hydroxyvitamin D (25OHD) levels less than 20 nmol/L.²²⁻²⁵ Vitamin D repletion in individuals presenting with vitamin D deficiency has been shown to have a positive effect on bone biology, resulting in mineralisation of osteoid, increases in bone mineral density measurements and reduced fracture rates.²⁶ This has led to overzealous use of vitamin D particularly in Kashmir valley where it is being prescribed or even given without prescription for non descript symptoms.⁸ Vitamin D repletion can improve bone mineral density and reduce fracture risk. In the absence of adequate sunlight exposure, supplementation becomes important. The target for vitamin D supplementation is suggested to be a serum level of 50 nmol/L, which is protective against secondary hyperparathyroidism and decreased bone density.

Vitamin D toxicity has been reported either due to over fortified food supplements taken accidentally for prolonged period, after the topical application of vitamin D ointment or iatrogenic in some unusual cases especially after injectable form.²⁻⁵ The excessive and prolonged use of injectable form can lead to vitamin D intoxication. Excretion of vitamin D is negligible and hence excessive administration can lead to toxicity. The clinical manifestations of this intoxication are kidney disorders (65%), renal insufficiency (51%), gastrointestinal tract disorders (23%), and arterial hypertension (52%). Symptoms may include-weakness, polyuria, intense thirst, weight loss, nausea, vomiting, difficulty in speaking and confusion. Patient may lapse into coma, while cardiac arrhythmias and renal failure can occur. These effects are due to hypercalcemia induced by increased intestinal absorption and mobilization of calcium from bone.^{1,4,5}

These two cases of Vitamin D intoxication are a continuum of many such cases being seen in the Nephrology department on intermittent basis over last two years.^{1,8} Both our patients had received massive doses of slow-release preparation of vitamin D for a prolonged period of time leading to a cumulative dose of millions of units. This emphasizes the need to regularly assess the levels of vitamin D in patients suspected of its deficiency and who are put on vitamin D replacement therapy. Also a general awareness about the potential toxic effect of excessive use of injectable vitamin D needs to be done at the district and village level.

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