Primary hyperparathyroidism associated with vitamin D toxicity in a patient with severe osteoporosis receiving teriparatide

Sir,

We present an elderly female with severe osteoporosis receiving terparatide, who presented with generalized body ache and joint pains. The patient was started on teriparatide and vitamin D supplementation, based solely on a serum calcium that was within the normal biochemical range. She was subsequently diagnosed to have primary hyperparathyroidism and vitamin D intoxication (iatrogenic). The case cannot exemplify enough the need for an appropriate endocrine evaluation before prescribing teriparatide therapy even if the presenting calcium is normal as was seen in the case. Another point of concern is the rampant unsupervised use of vitamin D by healthcare providers without an appropriate monitoring plan, risking vitamin D toxicity.

We want to present a 68-year-old married lady, who was referred to our endocrine practice by an orthopedic surgeon, on the background of hypertension (since 10 yrs), with the complaints of persistent lower backache (non- radicular), multiple joint pains and generalized weakness since 1 year. She was diagnosed with severe osteoporosis (dual energy X-ray absorptiometry {DEXA} T-score-2.6 at lumbar spine;-3.2 at femoral neck and -4.4 at radius) by a physician one year ago and was suggested vitamin D replacement (60,000 units of cholecalciferol) as bolus therapy once a week for 3 months (against a corrected calcium of 9.7 without any other biochemical evaluation relevant to the bone) and teriparatide. Examination showed proximal muscle weakness (4/5 in all four limbs). Biochemistry revealed moderate renal impairment (creatinine 1.4 mg% [estimated glomerular filtration rate (eGFR) 55], elevated alkaline phosphatase 176 IU/L (50-136), hypercalcemia 13.4 mg/dl (9-10.5mg%), parathormone 121 pg/mL (11–54), vitamin D3 144.4 ng/ mL (11-42) and hypercalciurea [24 hr urine calcium 446mg%] (50-300 mg%)] on the background of use of recombinant teriparatide. Teriparatide was stopped and biochemistry repeated after 7 days. The repeat tests suggested persistent parathormone-dependent hypercalcemia with a corrected calcium of 12.5 mg%. A follow-up DEXA surprisingly showed a mild improvement of T-scores at the level of hip -2.9 along with mild worsening at the level of the spine -2.7 and radius -4.6. A sonography of the pelvis and abdomen revealed bilateral nephrocalcinosis. Doppler ultrasound of neck suggested a mass at inferior pole of right lobe of thyroid gland that was confirmed by a SESTAMIBI scan. A parathyroidectomy was undertaken after rendering the patient eucalcemic (9.4 mg%). A 2.0 × 1.5 cms mass was excised that was consistent with parathyroid adenoma [Figure 1]. The routine use of vitamin D should be a subject of concern in patients on teriparatide, as it may augment the risk of hypercalcemia. Stringent guidelines regarding routine use of vitamin D and strict monitoring guidelines need to be clarified while on teriparatide. The routine use of vitamin D in large bolus doses should be strongly discouraged as it may risk severe hypercalcemia even in the absence of primary hyperparathyroidism (PrPTH). The case exemplifies the importance of ruling out PrPTH[1-4] before starting teriparatide. In patients presenting with a normal serum calcium (< 10.2 mg%), although measurement of a serum parathormone is imperative (> 65 ng/dl; sensitivity 90% and specificity 77% to detect PrPTH), other marker that may help differentiate a PTH- dependent etiology from a non-PTH dependent cause is a *calcium- to- creatinine ratio* > 150 mg/gm (7.07 fold greater risk of PrPTH); *calcium*

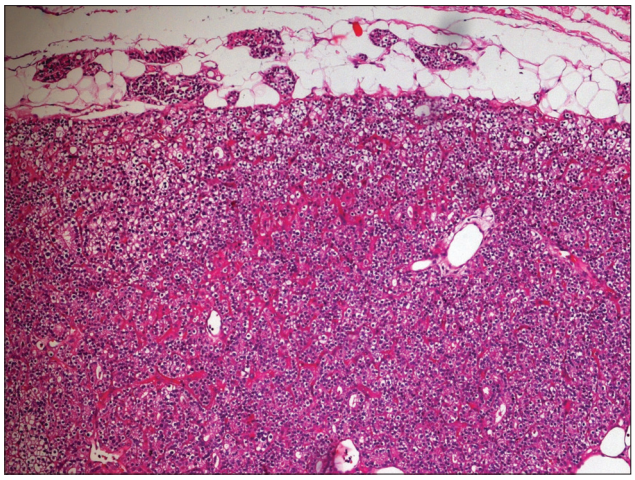

Figure 1: H and E, ×10, Histopathology showing parathyroid adenoma

per kg of > 4 mg/kg (8.03- fold greater risk of PrPTH) and *hypercalciuria* (4.38-fold greater risk of PrPTH).[5] The average Indian diet is relatively poor in calcium and vitamin D, which often protects against the development of hypercalcemia. The presence of musculoskeletal complains such as (myalgias, bone pains, etc) with osteoporosis more severe at hip and radius compared to spine should prompt a search for a relevant metabolic cause (PrPTH) even if the serum calcium is< 10.2 mg%.

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