Title

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CLINICAL VIGNETTE

Hypercalcemia Secondary to Teriparatide in a Patient with Primary Hyperparathyroidism

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Case Presentation

A 69-year-old female presented for a second opinion of her osteoporosis and primary hyperparathyroidism. She had post-surgical hypothyroidism for more than 30 years after right thyroid lobectomy for goiter. Intermittent mild hypercalcemia was first noted on routine laboratory evaluation four years earlier with slightly elevated calcium levels and intact parathyroid hormone (iPTH) in the high normal range. Thyroid/parathyroid ultrasound at an outside facility did not localize a parathyroid adenoma and parathyroid sestamibi scan with single photon emission computed tomography (SPECT) was suspicious although not definitive for parathyroid adenoma along the left thyroid lobe. Further evaluation was deferred and she was not referred to a surgeon.

A few months later she was found to be osteoporotic on dual energy x-ray absorptiometry (DXA) bone density scan and treated with Vitamin D supplementation and advised to avoid calcium supplements. The following year she was started on denosumab 60 mg subcutaneous injection every 6 months for total of 5 injections. Repeat SPECT/CT showed findings suggestive of a left superior adenoma, but she was not referred to surgery. DXA bone density scan after 3 years of denosumab showed worsening bone density with T-scores of -3.0 at the lumbar spine, -2.8 at the left femoral neck, and -2.6 at the left total hip. She then developed severe back pain without trauma and spine x-ray showed a lumbar compression fracture. Her physician then recommended teriparatide 20 mcg subcutaneous injection daily. She developed worsening hypercalcemia of 11.5 (8.9-10.1) and was treated in an emergency room with intravenous fluids and recommended to discontinue teriparatide. Calcium improved to 10.3 mg/dL and she was discharged from the ED. Repeat labs three days later showed calcium 12.3 mg/dL, iPTH 60.9 (15.0 to 65.0 pg/mL), and Vitamin D,25-OH 118.4 (20.0 to 80.0 ng/mL), prompting referral to UCLA.

She was evaluated by endocrine surgery with ultrasound showing a rounded hyperechoic mass in the left anterior neck (anatomically at nodal level IV), sitting between major blood vessels. Parathyroid 4D CT demonstrated a 13 mm left paraesophageal mass consistent with a parathyroid adenoma posterior to the small superior extension of the left thyroid lobe and along the medial margin of the common carotid artery, consistent with findings of the clinic ultrasound. She underwent parathyroidectomy with surgical pathology showing an enlarged (108 mg), hypercellular left superior parathyroid gland with decreased fat. Postoperative laboratory evaluation showed resolution of hyperparathyroidism, with calcium 10.0 (8.6-10.3 mg/dL) and iPTH 38 (11-51 pg/mL). She restarted teriparatide following parathyroidectomy, with normal calcium levels on follow up laboratory evaluations. DXA bone density scan two years after prior DXA showed improvement of bone density, with T-scores of -1.5 at the lumbar spine (L2-L4), -2.4 at the left femoral neck, and -2.6 at the left total hip.

Discussion

Primary hyperparathyroidism is a disorder in which one or more parathyroid gland(s) become overactive. This leads to excess parathyroid hormone secretion resulting in hypercalcemia. Primary hyperparathyroidism causes secondary osteoporosis as a consequence of its catabolic effect, promoting osteoclast activity and bone resorption. Current osteoporosis guidelines recommend routine assessment of iPTH in all patients with osteoporosis, with additional recommendation to assess serum calcium and iPTH prior to treatment with teriparatide.[1]

Teriparatide-recombinant human PTH (1-34) is a synthetic, recombinant polypeptide hormone consisting of the 1-34 fragment of human parathyroid, and is the biologically active N-terminal region of the 84-amino-acid native hormone.[2,3] Teriparatide is an anabolic agent that increases new bone formation on both cancellous and cortical bone.[4] Teriparatide is contraindicated in pregnancy, breastfeeding, Paget's disease of bone, unexplained elevations of alkaline phosphatase, history of skeletal radiation therapy, history of osteosarcoma of bone, and in children and persons with hypercalcemia. It should be used with caution in patients with low blood pressure and history of renal stones. Teriparatide has not been studied in patients with pre-existing hypercalcemia, and such patients should be excluded from treatment due to possible hypercalcemia exascerbation. An initial important study of teriparatide in postmenopausal women reported serum calcium elevation in 11% of patients on teriparatide 20 mcg/daily within four to six hours after an injection, with only 3% having persistent hypercalcemia following reduction of calcium intake.[5]

Our patient had intermittent hypercalcemia secondary to primary hyperparathyroidism, and she exemplified risk of worsening hypercalcemia when treated with teriparatide. Ideally initial parathyroid surgery to cure primary hyperparathyroidism

should have been performed prior to teriparatide therapy, especially given her underlying osteoporosis.[6] Following one year after parathyroidectomy, up to one half of postmenopausal women with primary hyperparathyroidism and low bone mineral density have significant response in bone remineralization.[7] Following parathyroidectomy, teriparatide has been shown to be a safe and effective treatment of osteoporosis, with most pronounced effects at the lumbar spine,[8] similar to what was observed in our patient.

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