Acute neurological syndrome complicating secondary hyperparathyroidism

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ABSTRACT

Longstanding severe hyperparathyroidism can lead to the formation of “brown tumors,” benign but locally aggressive neoplasms. We present the case of a young woman with end-stage renal disease on hemodialysis with uncontrolled secondary hyperparathyroidism. The patient presented with progressive lower extremity weakness and back pain. Imaging showed multiple lytic bone lesions, the most impressive being a T3 spinal lesion causing cord compression. She underwent urgent neurosurgical resection of the tumor at T3 followed by subtotal parathyroidectomy. Our case touches upon the pathophysiology, consequences, and treatment of secondary hyperparathyroidism in patients with end-stage renal disease.

KEYWORDS Brown tumor; end-stage renal disease; hyperparathyroidism; spinal cord compression

Hyperparathyroidism can be primary, secondary, or tertiary. Primary hyperparathyroidism is most commonly due to an adenoma of the parathyroid glands, whereas the pathogenesis of secondary hyperparathyroidism (SHPT) is an intricate interplay of hypocalcemia, vitamin D deficiency, reduced formation of calcitriol, and phosphate retention.^{1,2} Impaired phosphate clearance increases the level of fibroblast growth factor-23, which in turn inhibits the formation of calcitriol.^{3–6} The decrease in calcitriol exacerbates hypocalcemia as intestinal absorption of calcium decreases. The combination of these factors contributes to a relentless rise in parathyroid hormone (PTH) levels. Persistently high PTH levels produce a high-turnover bone state, which can result in the production of brown tumors.^{7,8} Patients usually are asymptomatic, and brown tumors are an incidental finding.⁹ Here, we describe an unusual case of acute spinal cord compression caused by a brown tumor.

CASE DESCRIPTION

A 33-year-old Hispanic woman, dialysis dependent for 9 years, presented to the emergency department for an acute exacerbation of back pain and bilateral lower extremity

weakness. She was undergoing “compassionate” dialysis due to lack of insurance and, as such, her treatment of SHPT was often insufficient. She had persistent hyperphosphatemia, hypocalcemia, and progressive hyperparathyroidism. She was treated with calcium carbonate, calcium acetate, and samples of cinacalcet. Despite these interventions, her parathyroid levels escalated to the 5000s (normal 10–65 pg/mL). On physical exam, pertinent positive findings were a palpable mass along the lower rib cage and tenderness of the thoracic spine. Laboratory results were significant for a calcium level of 10.3 mg/dL and PTH of 2476 pg/mL. Magnetic resonance imaging (MRI) confirmed two masses causing cord compression at T3 and moderate spinal canal stenosis at T12 (*Figure 1a*).

Due to the patient’s bilateral lower extremity weakness and spinal cord compression, she underwent urgent T2 to T4 laminectomy with resection of the T3 tumor. No intervention was made at T12. Intraoperative pathology evaluation of the T3 mass demonstrated giant cell proliferation and tan-brown soft tissue fragments admixed with tan porous bone fragments, confirming the diagnosis of brown tumor (*Figure 2*). One week later, she underwent subtotal

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Received May 29, 2018; Revised July 5, 2018; Accepted July 7, 2018.

Figure 1. MRI imaging before and after treatment. (a) Severe spinal canal stenosis and cord edema at T3; moderate spinal canal stenosis at T12. (b) Stable resection site at T3 and regression of T12 tumor 3 months after resection of the T3 lesion and parathyroidectomy.

parathyroidectomy. Her PTH dropped from 2358 pg/mL before surgery to 268 pg/mL after surgery. The rest of her hospitalization was uneventful except for the development of hungry bone syndrome, which was treated with calcium and phosphorus replacement.

A few months after spinal decompression and parathyroidectomy, repeat MRI showed no recurrence at T3 and regression of the T12 tumor (*Figure 1b*). Her PTH level was at goal in the 200 range, and both calcium and phosphorus were at target with medical management (*Figure 3*).

DISCUSSION

The incidence of brown tumors in patients with end-stage renal disease remains quite rare, estimated at around 1.5%.^{10,11} Brown tumors are not malignant, but are destructive neoplasms made up of osteoclast-like multinucleated giant cells and hemosiderin-filled macrophages, which give them the “brown” name.^{10,12} They present as either single or multiple lesions and can be localized in any skeletal bone; most common are the mandible, maxilla, or hard palate.^{7,10,13} Most brown tumors are asymptomatic, whereas others can cause local swelling or pain.^{5,14,15} Severe manifestations such as cauda equina syndrome, paraparesis, and even paraplegia have been reported as well.^{16,17}

We found 16 published cases of patients on dialysis with symptomatic brown tumors involving the spine published between 1977 and 2017. Of those case reports, there was no significant difference in gender, age, or duration on dialysis. Brown tumors do not have specific laboratory findings. On imaging, the lesions can mimic a host of other disease

Figure 2. Pathology results of the T3 brown tumor showing (a) multinucleated giant cells and (b) hemosiderin deposits.

processes such as myeloma, giant cell granulomas, or beta-2 microglobulin amyloidosis.¹⁸ Therefore, tissue biopsy and histopathology are key to diagnosis.

In terms of management of brown tumors, no societal recommendations or clinical trials exist to guide treatment. The main focus of medical management involves aggressive lowering of PTH by reducing dietary phosphate intake, phosphate binders, calcium, vitamin D, calcitriol supplements and, most important, the addition of a calcimimetic-like cinacalcet. The increasingly prominent role of calcimimetics was emphasized in the post hoc analyses of the EVOLVE (Evaluation of Cinacalcet Hydrochloride Therapy to Lower Cardiovascular Events) trial, which found that cinacalcet significantly reduced progression of SHPT.¹⁹ When medical management fails, parathyroidectomy is the next best option. There are data demonstrating remineralization of bone and regression of the tumors just months following parathyroidectomy.^{12,13,20}

This case illustrates a rather dramatic presentation of a brown tumor. Yet, aggressive management led to a successful outcome. We believe that brown tumors are both underrecognized and underreported and hope that this case report prompts further discussion of this rare pathology.

Figure 3. Metabolic bone profile of (a) parathyroid hormone, (b) calcium, and (c) phosphorus showing stabilization after parathyroidectomy.

ACKNOWLEDGMENTS

The authors express great gratitude to Daniel Savino, MD, of the Department of Pathology at Baylor University Medical Center and Gregory de Prisco, MD, of the Department of Radiology at Baylor University Medical Center for their time and discussion of this case.

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