

Diaphyseal Femoral Fracture Associated with Hyperparathyroidism and Brown Tumor with Sclerotic Bone Response to Parathyroidectomy

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Abstract

Brown tumor is a rare complication of long-standing hyperparathyroidism (HPT). The pathology is well defined but the radiologic appearance has previously been described as lytic with rare reports of sclerotic lesions after therapy.

Brown tumors can affect the mandible, maxilla, ribs, clavicles and rarely long bones. When multiple, these lesions may mimic malignancy, metastatic to bone.

We present a 35 year-old East Indian woman who presented with a pathological, atraumatic right femoral diaphyseal fracture. Curettings of the femoral shaft at the time of surgical nailing showed "brown tumor of bone" but did not show malignant change. Subsequent isotope bone scan showed multiple skeletal areas of uptake in proximal femur, and T12 vertebra. Imaging studies showed lytic lesions at these locations. Parathyroidectomy surgery yielded a 1.2cm solitary parathyroid adenoma. There was postoperative normalization of hypercalcemia and elevated PTH levels. Subsequent radiographs and DXA BMD studies showed an intense blastic response at the sites of prior bone scan uptake and radiographic lytic lesions.

We described an atypical diaphyseal femoral fracture associated with hyperparathyroidism and solitary parathyroid adenoma. Surgical cure of her primary hyperparathyroidism resulted in an atypical blastic appearance of the previously lytic lesions. These abnormalities might be easily confused with bisphosphonate-related atypical femoral fracture or bone metastatic disease.

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Introduction

Osteitis fibrosa cystica (brown tumor) is a rare clinical consequence of untreated severe primary or secondary hyperparathyroidism (HPT) [1]. Reported in about 3% of patients with primary HPT and 1.5% of those with secondary HPT disease [2].

Clinically, hyperparathyroidism (HPT) presents as stones, bones and groans. The stones refer to recurrent kidney stones. Bones refers to the bone lesions that occur in severe or prolonged cases. Groans are meant to describe the gastrointestinal symptoms of

nausea, vomiting, peptic ulcers and pancreatitis. However, Up to one third of patients may be asymptomatic [3,4].

Hyperparathyroidism is frequently caused by a solitary adenoma in 80% of patients, multiple adenomas in 5%, parathyroid hyperplasia in 15%, and carcinoma in less than 1-5% [2,4].

Hypercalcemia is often discovered incidentally during routine laboratory testing hypophosphatemia and increased alkaline phosphatase level in blood may also be seen [3,4].

In daily practice, hip and thigh pain are commonly attributed to arthritis or soft tissue inflammation, however an unusual pain

pattern should alert the clinician to search for underlying causes such as metabolic bone disease.

We herein present a case of primary HPT secondary to single adenoma and concurrent brown tumor that presented with persistent thigh pain ultimately femur fracture.

Case report

This is a case of a 35 year-old Indian lady who recently immigrated to Canada. She had an intermittent right-sided thigh pain, which gradually increase in severity over the course of four months. She had frequent visits to walk in clinic and emergency room in which pain was treated with analgesics. While attempting to get out bed, she sustained a mid-shaft fracture of the right femur.

She has previously been very active; she has not had any other fracture. There was no history of peptic ulcer, renal stone, increased thirst, urinary frequency, constipation, and weight loss. There was no exposure to radiation or industrial toxin. She takes only one dairy serving per day. She does not take calcium or vitamin D; she does not drink alcohol or smoke cigarettes. She never had a tumor diagnosed.

On physical examination, her head and neck were normal; no cervical adenopathy and no enlargement of the thyroid or nodularity palpable in the thyroid bed.

Her radiograph showed cortical thinning within the mid diaphysis of the femur (**Figure 1**).

Curettings from the right femur medullary canal revealed giant cells with no evidence of fibrous dysplasia or malignancy.

An isotope bone scan showed left hemimandible uptake, as well as uptake in the proximal humeri, humeral neck, left scapula, left clavicle and ribs bilaterally uptake was also noted in T 12, in addition to multiple areas of the pelvis and right femoral diaphysis, distal femurs and proximal tibias bilaterally (**Figure 2**).

Radiographs obtained four months later demonstrates dense blastic lesion within the inferior aspect of the left greater trochanter. Additional sclerotic lesions are present over both iliac wings in the region of the right sacroiliac joint. Gamma nail remains is seen in the right proximal femur (**Figure 3**).

Parathyroid scan showed an increased activity at the inferior pole of the left lobe, with delayed washout. There are no other reproducible abnormalities to suggest parathyroid abnormality elsewhere.

The serum level of calcium was markedly elevated at 3.79 mmol/L (normal range 2.10-2.55mmol/L), phosphorus level was low at 0.72 mmol/L (normal 0.80-1.40 mmol/L). Parathyroid hormone was elevated at 160 Pmol/L (normal<6.4). Serum alkaline phosphate was high at 258 U/L (normal 48-138 U/L). Co-existing



Figure 1 AP and lateral radiographs demonstrating a displaced transverse fracture at the junction of the mid and distal thirds of the right femoral diaphysis, which appears centered on a lucent bony lesion. Cortical thinning is demonstrated, but no definite periosteal reaction is identified within the limitations of this view (with bandages overlying the area of the fracture).



Figure 2 An isotope bone scan demonstrating uptake in the left hemimandible, as well as uptake in the proximal humeri, humeral neck, left scapula, left clavicle and ribs bilaterally uptake was also noted in T 12, in addition to multiple areas of the pelvis & right femoral diaphysis, distal femurs & proximal tibias bilaterally.

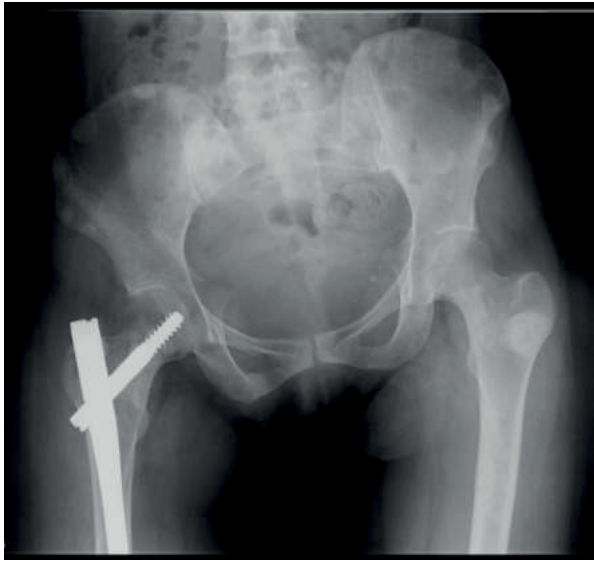


Figure 3 AP radiograph of the pelvis obtained four months later demonstrates dense blastic lesion within the inferior aspect of the left greater trochanter. Additional sclerotic lesions are present over both iliac wings in the region of the right sacroiliac joint. Gamma nail is seen in the right proximal femur.

Vitamin D deficiency was noted at 23 nmol/L (reference range 75-150 nmol/L).

Neck exploration revealed 1.2 x 1.2 cm left inferior parathyroid adenoma, which has been resected and histopathology confirmed parathyroid adenoma. Patient tolerated the surgery very well. Subsequently, her PTH post operatively returned to normal at 0.9 Pmol/L as well as the ionized calcium at 1.07 mmol/L (reference range: 1.03-1.23 mmol/L).

At four months follow-up, L2-4 bone mineral density was 0.688 g/cm², which was 3.5 standard deviations below age matched. Total hip bone density was 0.627 g/cm², which was 2.5 standard deviations below age matched and distal third of radius was 0.377 g/cm², which was 3.5 standard deviations below age matched. Follow up bone mineral density 1 year later showed that total hip BMD is 0.851 g/cm², which is 0.7 standard deviations below age matched, reflecting a significant increased by 35.8% from previous.

Discussion

In 1891, Von Recklinghausen described the classic bone disease termed osteitis fibrosa cystica. In 1925, the Viennese surgeon Mandl performed the first parathyroid exploration and adenoma resection. Mandl noted improvement of the patient's severe skeletal abnormalities post operatively, thereby linking HPT with bone disease. Albright later in 1930s described the clinical entity of classic primary HPT on the basis of 17 cases from his clinical practice [5].

The term "Brown Tumor" is a misnomer, because it is not a true neoplasm. It represents a localized accumulation of osteoclast, fibrous tissue and blood. High hemosiderin content gives the lesion characteristic brown color so it's called Brown tumor [3].

Brown tumor of the bone typically involves the jaws, clavicle, ribs, pelvic bone and infrequently the long bone such as the femur. There have been occasional reports of involvement of the femur [6-18] and one report in pediatric patient [19].

Diagnostic confusion arises mainly when the clinician encounters multiple lytic lesions involving different areas of the skeleton, as was the case in our patient. Metastatic bone tumor is a rational consideration whenever multiple osteolytic lesions are found. However, serum calcium, phosphate and PTH level should be checked before the whole set of tumor survey is initiated, Although hypercalcemia with high intact PTH level and imaging evidence of parathyroid adenoma all indicated that brown tumor is highly possible, the definite diagnosis is histopathology of bone biopsy, which will reveal a dense fibroblastic stroma, area of cystic degeneration, osteoid, microfractures, hemorrhage, macrophages with hemosiderin, and multinucleated osteoclastic giant cells.

Brown tumor has similar radiologic features seen in other cystic bony lesions such as giant cell tumor, fibrous dysplasia and aneurismal bone cyst. Differentiating between a brown tumor and other giant cell tumor may be very difficult, even with histology. However, after treatment of hyperparathyroidism, brown tumors may heal with calcification, sclerosis and subsequently lesion disappearance [20].

Vitamin D insufficiency is common in patients with primary HPT and may be associated with more severe and progressive disease. Epidemiological studies suggest that vitamin D deficient patients with HPT have higher level of PTH and markers of bone turnover, larger parathyroid adenomas, and more frequent fractures than vitamin D replenished patients [21]. Vitamin D repletion reduces levels of PTH and bone turnover in HPT [22].

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