The case:

A 79-year-old woman presents with left anterior knee pain after a fall.

Figure: Lateral (A) and sunrise (B) view radiographs of the left knee.

Your diagnosis?

For answer see page 564
Diagnosis:
Multiple Brown Tumors and Pathologic Patellar Fracture in a Patient With Secondary Hyperparathyroidism

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A 79-year-old woman presented with left anterior knee pain after history of a fall. Multimodality imaging diagnosed a minimally displaced pathologic fracture through the left patella and multiple lytic lesions. Of note, the woman had a known history of renal failure with elevated serum creatinine, parathyroid hormone (PTH), and alkaline phosphate. Image-guided biopsy eventually confirmed the diagnosis of multiple Brown tumors and pathologic patellar fracture in the setting of secondary hyperparathyroidism (HPT). This case report reviews the imaging findings of Brown tumors, the differential diagnosis of multiple osseous lesions, as well as the pathophysiology and surgical treatment of HPT.

PATHOPHYSIOLOGY OF HYPERPARATHYROIDISM AND BROWN TUMORS

Hyperparathyroidism is the overactivity of the parathyroid glands resulting in excess production of PTH.\(^1\)\(^2\) Hyperparathyroidism can be primary, secondary, or tertiary and, when left untreated, can escalate into abnormal bone metabolism, resorption leading to demineralization and increased porosity of bone, fractures, and Brown tumors.\(^2\) Primary HPT is caused by parathyroid adenomas in 85% of cases, leading to hyperplasia and oversecretion of PTH.\(^1\)\(^3\) Diagnosis stems from abnormal levels of serum calcium, phosphate, and PTH and/or the identification of an enlarged parathyroid gland on sonography or computed tomography (CT). Abnormal serum levels differ in patients with primary and secondary HPT, with primary HPT characterized by high serum levels of calcium (above 10.5 mg/dL) and low phosphate (below 2.0 mg/dL).

Excessive PTH secretion in secondary HPT is caused by the parathyroid glands’ effort to correct serum hypocalcemia in the setting of renal failure and inability to reabsorb calcium from ultra-filtrate, leading to a cascade of events. Phosphate retention causes reduced ionized serum calcium, due to the binding of phosphate and ionized calcium. Parathyroid glands are then further stimulated to produce PTH due to the decreased vitamin D production triggered by the elevated phosphate.\(^3\) Skeletal resistance to PTH and renal failure will stimulate the parathyroid glands to maintain or increase the elevated PTH levels.\(^3\) Secondary HPT typically yields serum calcium below 8.5 mg/dL and serum phosphate above 5.0 mg/dL.\(^4\) In the current patient’s panel, the serum creatinine level reached as high as 3.29 mg/dL, PTH level was 392 pg/mL, and alkaline phosphate was 290 U/L. The hypocalcemia that secondary HPT triggers leads to oversecretion of PTH; the normal range for serum PTH is 10 to 55 pg/mL.\(^3\) The serum PTH level in this patient was 392 pg/mL (normal, 10-55 pg/mL), a classic finding in patients with HPT (secondary and primary).

Brown tumors, also known as osteitis fibrosa cystica, are not true neoplasms but rather focal lytic lesions caused by excessive osteoclastic activity in the setting of HPT.\(^3\)\(^8\) These lesions are named for the microhemorrhage that leads to
hemosiderin deposition within the Brown tumor, resulting in the characteristic reddish-brown color. Brown tumors are most commonly found in the cortical region of bones, where bone resorption due to HPT is at its highest.

**IMAGING**

Radiographs detected a nondisplaced pathologic fracture through the left patella, lytic expansile remodeling of both patellae, multiple lytic lesions throughout both tibiae, and extensive vascular calcifications attributed to atherosclerosis accelerated by renal failure (Figure 1). Brown tumors are classically lytic with well-defined borders on radiographs or CT (Figures 1-2), although healing lesions will demonstrate various levels of sclerosis. Brown tumors are more commonly found in patients with primary HPT, but can also present in secondary HPT, as in the current patient. The differential diagnosis of multiple osseous lytic lesions includes metastases, myeloma, polyostotic fibrous dysplasia, multifocal osteomyelitis, and giant cell granuloma. However, because the distribution of the lytic lesions was isolated to the lower extremities, this would be highly atypical for metastases or myeloma.

The classic findings of HPT include osseous resorption by osteoclasts along osseous surfaces. This includes the periosteal, endosteal, and articular surfaces, as well as along the medullary bony surfaces. Resorption along the radial surfaces of the phalanxes and medial surfaces of the proximal tibiae is characteristic of HPT. Resorption along the distal clavicles and the sacroiliac joints, as in this patient, is also classic for involvement of HPT (Figure 2). Looser zones are incomplete fractures that can occur due to failed osseous healing, resulting in lucent linear defects in transverse orientation to the axis of the bones.

Magnetic resonance imaging was performed for the left knee, which delineated the pathologic fracture and the extent of the multiple marrow replacing lesions (Figure 3). Magnetic resonance imaging is uncommonly obtained for evaluation of Brown tumors. Lesions are heterogeneously hypo- and isointense to skeletal muscle on T1-weighted images, although signal characteristics depend on the level of sclerosis (Figure 3).

Skeletal scintigraphy will demonstrate increased radiotracer uptake in Brown tumors, due to bone turnover at the margins of the lesions. Skeletal scintigraphy was obtained for evaluation of suspected metastases in this elderly patient with multiple lytic lesions; however, lesions were only confined to the lower extremities (Figure 4). The purpose of scintigraphy is typically to determine if lesions are multiple and, if so, the distribution pattern.

Fluoro-deoxyglucose positron emission tomography/CT is effective for detection of osseolytic lesions such as Brown tumors. Uptake of fluoro-deoxyglucose in osseous lesions can assist in diagnosis of Brown tumors with HPT, and abnormal uptake of fluoro-deoxyglucose can differentiate primary neoplasms. Fluoro-deoxyglucose positron emission tomography/CT can be used to evaluate Brown tumors and can provide additional information about the extent and distribution of disease.

![Figure 1: Multiple Brown tumors with pathologic fracture of the left patella (A and B). Lateral (A) and sunrise (B) view radiographs of the left knee showing a nondisplaced fracture (arrowheads) through the lytic expansile lesion occupying the majority of the patella. Notice the joint fluid in the suprapatellar pouch (white arrow), consistent with hemarthrosis and further sclerosis of the proximal tibial lesion (black arrow). Lateral radiographs of the knees and calves demonstrating multiple lytic lesions throughout both tibiae and patellae (arrows), with expansile remodeling of both patellae (C and D). Nondisplaced left patellar fracture identified on knee radiograph (not shown) is not well visualized in this projection.](image-url)
Computed tomography of Brown tumors. Resorption about the sacroiliac joints in hyperparathyroidism. Axial computed tomography showing irregularity and osseous resorption about both sacroiliac joints (arrows), which is characteristic for hyperparathyroidism (A). Axial computed tomography through the patella delineating the extent of lytic involvement of the vast majority of the patella (asterisk), destruction of the anterior cortex, narrow zone of transition, and sclerosis of the remaining patella (B). Computed tomography was used to guide percutaneous biopsy of the proximal lateral tibial lesion. CT can be used to show metabolic regression of Brown tumors after treatment has been administered.13

**BIOPSY AND HISTOLOGY**  
Computed tomography-guided biopsy of the left proximal tibial lytic lesion (Figure 5) failed to identify malignant cells, and the histologic findings were multinucleated giant cells admixed with fragments of bone, fibrohistiocytic cells, and hemosiderin. Surgical biopsy was then performed 6 days later, with similar histologic findings. Histological findings of the tumor consist of giant cells and can be misidentified with other similar pathologies such as giant cell granuloma.3 It is difficult to differentiate the histological findings of Brown tumors from other lesions such as giant cell granuloma.5 The lesions also contain hyperactive osteoclasts and fibrous tissue among the giant cells.6,7 The histological findings of the CT-guided biopsy of the left proximal tibial lytic lesion in this patient included multinucleated giant cells admixed with fragments of bone, fibrohistiocytic cells, and hemosiderin. Histological confirmation of the diagnosis was made by a surgical biopsy 6 days later. 

**SURGICAL INTERVENTION**  
Primary HPT is most associated with hyperplasia and excess secretion of PTH from the parathyroid glands and, therefore, is subjected to a parathyroidectomy. The extent of the parathyroidectomy, whether complete or partial, is determined by the number of parathyroid glands that are affected. Primary HPT is usually treated successfully by parathyroidectomy.14-17 Secondary HPT is corrected by medical treatment to replenish or amend serum calcium and phosphorous levels to regulate elevated PTH levels. Oral calcium supplements should be taken along with limited dietary phosphorus consumption and phosphate binding antacids.3 The regulated PTH serum levels should correct the extensive PTH secretion, which will halt further development of Brown tumors and will eventually lead to their regression.9 Orthopedic surgical intervention for the osseous pathology of HPT patients is usually limited to the treatment of pathologic fractures.18-20 Pathologic fractures are induced by the formation of Brown tumors and porosity of bone tissue associated with extensive HPT. In some cases, pathologic fractures and osteolytic lesions due to HPT and Brown tumor formation can be fixed with surgical curettage, bone grafting, or prophylactic stabilization.10 Incomplete fractures of weight-bearing bones, particularly the femoral neck, often require surgical fixation. Complete, displaced fractures often require surgical fixation and stabilization.20 In rare cases, bone porosity and Brown tumor development of pathologic fractures along with other complications might be beyond repair and require amputation.16 Depending on the location of the Brown tumor, a surgical emergency may be required. This is most prevalent for Brown tumor development on the vertebrae, which could cause spinal compression or

Figure 2: Computed tomography of hyperparathyroidism and Brown tumors. 
Figure 3: Magnetic resonance imaging of Brown tumors. Sagittal fast spin echo proton density (A) and fast spin echo T2-weighted fat suppressed (B) images of the left knee demonstrating marrow replacing lesions occupying the vast majority of the left patella and another one in the proximal tibial metaphysis (arrows). The pathologic patellar fracture is better appreciated on radiographs. Notice also the small joint effusion.

Figure 4: Multiple Brown tumors detected with skeletal scintigraphy. Frontal projection of the lower extremities during skeletal scintigraphy showing multiple areas of increased radionuclide uptake in the tibial and patellar bones (arrows), corresponding to the lytic lesions. The patellar lesions have a “bull’s-eye” appearance, with decreased central radionuclide uptake.
severe neurological defects. Surgical treatment of bone may require bone grafting and further bone construction to repair damaged bone tissue.

REFERENCES


