Multiple Brown Tumors

A Diagnostic Dilemma

Hai-long Zhang, MD

Abstract: Brown tumor is rarely seen today, probably because routine serum chemical tests identify patients with primary hyperparathyroidism before this skeletal complication develops. It has the appearance of a well-circumscribed expansible lytic lesion of the bone and is difficult to differentiate from giant-cell bone tumor and aneurysmal bone cysts. We report a case of multiple brown tumor case, in which we did not make the diagnosis in the first hospitalization. Three days after discharge, the patient was called back because of a serum parathyroid hormone level of 1305 pg/mL (15–65 pg/mL). Curettage, bone grafting surgery, and subtotal parathyroidectomy were performed. After subtotal parathyroidectomy, histopathology confirmed the diagnosis of parathyroid hyperplasia.

Key Words: brown tumors, hyperparathyroidism, osteitis fibrosa cystica

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Brown tumor was first described by Gerhard Engel in 1864 and then by Friedrich Daniel von Recklinghausen in 1890. Its association with hyperparathyroidism was confirmed in 1925.[1] It is a consequence of the onset of severe hyperparathyroidism. They are non-neoplastic, proliferative disorders of the bone with localized rapid osteoclastic turnover. They are intraosseous soft-tissue masses characterized by focal accumulations of active, vascular proliferating fibrous tissue, and giant cells in a hemorrhagic stroma. They usually occur in patients with hyperparathyroidism. They are rarely seen today in clinical medicine, because hyperparathyroidism is generally detected in its early stages, which eliminates the advancement of the disease into osteitis fibrosa cystica.[2]

CASE REPORT

A 42-year-old man complained of increasing pain of 2 months duration in his left forefoot and low back. Symptoms started when he had a fracture in his right ulna 4 months earlier, without any other unremarkable medical history. Physical examination was normal. There were no neurologic deficits. Radiography was performed in his feet, tibia, humerus, chest, and pelvic, which revealed an abnormality (Fig. 1). Computed tomographic (CT) images of the thoracic and lumbar spine were then performed to evaluate the abnormality (Fig. 2). Laboratory findings included a white blood cell count of 6.09×10^9/L ($4–10 \times 10^9$/L), calcium of 3.01 mol/L (2.15–2.60 mol/L), and phosphorus of 0.62 mol/L (0.82–1.6 mol/L). Liver function test results were normal. He had received curettage and bone grafting in the first, third, and forth metatarsal. Biopsy of the focus confirmed the proliferation of multinucleated giant cells (Fig. 3). After 3 days of his discharge, the patient was called back to the Department of General Surgery of our hospital because of the serum parathyroid hormone (PTH) level of 1305 pg/mL (15–65 pg/mL). The diagnosis of osteitis fibrosa cystica due to hyperparathyroidism was made. To confirm the diagnosis, magnetic resonance (MR) images of the neck and Tc-99m MIBI scintigraphy were

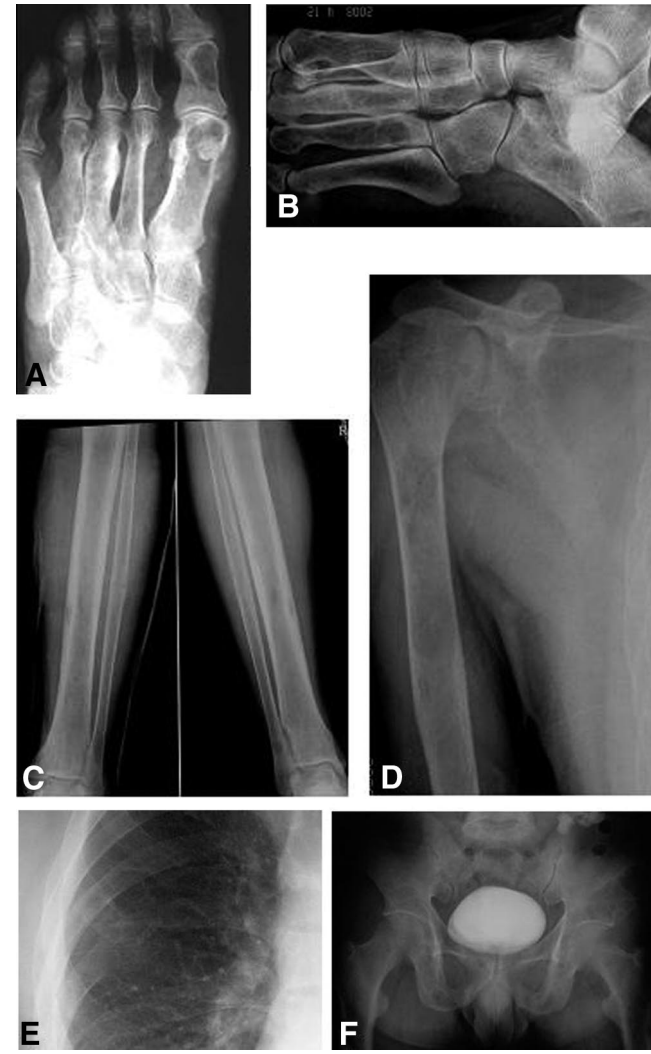

FIGURE 1. A, B, Anteroposterior and lateral radiographs of the foot revealed nearly complete destruction of the entire first, third, and forth metatarsal by a lytic lesion. C, D, Radiography of the tibia and humerus shows a lytic and expansile trabeculated lesion. E, F, A chest and pelvic radiograph shows a lytic lesion of the ribs, the inferior pubic ramus, and the left ala of ilium.

From the Department of Spine Surgery, Changhai Hospital, the Second Military Medical University, Shanghai, China.
Reprints: Hai-long Zhang, MD, Department of Spine Surgery, Changhai Hospital, the Second Military Medical University, 168 Changhai Rd, Shanghai 200433 China. E-mail: haroldzhang@gmail.com.

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performed (Fig. 4). Histopathology of the parathyroid gland confirmed the final diagnosis (Fig. 3). Two days postoperatively, the serum PTH level dropped to 20 pg/mL, and after 10 days, the PTH level was normal. He had no clinical evidence of recurrence at 6 months after this surgery. After the surgery, his bone pain disappeared.

DISCUSSION

Osteitis fibrosa cystica is focal bone lesion caused by increased osteoclastic activity and fibroblastic proliferation encountered in hyperparathyroidism. The overproduction of PTH may be either a primary or a secondary phenomenon. The most common cause of primary hyperparathyroidism is an adenoma of one of the parathyroid glands. Secondary hyperparathyroidism is generally the result of chronic renal failure.[3]

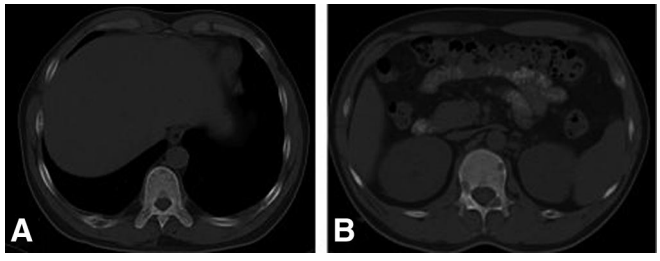

FIGURE 2. A, Noncontrast CT scan at the level of the thoracic vertebrae shows multiple tumors in the vertebras and ribs, with expansive appearance and ballooning of the thinned cortex. B, Noncontrast-enhanced CT demonstrates a lytic lesion in the right pedicle, lamina of the L1 vertebra.

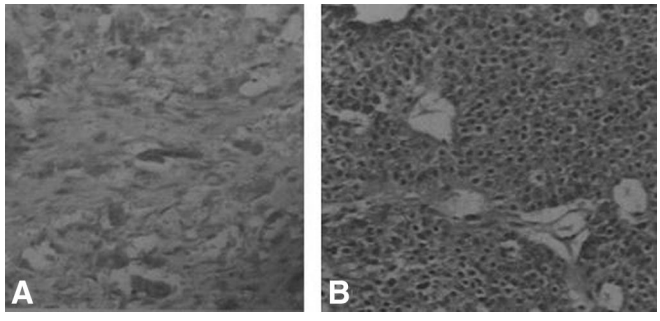

FIGURE 3. A, Biopsy specimen of the first metatarsal osteoclastic giant cells and mononuclear stromal cells are seen. B, H and E staining of the parathyroid. The histologic diagnosis was parathyroid adenoma.

Whether the disease is primary or secondary, it causes similar radiologic and pathologic features in the bone. It has the appearance of a well-circumscribed expansile lytic lesion. Any bone can be involved, but it tends to occur preferentially in the mandible, clavicle, ribs, pelvis, and femur.

Although diffused osteopenia is seen on roentgenographic examination, the most characteristic findings are seen on roentgenograms of the hands, where erosion of the tufts of the phalanges and subperiosteal cortical resorption, especially on the radial side of the phalanges, are apparent. The spine is an uncommon site of brown tumor development.[4]

On plain radiographs, brown tumor is seen as an area of osteolysis with a jagged sharp outline and no sclerotic rim. On CT, the diagnosis of brown tumor is suggested by the presence of a lytic lesion with associated soft tissue in a patient with other features of either primary or secondary hyperparathyroidism. However, the appearance on CT is not specific, and metastases or myeloma may have a similar appearance. Lytic bone lesions that contain hemosiderin include giant cell tumors, giant cell reparative granulomas, pigmented villonodular synovitis, and brown tumors, all of which contain multinucleated giant cells.[5] The MRI appearance of brown tumor has been described in the literature as hypointense on T1-weighted images, strongly enhancing after administration of gadolinium-based intravenous contrast, and hyper- or hypointense on T2-weighted images.[6] The Tc-99m MIBI scan is highly sensitive. Increased uptake in the areas is proportional to regional blood flow, osteoid formation, and mineralization.[7] Our patient had increased uptake in the parathyroid glands. Biopsy and correlation of radiology and pathology findings with laboratory and clinical findings will be required to diagnose brown tumor and to differentiate it from other lesions containing hemosiderin.

The previous report described the major symptoms of brown tumor as muscle weakness, weight loss, anorexia, nausea, vomiting, polyuria, recurrent stone formation, bone pain, and recurrent fractures.[8] These are the symptoms of hyperparathyroidism. The classic findings in brown tumors are pathologic fractures. Review of the laboratory data in our case showed an elevated calcium and alkaline phosphatase. Renal function was normal. Serum PTH was 1305 pg/mL (15–65 pg/mL), calcium 3.01 mol/L (2.15–2.60 pg/mL), and phosphorus 0.62 mol/L (0.82–1.6 pg/mL), diagnostic of hyperparathyroidism.

The patient had received curettage and bone grafting in the first, third, and forth metatarsal bones. An open biopsy of one of the

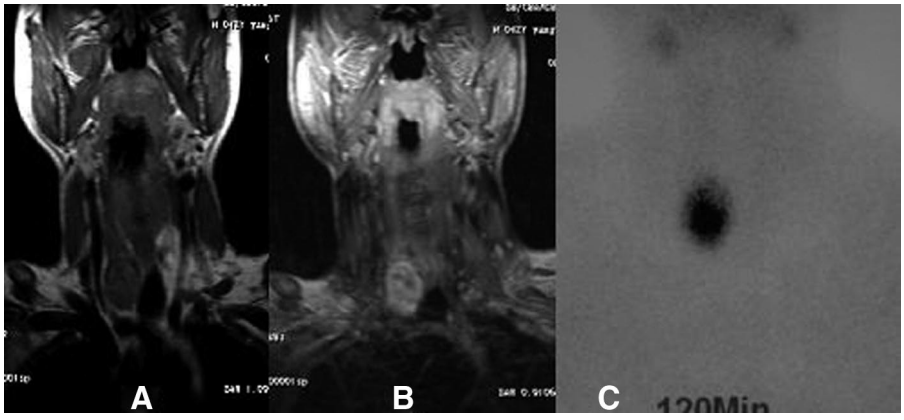

FIGURE 4. A, B, The parathyroid tumor showed a high signal on T2 and enhanced images on MRI compared with surrounding tissues. C, Tc-99m MIBI scintigraphy of the parathyroid showed increased uptake.

metatarsal lesions revealed the proliferation of multinucleated giant cells. He underwent a right thyroid lobectomy and parathyroidectomy. After the second surgery, his bone pain disappeared. Two days post-operatively, serum PTH level dropped to 20.23 pg/mL, and after 10 days, the PTH level was normalized. The patient had no clinical evidence of recurrence at 6 months after surgery.

REFERENCES

1. Buchanan WW, Kraag GR, Palmer DG, et al. The first recorded case of osteitis fibrosa cystica. *Can Med Assoc J*. 1981;124:812–815.
2. Rao DS, Agarwal G, Talpos GB, et al. Role of vitamin D and calcium nutrition in disease expression and parathyroid tumor growth in primary hyperparathyroidism:a global perspective. *J Bone Miner Res*. 2002; 17(suppl 2):75–80.
3. Triantafillidou K, Zouloumis L, Karakinaris G, et al. Brown tumors of the jaws associated with primary or secondary hyperparathyroidism. A clinical study and review of the literature. *Am J Otolaryngol*. 2006;27:281–286.
4. Vandenbussche E, Schmider L, Mutschler C, et al. Brown tumor of the spine and progressive paraplegia in a hemodialysis patient. *Spine*. 2004; 29:251–255.
5. Knowles NG, Smith DL, Outwater EK. MRI diagnosis of brown tumor based on magnetic susceptibility. *J Magn Reson Imaging*. 2008;28:759–761.
6. Gould CF, Ly JQ, Lattin GE, et al. Bone tumor mimics: avoiding misdiagnosis. *Curr Probl Diagn Radiol*. 2007;36:124–141.
7. Mettler FA, Guiberteau MJ. *Essentials of Nuclear Medicine Imaging*. 3rd ed. Philadelphia, PA: W.B. Saunders Co; 1991:209–213.
8. Younes NA, Mahafza WS, Agabi SS. Brown tumor of the femur associated with double parathyroid adenomas. *Saudi Med J*. 2004;25:1701–1703.