Oncology and Translational Medicine
DOI 10.1007/s10330-018-0301-1

April 2019, Vol. 5, No. 2, P98–P101

CASE REPORT

Brown tumor of the femur and ulna in a woman with hyperparathyroidism

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Abstract

Objective A typical brown tumor caused by hyperparathyroidism (HPT) is rare. In this report, we describe our pathological findings along with a review of the literature to enhance understanding of the disease and prevent misdiagnosis, as well as to provide evidence for treatment and prognosis.

Methods We present a case of brown tumor of the left proximal femur and pelvis in a 57-year-old woman who was admitted to our hospital (Dalian Municipal Central Hospital, Dalian, China). Pelvic computed tomography (CT) showed cystic expansile lesions in the left proximal femur and pelvis. Lung and abdominal CT also revealed multiple lytic lesions in the ribs and lumbar spine. X-ray of the left ulna and radius showed that the middle of the left ulna had a fracture caused by a brown tumor. A bone biopsy from the left proximal femur showed focal distribution of giant cells, with hemorrhage and fibrin hyperplasia.

Results The patient underwent internal fixation of the left intertrochanteric fracture, and postoperative bone biopsy showed focal distribution of giant cells with hemorrhage and fibrin hyperplasia. The patient had a parathyroidectomy 5 months after discharge. Two weeks later, the patient developed a fracture in the right femoral neck and pain in the left forearm. X-ray of the left ulna and radius showed that the middle of the left ulna was affected by a pathological fracture caused by a brown tumor. The patient was debilitated and declined surgical treatment. The patient and her family chose discharge.

Conclusion Brown tumor of bone, also called osteitis fibrosa cystica, is a rare non-neoplastic lesion that reflects abnormal bone metabolism in patients with HPT. However, with fine needle aspiration cytology in combination with biochemical tests, a correct diagnosis can be reached. The increase in osteoclast activity leads to decalcification and dissolution of bone, and formation of a cystic bone defect with hyperplastic fibrous tissue. This eventually becomes a brown tumor, with deformed and bleeding fibrous tissue. The patient had a typical brown tumor, as well as osteoporosis, anemia, and pathological fractures.

Received: 15 September 2018
Revised: 21 October 2018
Accepted: 21 November 2018

Key words: brown tumor; hyperparathyroidism (HPT); fibrocystic osteitis; pathological fractures

Brown tumor is known to occur in primary hyperparathyroidism (HPT) and also in secondary HPT caused by renal failure [1]. If unchecked, sustained HPT can result in the development of a hemorrhagic destructive lytic brown tumor and severe skeletal deformities, a condition called osteitis fibrosa cystica [2]. Brown tumor commonly affects the mandible, clavicles, ribs, pelvis, and femur [3]. This disease is rare and is often misdiagnosed as a true bone tumor, osseous tuberculosis, or other disease. Herein, we illustrate the characteristic cytomorphological features of a brown tumor in the femur, seen as a manifestation of primary HPT.

Case report

A 57-year-old woman was admitted to our hospital (Dalian Municipal Central Hospital, Dalian, China) because of a left subtrochanteric fracture. Biochemical assays revealed parathyroid hormone (PTH) levels > 1900 (normal 8–50) pg/mL, a serum calcium level of 4.06 (normal 2.10–2.55) mmol/L, phosphorus level of 2 (normal 2.5–4.5) mg/dL, and alkaline phosphatase levels of 684 (normal 40–125) U/L. The hemoglobin level was 80 g/L. Computed tomography (CT) of the pelvis revealed multiple lytic lesions in the left ilium, acetabulum, and proximal femur (Fig. 1). Lung and abdominal CT also

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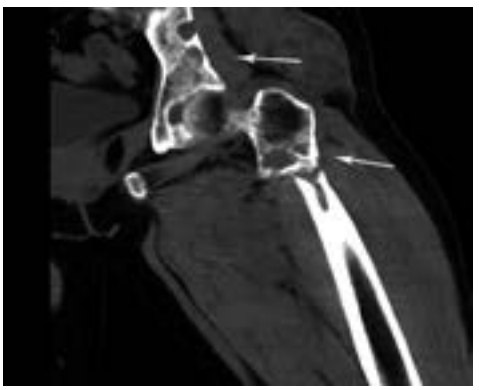

Fig. 1 Computed tomography image of the right femur reveals multiple expansile osteolytic lesions in the pelvis, involving the left ilium, acetabulum, and proximal femur, with a subtrochanteric fracture

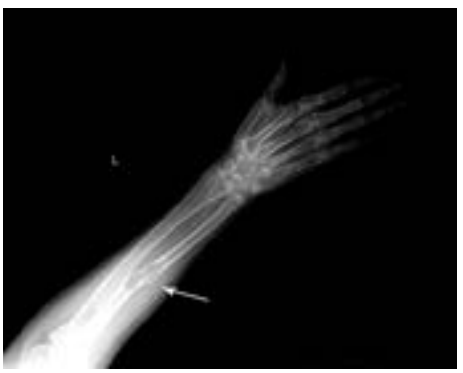

Fig. 3 X-ray shows multiple lytic lesions in the left ulna with left middle ulna fracture caused by brown tumor

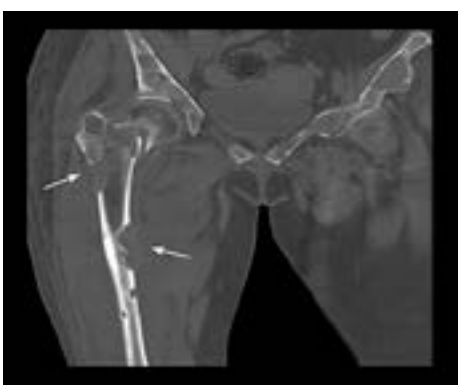

Fig. 4 Computed tomography image of the right femur reveals a cortical osteolytic expansile lesion in the middle and proximal aspect of the right femur, with bulging of surrounding soft tissue and a femoral neck fracture

revealed multiple lytic lesions in the ribs and lumbar spine. Ultrasonographic examination of the neck showed a parathyroid adenoma. The kidney was unaffected on abdominal CT and ultrasound. The patient underwent

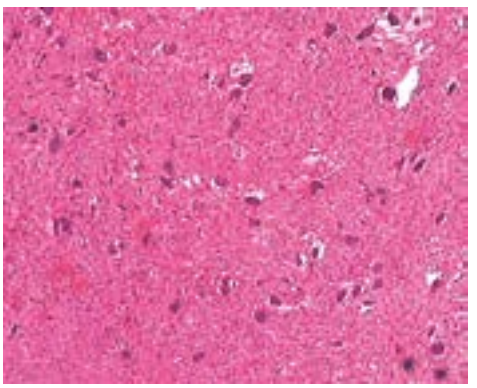

Fig. 2 Histopathology report on the biopsy taken from the left proximal femur shows focal distribution of giant cells, with hemorrhage and fibrin hyperplasia (deep dyeing with hematoxylin and eosin, × 100)

internal fixation of a subtrochanteric fracture, during which the fracture site was found to have a small amount of tan-colored liquid. Postoperative bone biopsy of the left proximal femur showed focal distribution of giant cells, with hemorrhage and fibrin hyperplasia (Fig. 2). The slides were reviewed by a pathologist. Based on the combined clinical, biochemical, radiological, and histopathological data, the case was diagnosed as osteitis fibrosa cystica, with multiple cystic lesions secondary to brown tumor in the pelvis and femoral bones. We advised the patient to consult the department of thyroid and breast surgery for further examination after discharge. The patient also underwent parathyroidectomy after 5 months.

Two weeks later, the patient again developed a fracture of the right femoral neck. We obtained additional history of palpitations and painful swelling in the left arm, with no systematic treatment after the first discharge. Physical examination revealed high blood pressure and a rapid heart rate. X-ray of the left ulna and radius showed that the middle of the left ulna had a fracture induced by a brown tumor (Fig. 3), and CT of the right proximal femur revealed multiple brown tumors, with massive bone destruction (Fig. 4). Biochemical analysis revealed a serum calcium level of 1.71 mmol/L. The hemoglobin level was 85 g/L. Testing was limited by the patient's economic status. The patient was debilitated and not suitable for surgery. Finally, she chose discharge.

Discussion

HPT is one of the most common endocrine disorders encountered in endocrinology practice [4]. Adenomas are the cause in 85% of cases [5]. Incidental discovery of hypercalcemia accounts for 80% of diagnoses [5]. Secondary HPT occurs in the setting of chronic renal failure, where

hypocalcaemia or vitamin D deficiency acts as a stimulus for PTH production [5–6]. Brown tumor of bone, also called osteitis fibrosa cystica, is a rare non-neoplastic lesion resulting from abnormal bone metabolism in HPT [6]. Commonly affected sites are the mandible, clavicles, ribs, pelvis, and femur. In severe and late stages of HPT, skeletal changes can be observed. In recent years, typical brown tumor caused by HPT is rare due to earlier detection of the disease [7]. Parathyroid adenomas can cause the body to secrete large amounts of PTH, which can make osteoclasts proliferate and become more active leading to decalcification and dissolution of bone and the formation of cystic bone defects. The cystic bone defects are gradually replaced by hyperplastic fibrous tissue. The fibrous tissue shows degeneration and hemorrhage with hemosiderosis. Finally, the cystic tissues become brown, resulting in a so-called brown tumor [2]. The dissolution of bone can result in osteoporosis, with elevated serum calcium and alkaline phosphatase. Anemia is caused by fibrous tissue degeneration and hemorrhage. Simultaneously, increased PTH can inhibit the absorption of phosphorus by renal tubules, resulting in massive loss of phosphorus in urine and decreased phosphorus in blood [2]. The patient had a typical brown tumor, osteoporosis, anemia, and pathological fractures. This case was rare. As originally described by Wu *et al* [8], this disease is often misdiagnosed as a giant cell tumor or osseous tuberculosis, which was the initial diagnosis in our patient. With histopathology alone, it is difficult to differentiate between the two [9]. When the histopathology was reviewed in the context of the patient's history, clinical findings, laboratory investigation, and radiological findings, the diagnosis of a brown tumor was made and treated appropriately.

In our case, the patient presented with a pathological fracture and involvement of the ulna, ribs, lumbar spine, pelvis, and femoral bone. The patient's PTH, serum calcium, phosphorus, and alkaline phosphatase levels were significantly elevated and moderate anemia was present. Ultrasonographic examination showed a parathyroid adenoma. Imaging examinations and bone biopsy led to a diagnosis of brown tumor. Although the patient underwent hip surgery, parathyroidectomy was only performed 5 months after internal fixation. As a result, the fracture recurred.

Treatment for brown tumor caused by parathyroid adenomas mainly includes parathyroidectomy. Agarwal *et al* [10] reported that areas of the bone affected by osteitis fibrosa cystica start to recover as early as 1 week after successful parathyroidectomy, and can be demonstrated by changes in biochemical markers of bone turnover. After successful parathyroidectomy, recovery of bone mass occurs earlier at sites with cancellous bone as compared to sites consisting of cortical bone [10]. The reason for fracture recurrence in our patient was the lack of timely parathyroidectomy.

As a brown tumor is rare, we lacked understanding of this disease and initially misdiagnosed it as a giant cell tumor of bone. Brown tumors are very similar to giant cell tumors, but in the context of HPT they are considered reparative granulomas [11]. Tumor is a misnomer because the lesion, although invasive in some instances, does not have neoplastic potential and should be differentiated from true bone cell tumors [12]. Cytologically, a brown tumor is indistinguishable from any other giant cell lesion with 2 main components being mononuclear spindle or stromal cells and multinucleated osteoclast giant cells [5]. The distinction is of importance as their management is vastly different [13].

In conclusion, the occurrence of a typical brown tumor is rare and is prone to being misdiagnosed. Only a few cases of brown tumor have been reported in the literature. Hence, we present a case of brown tumor from our hospital to enhance understanding of this disease and improve the diagnosis and treatment.

Conflicts of interest

The authors indicate no potential conflicts of interest.

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DOI 10.1007/s10330-018-0301-1
Cite this article as: Jiang L, Huang Y, Han YZ. Brown tumor of the femur and ulna in a woman with hyperparathyroidism. Oncol Transl Med, 2019, 5: 98–101.