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Case Report

Diagnosis and Treatment of Brown Tumor in the Femur Induced by Parathyroid Carcinoma: A Case Report

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Keywords
Brown tumor · Pathological fracture · Parathyroid carcinoma

Abstract
Brown tumors are rare destructive bone lesions caused by hyperparathyroidism. As their clinical symptoms, radiographic findings, and laboratory results closely mimic those of metastatic tumors or multiple myeloma, the diagnosis may often be mistaken. We report a case of a 61-year-old woman with brown tumors in both femurs due to parathyroid carcinoma. The patient presented with multiple osteolytic lesions that caused pain in the right thigh. Whole-body computed tomography (CT), including the neck, suspected a parathyroid tumor, and a biopsy of the bone lesion revealed no malignancy. Following parathyroidectomy, she was diagnosed with a brown tumor with hyperparathyroidism due to a very rare parathyroid carcinoma. Although the right femoral lesion was indicated as an impending fracture, conservative treatment was performed because of the instability of her general condition after parathyroidectomy and her wishes. Bone remodeling of the right femur progressed, and the patient was ambulatory; however, 9 months postoperatively, the patient fell, developed a pathological fracture, and underwent internal fixation. When multiple osteolytic bone lesions are present, CT imaging of the neck should be performed to determine the possibility of a brown tumor due to parathyroid disease. Bone lesions of brown tumors are known to be naturally cured after treatment for hyperparathyroidism. However, when the lesion of a brown tumor in the femur is an impending fracture, prophylactic internal fixation is recommended aggressively if the patient's general condition permits.

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Introduction

Brown tumors are benign osteolytic lesions of the bone resulting from primary hyperparathyroidism. The lesion is caused by the excessive functioning of osteoclasts and the resorption of mineral components [1]. The incidence of brown tumors in patients with primary hyperparathyroidism is lower than in patients with secondary hyperparathyroidism [2]. Multifocal lesions are located in the jaws, ribs, clavicles, extremities, and pelvic girdles [3, 4]. Because these lesions clinically cause swelling, pathological fracture, and bone pain, brown tumors can frequently be mistaken for metastatic lesions.

Diagnostic and therapeutic strategies for impending fractures of brown tumors in the lower extremities have not been established. The bony osteolytic lesion of a brown tumor is difficult to differentiate from a metastatic bone tumor or multiple myeloma; delays in diagnosis and treatment can lead to disease progression and complications [5]. Usually, osteolytic lesions tend to be naturally cured through the treatment of hyperparathyroidism [6]. However, when a lesion in the lower extremity is an impending fracture, whether it should be treated with prophylactic internal fixation or treated conservatively is unclear. We encountered a case of a brown tumor in the femur, which was treated with internal fixation for pathological fracture after conservative treatment, and the diagnostic and therapeutic approach is discussed. This case is reported in conformance to the CARE checklist (online supplementary file; see www.karger.com/doi/10.1159/000527637 for all online suppl. material).

Case Presentation

A 61-year-old woman presented at a local hospital with right thigh pain after stepping on. The patient was referred to our hospital for a detailed examination. The patient had no history of cancer. Radiography of both femurs revealed multiple osteolytic bone lesions and thinning of the cortical bone in the right proximal femur (Fig. 1). Computed tomography (CT) from the chest to the lower extremity revealed multiple osteolytic lesions on the ribs, pelvis, tibia, and first metatarsal bone, with no findings suggestive of a primary tumor. Magnetic resonance imaging of the right femoral lesion revealed low signal intensity on T1-weighted axial imaging and high signal intensity on T2-weighted axial imaging. Contrast-enhanced magnetic resonance imaging revealed peripheral enhancement but no internal enhancement. Consequently, we suspected metastatic tumors or multiple myeloma. Initial blood tests indicated that the calcium (Ca) level was 15.2 mg/dL (normal, 8.8–10.1 mg/dL), alkaline phosphatase level was 2082 U/L (normal, 38–113 U/L), and phosphate level was 2.2 mg/dL (normal, 2.7–4.6 mg/dL). However, the tumor markers (AFP, CEA, CA19-9, CA125, SCC, IL-2 receptor) and Bence-Jones protein levels were normal. To diagnose osteolytic lesions, an incisional biopsy of the first metatarsal bone was performed. Histology revealed hemosiderin deposition, mild fibrosis, a few osteoclasts in the trabecula, and no neoplastic changes. The histology of the incisional biopsy could not determine a diagnosis; therefore, contrast-enhanced CT, including the neck, and additional blood tests were performed. CT revealed a parathyroid lesion (Fig. 2), and the intact parathyroid hormone (PTH) level was markedly increased to 2,080 pg/mL (normal, 10–65 mg/dL). To reveal the cause of hyperparathyroidism, neck ultrasonography and a parathyroid scan (99mTc-MIBI: technetium 99m-methoxyisobutylisonitrile) were performed. Ultrasonography showed a hypoechoic lesion of the parathyroid gland, and the 99mTc-MIBI scan showed increased uptake in the left enlarged parathyroid in the delayed phase. Resultantly, a parathyroid tumor was suspected, and the left thyroid lobe, including the parathyroid gland, was resected. Pathological examination revealed parathyroid carcinoma.

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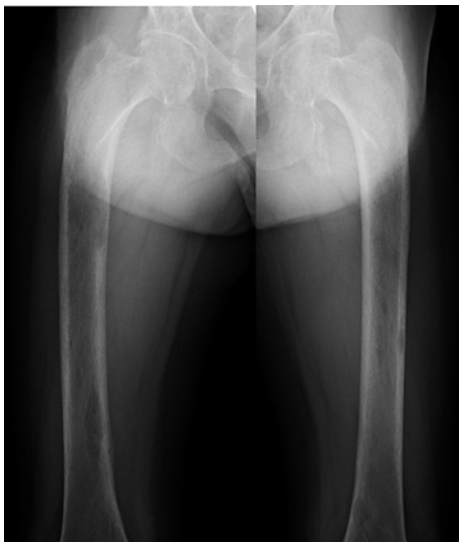

Fig. 1. Plain radiographs showing multiple osteolytic lesions in the shaft of both femurs. In particular, the proximal metaphysis of the right femur showed cortical thinning.

Consequently, the diagnosis of multiple bone lesions was a brown tumor caused by primary hyperparathyroidism. One week after the operation, the Ca and intact PTH levels returned to normal.

The patient was instructed to walk without weight-bearing on the right lower extremity. Mirels' rating system for the prediction of pathologic fracture risk was a total of 11 for the right femur on admission, which indicated a high risk for impending fracture [7]. Hence, Mirels' treatment recommendation was prophylactic stabilization; however, it was treated conservatively. This was because the patient's general condition was unstable owing to hypocalcemia and renal dysfunction after parathyroidectomy, and the patient did not wish to undergo surgery on the right femur. Six months after the parathyroidectomy, she had no pain in her right thigh. Radiographic findings of her right proximal femoral lesions revealed cortical bone thickness and marginal sclerotic change, and Mirel's score improved to 7 points (Fig. 3a). Therefore, she was allowed to walk with full weight bearing. Nine months after the operation, she walked indoors and fell, leading to a fracture at a site where a brown tumor of the right proximal femur was observed (Fig. 3b). Internal fixation with intramedullary nailing was performed (Fig. 3c). After the postoperative treatment, the patient remained non-weight-bearing for 4 weeks. After partial weight-bearing was started, full weight-bearing was allowed after 8 weeks. At the 2-year follow-up, fracture union was confirmed (Fig. 3d). The patient had no pain in the right thigh, could walk without canes, and did not require admission for any recurrence or metastasis.

Discussion

Our case identified two important clinical issues regarding the diagnosis and treatment of brown tumors. First, it is necessary to evaluate CT imaging, including that of the neck, when searching for the cause of multiple bone lesions. Second, when bone lesions of brown tumors in the femur are impending fractures, whenever possible, operative treatment should be considered first because of the high risk of pathological fractures, even if they tend to improve with conservative treatment.

When multiple osteolytic lesions are observed, the possibility of a brown tumor should be considered, and CT imaging should include the neck. Brown tumors are caused by PTH

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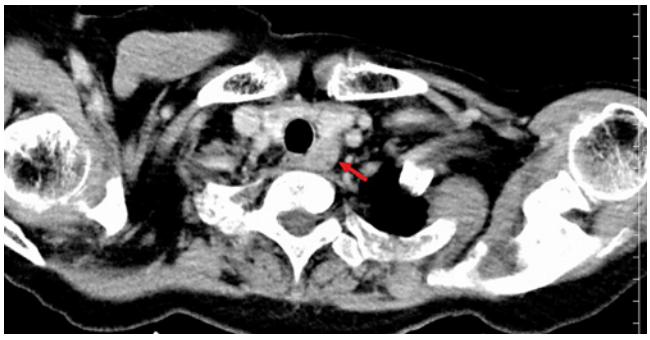

Fig. 2. CT was performed again to include the neck and revealed the left parathyroid lesion.

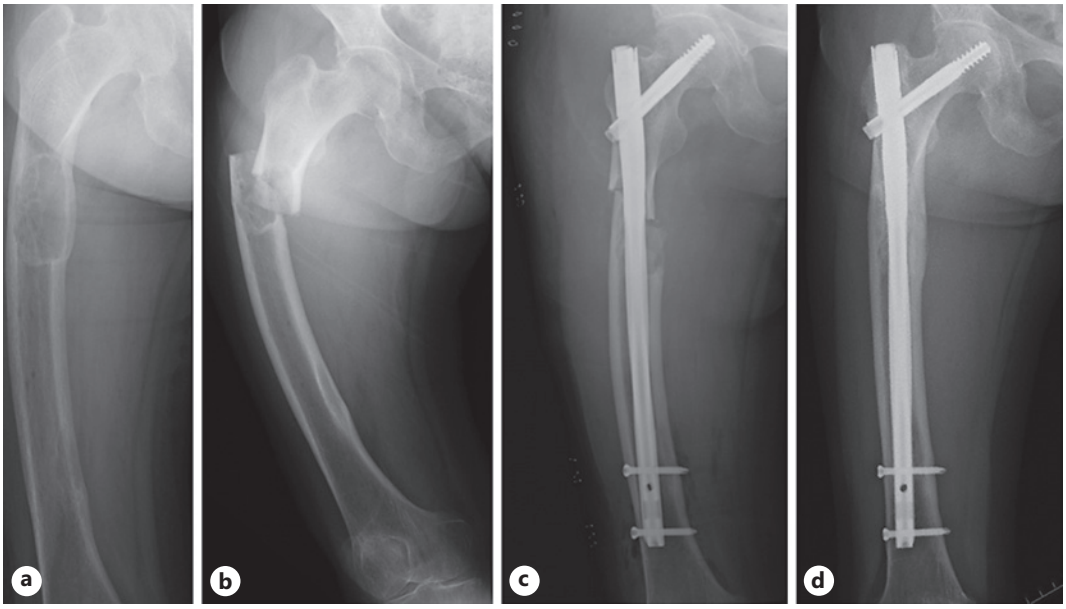

Fig. 3. Plain radiographs showing the right femoral lesion after parathyroidectomy conservatively at 6 months (**a**), pathological fracture at 9 months (**b**), internal fixation with the intramedullary nailing (**c**), and 2 years follow-up after surgical treatment (**d**).

hypersecretion due to hyperparathyroidism, which activates osteoclasts and leads to bone resorption. On radiography and CT, the lesion of a brown tumor shows osteolysis without marginal sclerotic change, and its findings can be confused with malignant bone lesions, such as metastases of carcinoma, multiple myeloma, and bone sarcoma. Thus, when multiple osteolytic bone lesions are observed, brown tumors should also be differentiated, and imaging tests should be performed, including in the neck, to search for parathyroid disease. In our case, a CT scan was initially performed only from the chest to the lower extremities and did not include the neck. Therefore, the parathyroid gland lesions were not detected.

Parathyroid carcinoma is a rare tumor that induces hyperparathyroidism. Primary hyperparathyroidism is a disorder of the parathyroid glands caused by a solitary adenoma in 85% of patients, parathyroid hyperplasia in 10–15%, and carcinoma in 1–5% [8]. Parathyroid carcinoma has a rather low malignant potential, and distant metastases occur in 25% of patients, mostly in the lungs but also in bones [9]. The diagnosis is based on symptoms of hyperparathyroidism, and imaging tests such as CT, ultrasonography, and 99mTc-MIBI are

Table 1. The serum levels of calcium (Ca), intact parathyroid hormone (PTH), alkaline phosphatase (ALP), and creatinine (Cr) before and after parathyroidectomy

	Normal range	Pre-op	Post-op 1 week	Post-op 1 month	Post-op 3 month	Post-op 2 years
Ca, mg/dL	8.8–10.1	15.2	8.8	7.1	9.2	9.1
Intact PTH, pg/mL	10–65	2,080	23	55	28	41
ALP, U/L	38–113	2,082	4,016	2,056	870	87
Cr, mg/dL	0.47–0.79	1.24	2.34	2.00	2.71	1.85

ALP, alkaline phosphatase; Cr, creatinine.

performed. In the treatment of parathyroid carcinoma, parathyroidectomy is the single most effective procedure and generally leads to the normalization of Ca and intact PTH levels. Consequently, osteolytic lesions are naturally cured through primary hyperparathyroidism treatment [6]. One week after parathyroidectomy, the serum levels of Ca and intact PTH were normalized in our patient (Table 1). However, postoperative hypocalcemia may have occurred, as in our case.

The diagnosis of a brown tumor is indispensable for the biopsy of the bone lesion. Clinical manifestations, radiological findings, and laboratory tests, including serum Ca, alkaline phosphorous, and intact PTH levels, are also essential diagnostic tools [2, 10, 11]. However, the clinical symptoms, osteolytic lesions on radiographs, and hypercalcemia may closely mimic those of metastatic tumors or multiple myeloma; therefore, surgical biopsy plays an important role in the differential diagnosis [5, 6]. Biopsy is useful to rule out bone metastasis of the lesion itself, especially in the case of parathyroid carcinoma. The histopathological findings of brown tumors include osteoclastic resorption of the bone, irregularly thickened woven trabecular bone, large numbers of osteoblasts and osteoclasts, and areas of granulation tissue, inflammatory cells, giant cells, hemorrhage, and hemosiderin deposition [6, 12]. Here, histopathological examinations showed characteristic features of a brown tumor and no malignant cells. Biopsy ruled out other diseases, and a definitive diagnosis of brown tumors was made.

When a brown tumor accompanies an impending fracture in the femur, surgical treatment should be the first option if the patient's general condition permits. Brown tumors began to be repaired 4–6 months after treatment of hyperparathyroidism and disappeared within 1–2 years [13]. Therefore, conservative treatment is often considered even in cases of impending fractures. However, there are some reports of pathological fractures after conservative treatment of brown tumors [1, 5, 6]. Mirels' rating system is a method of classifying pathological fracture risk and recommends treatment based on the risk of fracture [7]. Our patient's score of the right femur was a total of 11, which indicated an impending fracture and recommended prophylactic stabilization, but we selected conservative treatment, considering the patient's general condition and wish. After parathyroidectomy, osteolytic lesions of the right femur and other bones gradually remodeled, which resulted in the disappearance of thigh pain, and Mirel's score improved to 7 points. Unfortunately, a fracture of the right femoral lesion occurred 9 months after the operation despite the tendency for bone remodeling. As shown in our case, there is a risk of fracture even if the impending fracture tends to improve with conservative treatment. Therefore, when the initial Mirel's score for the femoral lesion of a brown tumor is high, prophylactic fixation should be considered whenever possible, even if conservative treatment improves Mirel's score.

Conclusion

When there is a case of osteolytic lesions on radiographs and hypercalcemia, metastatic bone tumor, multiple myeloma, and brown tumors should all be considered for differential diagnosis, and CT imaging, including the neck, should be evaluated to search for parathyroid disease. When a brown tumor lesion in the femur is classified as an impending fracture according to Mirels' score, prophylactic internal fixation should be considered first if the patient's general condition permits.

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Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflicts of Interest Statement

We have no disclosure or financial support.

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Author Contributions

Ryota Yamauchi searched the literature and contributed to the care of the patient and to the writing of the final draft. Shusa Ohshika and Yasuyuki Ishibashi contributed to the writing of the final draft. Hiroya Ono, Tasturo Saruga, and Testuya Ogawa have contributed to the editing of the manuscript.

Data Availability Statement

All data generated or analyzed in this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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