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CASE REPORT
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Brown Tumor Related to Primary Hyperparathyroidism Mimicking Malignity in the Mandible: Case Report and Literature Review

ABSTRACT

Brown tumors can be found in any bone, during the course of primary hyperparathyroidism and may be misdiagnosed as tumors of bone origin. In this case report, we emphasized the importance of considering primary hyperparathyroidism in the differential diagnosis of a patient who presented with a mass in the mandible and was thought to have a malignant mass lesion originating from the mandible on tomography. A 27-year-old male patient applied to an external center due to enlargement of the left jaw and swelling in the mouth, which started 2 months ago and increased over time. Based on the biopsy and mandibular tomography results taken from the intraoral lesion, he was referred to our hospital from the external center for excision, considering a bone orginated malignant mass in the mandible. Laboratory examinations of the patient revealed a calcium serum level of 13.6 mg/dL and the parathyroid hormone level of 508 ng/L. In parathyroid ultrasonography, hypoechoic nodular formation adjacent to the thyroid capsule on the left inferior posterior, was evaluated as a parathyroid adenoma. Histopathological diagnosis from parathyroid ademocectomy, and the the mandibular mass , revealed a parathyroid adenoma and brown tumour respectively. We have compiled 5 cases in the literature, initially thought to be malignant bone tumors but later turned out to be brown tumors due to primary hyperparathyroidism. Increasing surgeons' awareness about primary hyperparathyroidism is important as patients with brown tumors are first admitted to surgeons. Considering primary hyperparathyroidism in masses of bone origin avoids unnecessary surgeries.

Keywords: Brown tumor, mandible, primary hyperparathyroidism

Introduction

Brown tumor is a rare tumor-like lesion of bone that is considered an end-stage lesion of abnormal bone turnover caused by elevated parathyroid hormone (PTH).

The term "brown tumor" comes from its brown appearance due to its vascularization and hemosiderin deposits. Brown tumors are not due to a malignant process. They are focal bone lesions due to bone remodeling resulting from hyperparathyroidism or paraneoplastic syndrome.[1] The incidence is lower in primary hyperparathyroidism (PHPT) than in secondary hyperparathyroidism (<5%).[2] Brown tumors can be found in any bone; they may be misdiagnosed as malignant tumors.[3] Common sites of brown tumors are the long bones such as the ribs, clavicle, tibia, and pelvic bones. Head and neck brown tumors are seen, and when they occur, the mandible is usually involved.[4] The diagnosis of a brown tumor is usually based on the history, clinical examination, laboratory results, and imaging findings. Detection of mononuclear cells mixed with multinucleated giant cells in the pathological examination is the gold standard for diagnosis.[5] However, pathological findings are similar in all giant cell tumors (GCT) and may lead to misdiagnosis. Imaging findings of brown tumors are similar, including bone metastases that appear as osteolytic lesions, amyloid cysts, chondroma, aneurysmal bone cysts, osteosarcoma, and GCT.[6] In addition, the most important factor in diagnosing brown tumors is bringing PHPT to mind. Parathyroid hormone and calcium are not routine tests. Therefore, PHPT can easily be overlooked. Brown tumor regresses spontaneously with hyperparathyroidism treatment.[7]

In this case report, we emphasized the importance of keeping PHPT in mind in the differential diagnosis of a patient who presented with a mass in the mandible and was thought to have a malignant mass lesion originating from the mandibular bone on tomography.

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Written informed consent was obtained from the patient to publish this case report and any accompanying images.

Case Report

A 27-year-old male patient applied to an external center due to enlargement of the left jaw, swelling, swelling in the mouth, pain, occasional bleeding, and enlargement of the wound, which started 2 months ago. As a result of the biopsy taken from the intraoral lesion, active inflammation was evaluated as a suspicious of malignancy, and a repeat biopsy was recommended. In the mandibular computed tomography, it was evaluated as a bone-origin malignant mass in the mandible, and tissue diagnosis was suggested. The patient, who was thought to have a malignant tumor in the mandible in an external center, was referred to the medical faculty's otolaryngology (ORL) clinic for excision.

During intraoral examination of the patient, it was observed that there was a painful, ulcerated 5 × 3 × 4 cm painful mass extending toward the cheek mucosa in the gingiva at the level of the left lower third molar tooth (Figure 1). Painful lymphadenopathies of approximately 1.5 cm were palpated in the left upper cervical and middle cervical. In the examinations of the patient, the corrected calcium level for albumin was found to be 13.6 mg/dL (reference range, 8.6-10 mg/dL), phosphorus was 1.36 mg/dL (reference range, 2.5-4.5 mg/dL), parathyroid hormone (PTH) level was 508 ng/L (reference range, 15-65 ng/L), 25-hydroxyvitamin D level was <10 ng/L (reference range, 20-70 ng/L), and creatinine level was 1.40. In the mandibular computed tomography (CT), it was thought that the 51 × 30 × 47 mm hypervascular bone-origin mass with marked contrast, starting from the neighborhood of the third molar root in the left half of the mandibular bone and extending to the posterior along the mandibular bone ramus, could be a primary bone orginated tumor. The mass is primarily located in the masticator space, and some soft tissue component is located in the buccal space. The mass caused slight erosion in the processus coronoideus in the anterior mandibular ramus (Figure 2).

With these findings, the patient was considered to have brown tumor in the mandible due to PHPT. He was admitted to the endocrinology service due to moderate hypercalcemia and acute renal failure. Intravenous hydration followed by furosemide treatment was applied for hypercalcemia. During the follow-up, the calcium value decreased to 10.8. In parathyroid ultrasonography (USG), a 12 × 19 × 23 mm hypoechoic nodular formation adjacent to the thyroid capsule on the left inferior posterior, was evaluated as a parathyroid adenoma (Figure 3). Sestamibi activity, prooved the adenoma in a area matching the left lobe lower pole inferior part of the thyroid gland.

MAIN POINTS

- Brown tumors can be found in any bone; they may be misdiagnosed as tumors of bone origin.
- Considering primary hyperparathyroidism (PHPT) in malignant masses of bone origin saves the patient from unnecessary surgeries.
- Increasing surgeons' awareness about PHPT is important as patients with brown tumors are ussually admitted to surgeans initially.

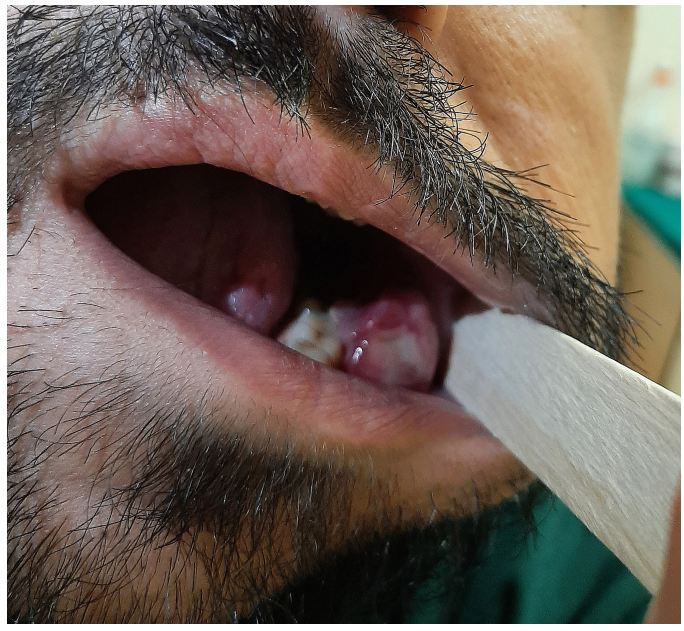

Figure 1. Brown tumor in the mandible.

Multiple endocrine neoplasia syndrome MEN1 and MEN2 components were screened because he was under 40. MEN 1 and MEN 2 was not detected.

A left parathyroid adenomectomy was planned after the left parathyroidectomy, the calcium level corrected for albumin was found to be 7.9 mg/dL (reference range, 8.6-10 mg/dL), phosphorus was 3.01 mg/dL (reference range, 2.5-4, 5 mg/dL) PTH level was 21 ng/L (reference range, 15-65 ng/L). Calcium and calcitriol replacement therapy was applied to the patient who developed hungry bone syndrome during the follow-up. The hungry bone syndrome lasted for 72 hours. During the follow-up, calcium and calcitriol replacements were discontinued, and the calcium levels remained normal. A loading dose of cholecalciferol was planned as 50 000 units/week for 8 weeks.

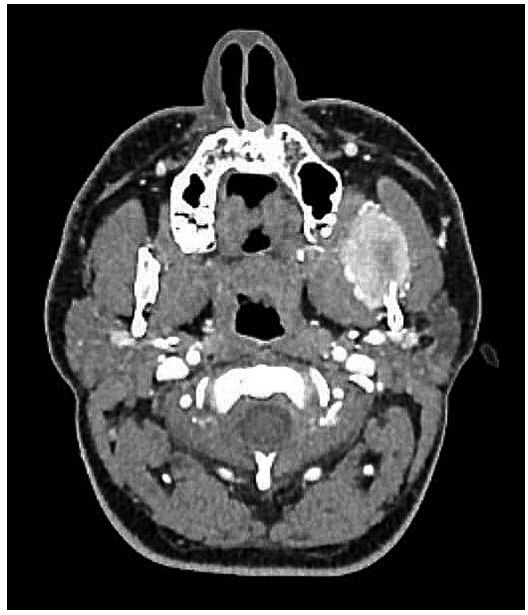

Figure 2. Computed tomography image of mandibular mass.

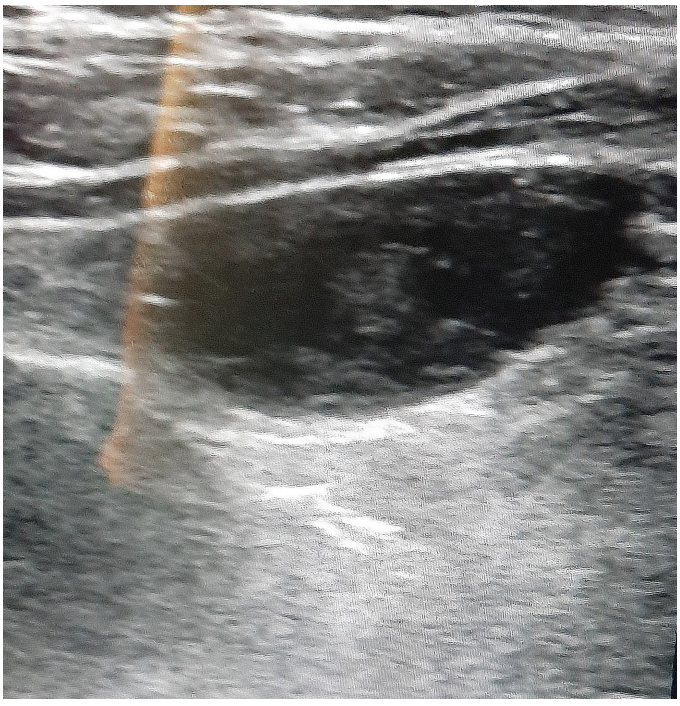

Figure 3. Ultrasonography image of parathyroid adenoma.

Histopathology revealed, parathyroid adenoma, giant cell reparative granuloma and brown tumor due to hyperparathyroidism (Figure 4).

Discussion

Hyperparathyroidism is a condition characterized by increased secretion of PTH. Hypersecretion of PTH leads to excessive calcium reabsorption from the kidneys, phosphaturia, increased vitamin D synthesis, and bone resorption. Parathyroid hormone increases osteoclastic activity in bones. The incidence of bone disease in primary hyperparathyroidism cases is around 10%-20%.[3] Due to routine blood calcium and phosphorus tests, PHPT is usually detected early when patients are asymptomatic. Brown tumor, one of the pathognomonic findings of PHPT, is a focally developing tumor-like bone lesion caused by the increased osteoclastic activity of bone. The incidence rate of brown tumors in patients with PHPT varies between 1.5% and 4.5%.[8,9]

Brown tumor is frequently found in the long bones, pelvis, ribs, and clavicle.[10] Involvement of the facial region is extremely rare. The mandible is most frequently involved, with a rate of 4.5%.[11] Maxillofacial tumors are more likely to affect women than men, with a reported female: male ratio of approximately 1.7 : 1, and the mean age of diagnosis is 34.[12]

Warnakulasuriya et al[13] showed that 10 of 300 patients with parathyroid adenoma had facial involvement. In another study involving 220 patients, only 4.5% were reported to have jaw involvement.[14]

Symptoms of brown tumor are atypical, presenting with local swelling, pain, and sometimes even pathological fractures. However, when surgeons are inexperienced in diagnosing brown tumors, the rate of misdiagnosis increases, and malignant masses are considered. Pathological examination is the gold standard in the diagnosis of brown tumors. Laboratory examinations and clinical findings guide the diagnosis of brown tumors. Brown tumors can be proven when clinical findings are combined with the pathological examination.[15]

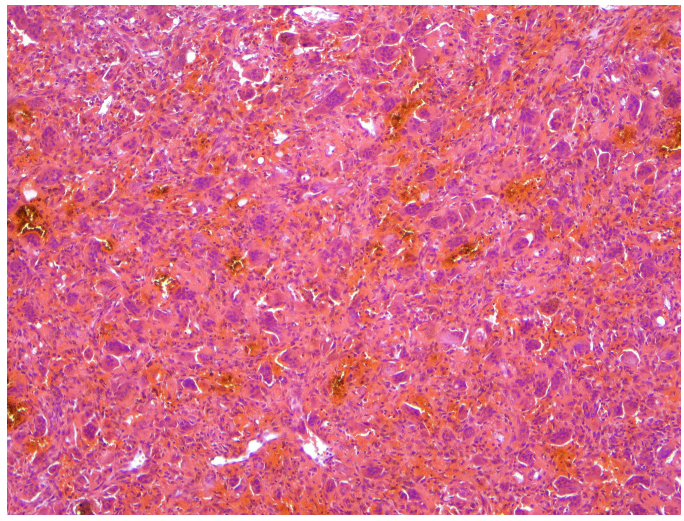

Figure 4. Brown tumor with multinucleated giant cells and deposits of hemosiderin (hematoxylin and eosin stain).

Sometimes the biopsy may not give us clear information. As in our case, the biopsy did not establish the diagnosis of the patient, who was initially thought to have a malignant bone tumor, and when evaluated with mandibular CT, a malignant bone tumor was considered. The patient first applied to the surgeon, and after the calcium PTH values PHPT was detected, and the patient was referred to the endocrinology outpatient clinic.

In the literature, some cases presented with a mass in the mandible and were thought to have PHPT at the time of diagnosis, as in our case. A 51-year-old woman was diagnosed with PHPT by measuring calcium and PTH at the initial diagnosis upon detecting a growing mass in the maxilla and mandible and lytic lesions in the ribs and humerus.[16] In addition, Çakır et al[17] reported on a case who presented with a mandibular mass and was diagnosed with primary hyperparathyroidism.

We have reviewed 5 cases in the literature, which were initially thought to be malignant bone tumors and underwent invasive surgical intervention, but were not considered at the time of diagnosis and were retrospectively diagnosed with PHPT-related brown tumors. Cases with secondary hyperparathyroidism due to chronic renal failure were excluded.

Panagopoulos et al[5] applied distal ulna resection, distal radius curettage, and cementoplasty to a 53-year-old patient with an osteolytic lesion on the direct radiograph of the left wrist. Histopathology resulted in a giant cell tumor (GCT). After the operation, osteolytic lesions were seen in many different bones and because multifocal GCT is rare, the pathology department warned that it might be a brown tumor, and calcium and PTH were examined, and they reported that they diagnosed it as a brown tumor. Calcium and PTH were not measured in the patient at the initial diagnosis. The patient had to undergo surgical intervention because the diagnosis was delayed.

Zhong et al[18] diagnosed an aneurysmal bone cyst in a 44-year-old male patient who presented with left shoulder pain, underwent proximal humeral resection, and had internal fixators to stabilize the bone. The pathology result was interpreted as GCT, and the diagnosis of PHPT was made by measuring calcium and PTH after the surgery with the histopathological findings.

Bohdanowicz-Pawlak et al[19] presented a 41-year-old female case with a size of 73 × 52 × 78 mm mass in the parieto-occipital region, which was thought to be a malignant mass, destroying the external bone lamina, and had multiple lytic lesions in other bones. Right parieto-occipital craniotomy and surgical resection of the tumor were performed, and a histopathology examination resulted in GCT. Two weeks after surgery, pathological fracture of the femur, left tibia, and ulna was considered metastasis, and radiotherapy was planned. As the pathology indicated that it might be a brown tumor, calcium and PTH levels were checked, and a diagnosis of parathyroid adenoma was made. Despite many clinical findings, the correct diagnosis was reached late.

Ekram Ullah et al[3] reported on a 23-year-old female with pathological fractures and lytic lesions in multiple bones. Malignant and polyostotic fibrous dysplasia was considered a preliminary diagnosis. The lower third of the right femur was removed; fixation was applied to the right femoral diaphysis; when the pathological diagnosis was a brown tumor, calcium and parathormone were examined, and the diagnosis of PHPT was made.

Schnyder et al[20] thought of bone metastasis in a 72-year-old patient with a history of breast cancer 7 years ago, with hypercalcemia and multiple bone lesions. However, they detected PHPT in the patient with high calcium and parathormone and reported that the bone lesions improved after parathyroidectomy.

In 5 cases we compiled from the literature, brown tumors were primarily considered bone-derived malignant masses. Calcium and PTH were not measured at the time of diagnosis because PHPT was not considered in the differential diagnosis of malignant masses. In the first 4 cases, the diagnosis of PHPT levels was made retrospectively by calcium and parathormone after the diagnosis of the patients was called brown tumor by the pathologist after mass resection. In the first 4 cases, the lesion was surgically removed in the patients, and wide surgical resections were performed because a malignant mass was considered. Fixators were used for bone stabilization. In the case we presented, PHPT was considered in the differential diagnosis at the time of the first diagnosis, thanks to the experience of the surgeon, and the diagnosis was made early by looking at calcium and PTH before a wide surgical resection of the mandible. The patient underwent left parathyroidectomy in the early period.

We present a rare case of a PHPT-induced brown tumor initially misdiagnosed as a malignant bone-origin tumor in the mandible. Histopathological diagnosis is not sufficient for the diagnosis of brown tumors. The diagnosis can be made by combining clinical symptoms, imaging, and laboratory tests. It is important to consider PHPT and check calcium and PTH in the differential diagnosis since cases with suspected bone-derived malignant masses first apply to surgeons. It is necessary to increase the awareness of surgeons about PHPT to avoid unnecessary interventions.

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