Case Report

Brown Tumor in Parathyroid Adenoma Mimicking Malignant Bone Tumor: A Case Report

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ABSTRACT

Brown tumors, also recognized as osteitis fibrosa cystica or osteoclastoma, represent a unique pathological entity intricately linked to hyperparathyroidism. Although benign in nature, brown tumor can manifest as focal bone abnormalities, presenting diagnostic challenges due to their striking resemblance to malignant bone tumors, particularly bone metastases. A 24-year-old woman presented with a lump on her left knee and right lower leg pain. Imaging unveiled multiple osteolytic lesions resembling aggressive bone tumors. Subsequent investigations, including abdominal USG, thyroid USG, bloodwork, and parathyroid hormone assessment, confirmed hyperparathyroidism with elevated PTH levels and nephrocalcinosis. HistoPA examination shows a brown tumor diagnosis, prompting parathyroidectomy. Brown tumor can mimic aggressive bone tumors both in clinical and radiological findings. Besides PTH level, thyroid and abdominal USG should be performed to find both parathyroid mass and nephrocalcinosis as the result of hypercalcemia. A HistoPA examination shoud be performed to diagnose the main cause of hyperparathyroidism, that is mostly parathyroid adenoma. As for the treatment, medical and surgical intervention can be done to treat hyperparathyroidism and brown tumor itself. Brown tumors pose a diagnostic challenge due to their association with hyperparathyroidism and their resemblance to aggressive bone tumors. Further research is needed to enhance diagnostic and therapeutic strategies for brown tumors associated with hyperparathyroidism.

Keywords **:** Brown tumor, bone tumor, hyperparathyroidism, parathyroid adenoma.

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INTRODUCTION

Brown tumors, also recognized as osteitis fibrosa cystica or osteoclastoma, represent a unique pathological entity intricately linked to hyperparathyroidism. The term "brown tumor" stems from their characteristic brown color, resulting from hemosiderin within the lesions. While they predominantly arise in the setting of hyperparathyroidism, particularly primary hyperparathyroidism (Hamidi & Radswiki, 2010).

Historically considered rare, brown tumors have garnered increasing recognition in recent years, owing to advancements in diagnostic imaging modalities and a better understanding of their pathophysiology (Manjunatha et al., 2019). Brown tumors, although benign in nature, manifest as focal bone abnormalities, presenting diagnostic challenges due to their striking resemblance to malignant bone tumors, particularly bone metastases. Clinically, brown tumors may present with various nonspecific symptoms, including bone pain, swelling, and pathological fractures, often leading to an initial suspicion of malignancy. Radiologically, they exhibit lytic bone lesions with variable degrees of sclerosis, mimicking features commonly observed in aggressive bone neoplasms (Hoshi et al., 2008; Meydan et al., 2006). Consequently, accurate diagnosis necessitates a comprehensive approach encompassing clinical, radiological, and histopathological assessments.

Herein, we present a case report of a brown tumor mimicking bone metastasis in a young adult patient with hyperparathyroidism, highlighting the importance of considering this differential diagnosis in patients with lytic bone lesions and a low possibility of malignancy. This case underscores the significance of accurate diagnosis and appropriate management to prevent unnecessary interventions and optimize patient outcomes.

CASE REPORT

A-24-year-old woman presented with a lump on her left knee since October 2022, accompanied by pain in the lump area, along with pain in her right lower leg since January 2023. The patient had previously suffered a fracture of the left thigh bone after falling in the bathroom in April 2022. Subsequently, she underwent implant placement surgery on the right thigh bone at Zainoel Abidin Hospital, Banda Aceh, in April 2022. In October 2022, she noticed a lump on her left knee and sought treatment at Awal Bros Hospital, Batam, where she was then referred to Dr. Soetomo Regional General Hospital for follow up and advanced examination.

In Dr. Soetomo General Hospital, the patient underwent several plain x-ray imaging of the femur, thorax, humerus, pelvis, and cruris. These images revealed multiple osteolytic lesions accompanied by cortical destruction and soft tissue masses. Additionally, the patient presented with pathological fractures in the proximal femur and ischium (Fig.1). These findings suggest an aggressive bone tumor. A bone survey was conducted on this

patient, revealing multiple lytic lesions distributed across the skull, lumbosacral region, femur, cruris, ankle, and pedis, along with a mass on the thoracic wall. Bone scan and ^{99m}Tc sestamibi (MIBI) scintigraphy was also conducted but the result were indeterminate.

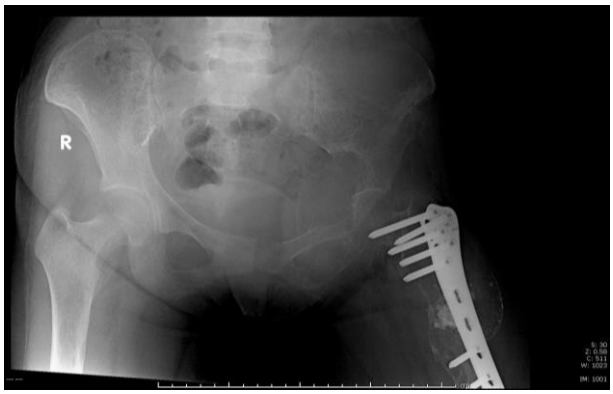

Figure 1. A plain pelvic x-ray shows lytic lesion on the diaphysis of proximal femur with internal fixation (plate and screw) with good apposition, osteolytic on the diaphysis of 1/3 proximal of right femur, and disuse osteopenia

From all these data, the initial diagnosis was bone metastasis with a differential diagnosis of metabolic bone disease. Regarding to investigate the possibility of metastatic bone disease, then an abdominal ultrasound was performed. The ultrasound revealed nephrocalcinosis in the right kidney with no signs of malignancy or mass detected within the abdominal cavity (Fig.2). Thyroid ultrasonography indicated the presence of a mass in the left parathyroid (Fig.3). Further examination of parathyroid hormone levels to investigate metabolic bone disease was suggested. Parathyroid hormone (PTH) examination revealed elevated PTH levels (415 pg/mL) and her bloodwork also discover a high calcium level (13,1 mg/dL1) and a normal phosphorus level (2,12 mg/dL).

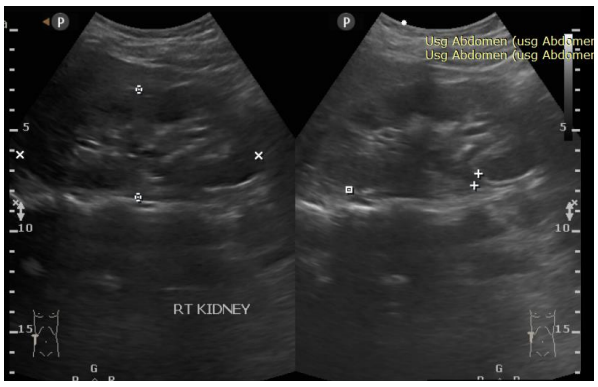

Figure 2. Abdominal USG shows right nephrocalcinosis with no metastatic process in the liver or lymphnode enlargement in the paraaorta.

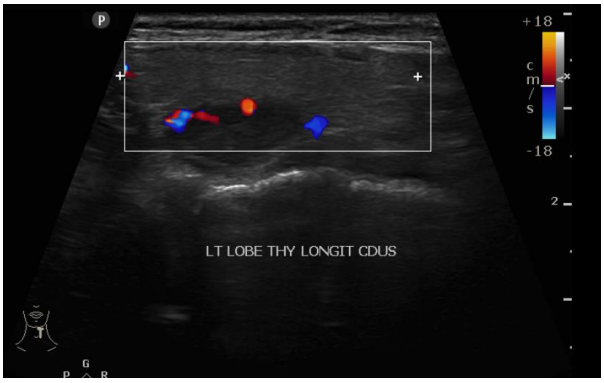

Figure 3. Thyroid USG shows a mass in the left infrathyroid, most likely to be a parathyroid mass. No lymph nodes enlargement are observed.

Subsequently, the patient underwent a core biopsy on the left cruris, and immunohistochemistry was performed using CD68, P63, and H3G34W antibodies, yielding results consistent with a brown tumor. Additionally, the thoracic biopsy revealed findings suggestive of a giant cell tumor and the differential diagnosis is brown tumor. Based on all the data, we suspected metabolic disease (hyperparathyroidism) as the underlying disease of this patient and brown tumor as the complication.

In order to find the underlying cause of HPT, patient underwent a cervical CT-scan examination. The CT revealing the presence of a mass in the left parathyroid gland, lytic lesions and bulging in the calvaria, mandible, cervical vertebra VII pedicle, right clavicle, and left scapula. Additionally, multiple lytic lesions accompanied by soft tissue bulging were observed in the ribs, along with nodules in the lung apex.

A subsequent histopathological examination (PA) was performed. The thyroid biopsy revealed the presence of adenomatous goiter, while the examination of the parathyroid tissue suggested a suspicious finding of an atypical parathyroid tumor (borderline malignancy) or parathyroid adenoma. Subsequently, the patient underwent parathyroidectomy and regular follow-up for weekly calcium levels. Post-operatively, there are no complaints of palpitations, cold sweats, weakness, nausea, vomiting, normal bowel movements, and urination within normal limits.

DISCUSSION

Brown tumors, also known as osteitis fibrosa cystica, are benign bone lesions that can occur in patients with hyperparathyroidism, particularly in the setting of primary hyperparathyroidism (Hamidi & Radswiki, 2010). These tumors result from excess hyperparathyroidism leading to increased bone resorption and fibrosis. Brown tumors, although rare, present a diagnostic challenge due to their radiological resemblance to

aggressive bone tumors. While brown tumors are benign lesions resulting from excessive osteoclast activity secondary to hyperparathyroidism, their aggressive radiographic appearance can lead to misinterpretation and inappropriate management.

Hyperparathyroidism is a condition characterized by overactivity of the parathyroid glands, resulting in excessive production of parathyroid hormone (PTH) (Khan et al., 2024) There are 2 types of hyperparathyroidism, primary and secondary. Primary hyperparathyroidism occurs due to the problem with parathyroid glands themselves. The most common cause of primary hyperparathyroidism is a parathyroid adenoma. Less commonly, primary hyperparathyroidism can result from hyperplasia of multiple parathyroid glands or, rarely, from parathyroid carcinoma (<1%) (Pokhrel et al., 2024). Although rare, parathyroid carcinoma should be concerned if the patients, who are typically younger by about 10 years, have high calcium and PTH level. The involvement of renal and skeletal disorders might also occurred (Bilezikian, 2018). The incidence of primary hyperparathyroidism is quite rare (0.025% to 0.065%). About 1,5-4,5% of those had brown tumor as their complication that is caused by parathyroid adenoma or parathyroid gland hyperplasia (Zhong et al., 2022).

Secondary hyperparathyroidism is usually a response to another underlying condition that causes low calcium levels in the blood. In secondary hyperparathyroidism, the parathyroid glands become overactive in an attempt to maintain normal calcium levels in the blood. The conditions that can lead to secondary hyperparathyroidism include chronic kidney disease, vitamin D deficiency, and malabsorption disorders, and pseudohyperparathyroid disease (Hoshi et al., 2008; Muppidi et al., 2024)

Brown's tumor is characterized by elevated levels of parathyroid hormone (PTH) secreted by the parathyroid glands, leads to hypercalcemia. The parathyroid glands function to regulate serum calcium levels. Under normal conditions, PTH secretion rises in response to low serum calcium levels, promoting calcium reabsorption and osteoclastic bone resorption. However, when the parathyroid glands malfunction, there is an abnormal increase in PTH secretion, resulting in heightened calcium reabsorption and bone resorption. Consequently, this leads to elevated levels of PTH and calcium in the bloodstream (Majumdar et al., 2022). In our case, there is a notable elevation in PTH levels (415pg/mL) accompanied by slight increase in calcium level.

Although brown tumors are considered benign, their appearance on imaging can resemble that of aggressive bone tumors. In the clinical presentation, brown tumor can present with non-specific symptoms that is also mimicking aggressive process such as pain, swelling, and pathological fractures. There are several reported cases presenting with brown tumors mimicking bone metastases in the literature. (Meydan et al., 2006; Parikh et al., 2021). While brown tumors can mimic aggressive bone tumors on imaging studies, certain features can help differentiate them, including a history of hyperparathyroidism, characteristic biochemical abnormalities, the radiographic presentations and the

histological findings on bone biopsy were important for differential diagnosis of underlying diseases (Meydan et al., 2006).

Benign lesion should always be considered in patients with and without an established cancer or a low-possibility of cancer. In plain X-ray imaging, brown tumors can exhibit radiographic features that resemble those of aggressive bone tumors. These features may include areas of bone destruction (lytic lesions), cortical thinning, periosteal reaction, and soft tissue extension (Meydan et al., 2006; Parikh et al., 2021). Brown tumor mostly affects the maxilla and mandible, even though it can also affect other bones such as the shafts of long bones, the pelvis or ribs(Wasiak et al., 2020). Another cases (Meher et al., 2023; Meydan et al., 2006) had also admitted with pathologic fracture of the distal femur like ours.

Ultrasound is a routine diagnostic tool in individuals suspected of having parathyroid adenoma, serving to evaluate the suitability of minimally invasive surgical procedures. Particular attention should be paid to the inferior aspect of the thyroid, as parathyroid adenomas are frequently located inferiorly, posteriorly, or laterally to this region. A comprehensive examination of the entire thyroid gland is warranted, as the superior parathyroid gland may be situated in the upper or middle pole of the thyroid (Xie et al., 2019). In our case, the patient has an infrathyroid mass, suspected to be parathyroid mass.

Besides thyroid USG, abdominal USG should also be done to detect renal calculi. This phenomenon arises due to the hyperparathyroid state, which can induce elevated levels of calcium in the bloodstream (hypercalcemia) and hypercalciuria. Consequently, this can predispose individuals to some renal complications (hypercalciuria, nephrolithiasis, nephrocalcinosis) (Lemoine et al., 2022). In another case reports other patients also have nephrolithiasis like ours (Iqbal & Syafril, 2021; Meher et al., 2023).

Parathyroid adenoma should not be ignored in brown tumor patients without proven parathyroid mass on imaging. A case documented a brown tumor patient with no mass in the parathyroid gland but the PTH level elevated and the thyroid uptake in MIBI scan was increased. However, parathyroidectomy was still performed and the HistoPA result came out as parathyroid adenoma(Can et al., 2016). Therefore, histopathological analysis (histoPA) must be performed in suspected brown tumors to confirm the diagnosis and characterize the tissue changes associated with this condition. In histoPA examination, a brown tumor appears as a soft tissue mass comprising clusters of multinucleated giant cells resembling osteoclasts within a fibrovascular stroma. This mass is situated within a cavity resembling a cystic lesion surrounded by connective tissue, with hemorrhage at the center of the lesion resulting from microfractures leading to hemosiderin release (Manjunatha et al., 2019). HistoPA examination can also provide insights into the underlying cause by assessing changes in the parathyroid gland itself such as parathyroid adenoma. In our case, the patient has parathyroid adenoma. Another case reports also

reported parathyroid adenoma as an underlying disease in brown tumor like ours(Meydan et al., 2006; Parikh et al., 2021; Phulsunga et al., 2016).

Treating Brown tumor primarily involves addressing its underlying cause (hyperparathyroidism). Parathyroid adenoma is a prevalent culprit behind HPT, although other conditions such as parathyroid carcinoma and hyperplasia can also contribute. Surgical procedures, such as removing the affected parathyroid tissue, are often effective. Parathyroid surgery swiftly reduces excessive PTH levels, leading to complete regression of lesions and bone remineralization. Medical interventions may complement surgical approaches. The overarching aim is to normalize serum calcium levels, thereby stabilizing the bone microenvironment (Hu et al., 2019). This patient and other brown tumor arises from parathyroid adenoma cases also underwent a parathyroidectomy (Hu et al., 2019; Ngo et al., 2021; Parikh et al., 2021). As a result, her condition improved and can be discharged for weekly control.

CONCLUSION

Brown tumors pose a diagnostic challenge due to their association with hyperparathyroidism and their resemblance to aggressive bone tumors. Our case highlights the importance of considering brown tumors in patients with lytic bone lesions and a low likelihood of malignancy. Through a multidisciplinary approach, we successfully identified hyperparathyroidism in our patient and managed it with parathyroidectomy. This underscores the importance of accurate diagnosis and tailored treatment to optimize outcomes. Further research is needed to enhance diagnostic and therapeutic strategies for brown tumors associated with hyperparathyroidism.

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