Dilemma in primary hyperparathyroidism with multiple brown tumors

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Abstract

Primary hyperparathyroidism (PHPT) is a disease characterized by excessive secretion of parathormone. During the disease, bone loss occurs, particularly depending on the resorption of the skeletal system. One of the complications of PHPT is fibrotic, cystic bony changes which are called a brown tumor (BT). Skeletal manifestations in the form of BTs are rare, and according to literature studies, it occurs in <2% of patients suffering from any form of HPT. As it is a rare disease and multiple benign lesions may simulate a malignant neoplasm and pose a real challenge for the clinician in its differential diagnosis. We present the case of a 35-year-old man who was evaluated for multiple lytic expansile lesions with a strong suspicion of malignancy and fibrous dysplasia but turned out to be a case of PHPT.

Keywords: Brown tumors, parathyroid adenoma, primary hyperparathyroidism

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a relatively common endocrine disorder, with prevalence estimates of one to seven cases per 1000 adults.\textsuperscript{[1‑4]} It is believed to be the most common cause of hypercalcemia, predominantly affecting elderly populations and women two to three times as often as men.\textsuperscript{[5]} The incidence of PHPT has been difficult to assess. Available estimates vary widely from 0.4 to 21.6 cases/100,000 person-years.\textsuperscript{[6]} Due to parathormone hypersecretion (PTH), several consequences occur, such as excess calcium reabsorption from kidneys, phosphaturia, increased Vitamin D synthesis, and bone resorption. Classical symptoms of hypercalcemia include “bony pain/bone fractures, renal stones, abdominal groans, and psychic moans.” PTH increases osteoclastic activity in the bones. While renal calculi have been reported in 10%–25% of the PHPT cases, the frequency of bone disease has been reported to be around 10%–20%. Patients with hypercalcemia also present with associated symptoms such as paresthesia, headaches, recent fractures, constipation, polyuria, and polydipsia. However, most of the patients are asymptomatic and are usually identified as part of routine investigations.\textsuperscript{[7]}

Brown tumor (BT) also is known as osteitis fibrosa, cystica generalisata, or Von Recklinghausen’s disease of bone is a metabolic bone disease that develops in primary, secondary, or tertiary HPT. It should be differentiated from other true giant cell tumors of bone, and it represents reparative granuloma rather than a true neoplastic process.\textsuperscript{[8,9]} They are called BTs because of the color that they get as a result...
of the hemorrhage in the tissue, and the hemosiderin deposits. The frequency of occurrence of BTs in the primary and secondary HPT is 4.5% and 1.5%–1.7%, respectively. The overall incidence is 0.1%. The frequency of occurrence is more among persons older than 50 years of age, with a male to female ratio of 1.3. BT is a localized bone cyst histologically benign and may cause swelling, pathological fracture, and bone pain in the skeletal system, and multiple BT with PHPT are very rare. Only six cases have been reported in the English medical literature. In this article, we present the radiological and clinical features of a case with PHPT caused by the parathyroid adenoma.

CASE REPORT

A 35-year-old Indian male presented to the Department of Surgical Oncology, Kidwai Memorial Institute of Oncology with pain in the left thigh, left ankle and right knee for about 2 months and was bedridden for the past 1 month due to increased pain and was on analgesics. He had a history of trivial trauma 4 months back with complaints of pain in his right ankle joint and was admitted to the orthopedic emergency department in a primary care center and was evaluated and found fracture of the right distal tibia and was treated with bone cement. He was being evaluated for malignancy and polyostotic fibrous dysplasia. On physical examination of the patient, tenderness was found to be present in the left knee, left ankle, right knee, and left thigh. On laboratory analysis, serum calcium level was 17.5 mgs% (normal 9–11 mgs%), serum albumin level was 3.8 g/dl (normal 3.4–5.5 g/dl), serum alkaline phosphatase level was 1375 U/l (normal 40–120 IU/l), serum parathyroid hormone level was >900 pg/ml (normal 11.1–79.5 pg/ml). The last follow-up visits which were conducted after about 1 month showed marked improvement in the patient’s clinical condition and radiological findings. Histopathological examination showed the presence of hypercellular nodules with nodular gray-white areas with necrosis with pinpoint hemorrhage with chief cell hyperplasia and surrounded by a thin capsule. The pattern of growth of chief cells was diffused, acinar/pseudoacinar, and pseudopapillary. The pathological diagnosis revealed parathyroid adenoma.

On day 11, biochemical markers had improved (urea 12.1 mg/dl, creatinine 1.1), and serum calcium had fallen to 11.2 mg/dl (normal 9–11 mg/dl). The patient underwent a neck exploration on day 14. During the exploration, the right inferior gland was found to be large, cystic, soft, and of a brown color. There was no evidence of local invasion and no lymphadenopathy [Figure 3]. As such, a diagnosis of adenoma was made. Intraoperative PTH assay was not routinely used at our unit and as such was not performed. The right inferior parathyroid gland was excised which was weighing approximately one gram. The right superior parathyroid gland was normal, and the contralateral neck was not explored as there was no uptake was found on Sestamibi scan. Two days’ postoperatively, the serum levels of serum calcium 9.6 mg/dl (normal 9–11 mg/dl) and serum parathyroid hormone level was 39 pg/ml (normal 11.1–79.5 pg/ml). The last follow-up visits which were conducted after about 1 month showed marked improvement in the patient’s clinical condition and radiological findings. Histopathological examination showed the presence of hypercellular nodules with nodular gray-white areas with necrosis with pinpoint hemorrhage with chief cell hyperplasia and surrounded by a thin capsule. The pattern of growth of chief cells was diffused, acinar/pseudoacinar, and pseudopapillary. The pathological diagnosis revealed parathyroid adenoma.

Figure 1: (a) Radiograph right tibia anteroposterior view shows geographic lytic expansile lesion with a pathological fracture in the meta-diaphyseal region of the right tibia. (b) The radiographs all showed similar lytic expansile lesions in the left mid tibia and (c) Outer table skull, but with no evidence of calcification in the lesions

Figure 2: (a) Ultrasound neck shows well-defined heterogeneous lesion noted inferior to the lower pole of right thyroid gland measuring 3.6 cm x 3.4 cm feeding artery noted with surrounding vascular vessel with no associated lymphadenopathy and a normal mediastinum. (b) Sestamibi scan showed increased uptake in the right inferior parathyroid gland
DISCUSSION

Multiple BT in the literature was associated with PHPT initially reported by Joyce et al. in 1994,[15¬17] In addition, five more cases have been observed since then. Such rare and multiple benign lesions may simulate cancer and pose a real challenge for the clinician during its differential diagnosis. BT is categorized by multiple lytic lesions is a misnomer, as it is not a true neoplasm. It may be observed in the facial bones, pelvis, ribs, and femur. Ninety percent of the patients with skeletal metastases present with multiple lesions.[19] Preoperative and even histological differentiation between benign or malignant pathology is often difficult, ultrasonography is the first and most common imaging methods and Sestamibi scan which has almost replaced the bilateral neck exploration is also very useful to locate the site of adenoma with even a small incision. Raised serum calcium and increased PTH will lead to suspicion for malignant disease as serum PTH levels are mildly elevated in benign disease, but carcinoma causes levels up to 10 times that of normal.[23] Robert et al. suggested that a PTH level < 4 times the upper limit of normal excludes a malignancy,[22] but none of these findings are specific. In the case of hypercalcemia and radiographic evidence of multiple lytic lesion, PHPT should always be kept in differential diagnosis and should be looked into once more common causes such as malignancy has been excluded. A high index of suspicion will lead to an early diagnosis. In our case, except for the bone-related symptoms, there were no other complaints related to gastrointestinal or central nervous system or renal was noted.

In summary, our case involves a gentleman presenting in hyperparathyroid crisis with a massively raised serum PTH level which is believed to be one of the highest reported in benign disease published to date. It represents the presentation of benign cystic adenoma mimicking malignant disease and reinforces the importance of prompt initial medical management, Preoperative diagnostic and localizing studies, and sound operative judgment, highlighting the difficulties facing the endocrine surgeon when dealing with lesions of the parathyroid gland.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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