Brown Tumor: Rare Skeletal Presentation Secondary to Hyperparathyroidism

Jagdish Patwa, Keyur Patel*, Parth Patel, Neel Patel and Parth Thakor

Sumandeep Vidyapeeth University, India

*Correspondence Info:
Keyur Patel
Sumandeep Vidyapeeth University, India
E-mail: kbp_87@yahoo.co.in

Abstract
Brown tumor is a giant cell lesion associated with hypoparathyroidism. It is a non-neoplastic condition and represents terminal stage of the remodeling process in hyperparathyroid state. This severe parathyroid bone disease is a rare clinical presentation of primary hyperparathyroidism which is due most often to a parathyroid adenoma, secreting parathormone(PTH). Elevated PTH levels cause bone resorption, the formation of polyostotic lesions and a reduction in bone mineral density, predisposing to pathological fractures. Here we report the case of young female having primary hyperthyroidism due to parathyroid adenoma with osteolytic cystic lesions at distal femur, distal end clavicle, iliac bone. She was treated with surgical excision of parathyroid with curettage, autogenous bone grafting, internal fixation with plate after confirming the biopsy report and biochemical, histopathological investigations. At the follow up time patient had no symptoms with full range of motions at knee with excellent fracture healing.

Keywords: Primary hyperparathyroidism, Brown tumor, Excision

1. Introduction
The incidence of untreated hyperparathyroidism has dramatically decreased.[1] Primary hyperparathyroidism most often is due to a parathyroid adenoma that secretes parathyroid hormone (PTH). The severity of hypercalcemia is correlated with the size and weight of the responsible parathyroid adenoma.[2] In the majority of patients with primary hyperparathyroidism (85%) caused by solitary parathyroid adenoma (single gland disease), whereas 13% have hyperplasia (multiple gland disease), 1-2% have double adenoma and 1% have carcinoma.[3] Due to parathormone hyperscretion, several consequences occur such as excess calcium reabsorption from kidneys, phosphaturia, increased vitamin D synthesis and bone reabsorption. Parathormone increases osteoclastic activity. Low density of bone and impaired bone quality predispose to a pathologic fracture. In this case report we have discussed brief review of literature and the rare presentation of the patient having parathyroid adenoma with multiple cystic skeletal lesions.

2. Case History
A 28 years old female patient came to our hospital with pain and swelling over left knee joint which was gradually increase in size since 8 months and was unable to bare weight on left lower limb for last 2 weeks.

On physical examination, painful swelling was determined over the left knee joint, firm to hard in consistency. On neck examination the right inferior thyroid lobe a 4 x 3 cm sized, palpable nodule, soft consistency was noticed. Other systemic examinations revealed no abnormality.

Laboratory analysis revealed serum calcium - 11.7 mg/dl, serum alkaline phosphatase - 200 IU/l, serum T3 – 3.43 ng/ml, serum T4 – 6.7 µg/dl, serum TSH – 2.36 µIU/ml and serum parathyroid hormone level was 1047 pg/ml.
On Roentgenography; multiple expansile, osteolytic lesion, eccentrically situated with sharp sclerosed margin with septations involving the left iliac bone, sacrum, lower ends of metadiaphyseal region of left femur and lateral end of right clavicle (Figure 1). There was paper pot appearance involving the skull vault (Figure 2). CT scan showed presence of Right cystic peripherally enhancing mass of size (coronal 4.6x2.5 cms, axial 2.5x2.6 cms, saggital 5.x2.3 cms.) which was thought to be compatible with parathyroid adenoma. On USG of neck, mass was seen oval, homogenous, hypoechoic, nodule localised behind thyroid gland separated from thyroid gland due to its capsule(Figure 3).

Biopsy was taken from the femur and sent for the histopathological examination. Right parathyroidectomy (Figure 4) and at distal femur curettage, autogenous bone graft and nonvascularized fibula of ipsilateral limb was grafted with open reduction and internal fixation by condylar buttress plate. Histopathological report confirmed the diagnosis of parathyroid adenoma and bone biopsy revealed brown tumor (Figure 5).

Macroscopic examination of the excised gland revealed greyish brown soft tissue mass measuring 5x3x2.5 cms and on cut section cystic area with thick brownish haemorrhagic material seen. Microscopic examination showed the presence of oxyphilic cells and chief cells arranged in nests, follicular and pseudopapillary patterns, separated by sinusoidal cells. Individual cells showed mild degree of pleomorphism, hyperchromatism and crowding of nucleus.

Post operatively patient’s serum level of calcium was 8.6 mg/dl and serum level of parathyroid was 274 pg/ml, patient was given oral calcium and vitamin D, above knee cast and advised non weight bearing for 8 weeks. We followed up the patient every monthly for 6 months (Figure 6) and patient was now able to bare weight on left leg with full range of movements and there were no other complications till the last follow up.
Figure 3: USG of neck

Figure 4: Sample histopathological examination of Right parathyroidectomy

Figure 5: histopathological examination of Right parathyroidectomy

Figure 6:
3. Discussion

The prevalence rate of primary hyperparathyroidism varies from 1% to 4%, with a female:male ratio of 3:1.[4] In 80% of cases the cause is a solitary adenoma and in 20% a glandular hyperplasia.5 Serum calcium, ionised calcium and PTH levels should be obtained to diagnose hyperparathyroidism. PTH plays a key role in calcium and phosphate metabolism.

Brown tumors are relatively uncommon lesions associated with hyperparathyroidism which are benign lesions, results in abnormal osteoclastic and osteoblastic activity resulting in bone resorption of the bone. The incidence of brown tumours in patients with primary hyperparathyroidism is 1.5% to 1.7%.[5] Nowadays hyperparathyroidism is usually treated before such lesions develop; therefore they have become extremely rare. Singhal et al[6] reported that 5-15% of patients with primary hyperparathyroidism have associated bony abnormalities. Radiological examination reveals osteopenia of the entire skeleton and multiple localised lytic lesions with a benign aspect. Hyperparathyroidism affects mainly cortical bone, and not cancellous bone. The bone marrow in these cysts may be replaced by vascularized fibrous tissue and giant cell reaction. Accumulation of blood pigment inside the cyst results in a reddish-brown hue and accounting for the term brown tumor. Clinically, brown tumours most often manifest as slowly growing, painful masses with tendency to pathological fracture.

Histologically, brown tumours are characterised by numerous giant cells, diffuse or arranged in clusters. Brown tumours may be indistinguishable from giant cell tumours of bone, and correlation with clinical and radiographical data is essential in making the correct diagnosis.[5] Brown tumours represent foci of haemorrhage within an enlarged fibrotic marrow space. Organisation of these lesions results in the release of haemosiderin and the accumulation of macrophages, fibroblasts and giant cells.

In our case patient had multiple cystic lesion in the skeleton. Similar radiologic features seen in other cystic bony lesions. However, the multiplicity of these lesions in combination with an elevated serum level of PTH confirms the diagnosis. Both ultrasound (USG) and CT scan of the neck are non-invasive and appropriate initial investigations, which may show the site of PTH producing adenoma in up to 75-90% of the cases.[7] Septamibi scan, however, is indicated if ectopic PTH producing adenoma is suspected or if the CT scan and the USG failed in localizing the PTH producing lesion.[8] In hyperparathyroid bone disease and hypercalcemia surgical exploration of the neck is recommended.[3]

After parathyroidectomy, the serum PTH level falls dramatically, bone resorption stops resulting in marked increase in bone uptake of calcium and phosphate (the so called hungry bone syndrome). We conclude that in a patient presenting with pathological fracture, primary hyperparathyroidism should be kept as differential diagnosis with screening of the whole skeleton. Symptomatic patient can back to normal with parathyroidectomy and fixation of the fracture with full range of movements.

Key Messages

Brown tumor is a benign lesion associated with hyperparathyroidism. Any patient with pathological fracture should be undergone Serum PTH level with whole skeleton screening. As multiple cystic lesions may present in brown tumor patient. Parathyroidectomy is the treatment with other orthopaedic interventions.

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