

Multiple Brown Tumors in a Normocalcemic Patient with Primary Hyperparathyroidism - A Case Report

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ABSTRACT

Brown tumor is a benign bone lesion that arises as a direct result of parathyroid hormone on bony tissue in some patients with hyperparathyroidism. Multiple brown tumors may simulate malignant disease and it is a real challenge for the clinicians in the differential diagnoses. Brown tumor as the only and initial symptom of normocalcemic primary hyperparathyroidism is a rare clinical entity. Here, we present a case with multiple brown tumors in a young normocalcemic woman as a sequela of primary hyperparathyroidism mimicking bone metastases.

Key words: Brown tumor, Parathyroid adenoma, Primary hyperparathyroidism, normal calcium homeostasis.

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INTRODUCTION

Brown tumors are a rare clinical consequence of primary hyperparathyroidism (1). These are non neoplastic lesions resulting from abnormal bone metabolism, localize in areas of intense bone resorption and the bony defect filled with fibroblastic tissue. Brown tumors arise secondary to both primary and secondary hyperparathyroidism and have been reported to occur in 4.5% of patient with primary hyperparathyroidism (PHPT) and 1.5-1.7% of these with secondary hyperparathyroidism (2). The reported prevalence of the brown tumour is 0.1%. The disease can manifest at any age, but it is more common among person older than 50 years, and is three times more common in woman than in man (3). Hyperparathyroidism is usually associated with high levels of serum calcium. Brown tumour as the only and initial symptom of

normocalcemic primary hyperparathyroidism is extremely rare (4). Multiple brown tumors may simulate cancer metastasis and it is a real challenge for the clinicians in the differential diagnoses (5). Although the measurement of serum calcium and parathyroid hormone (PTH) level provides early diagnosis and decreases the incidence of radiologic bone involvement, progressive major bone lesions may still be observed in developing countries. Here, we present a case with multiple brown tumors in a young woman as a sequence of PHPT without accompanying hypercalcemia mimicking bone metastases on radiography.

CASE REPORT

A 35 years young woman presented with generalized musculoskeletal pain, restricted limbs movement and radiographic findings of expanding osteolytic bone lesions in left clavicle, multiple ribs and fracture lower end of left humerus. Two years ago, she was treated with fracture femoral shaft. At that time her serum calcium, phosphate and alkaline phosphatase (ALP) were within the normal ranges. There was no family history of peptic ulcer, parathyroid disease or any other endocrine disorders. There was no history of increased thirst, urinary frequency, constipation, weight loss, cholelithiasis, exposure of ionizing radiation or industrial toxin exposure. On physical examination, the patient was ill-looking and anxious. There were no enlarged neck nodes. However, she had a swelling in the lateral aspect of left clavicle. She had tenderness over multiple bony areas. Considering the patient's history and clinical manifestations, serial

imaging and laboratory studies were conducted in light of the possibility of multiple bone metastases. Complete blood count and biochemical analysis, including blood urea, nitrogen, creatinine, albumin, calcium, and phosphorus were within normal ranges. Repeat of chest X-ray revealed expansile lucent lesions in lateral aspect of left clavicle with soft tissue swelling and multiple ribs mimicking metastases. Right arm X-ray including elbow joint showed fracture of lower end of right humerus (Figure 1).

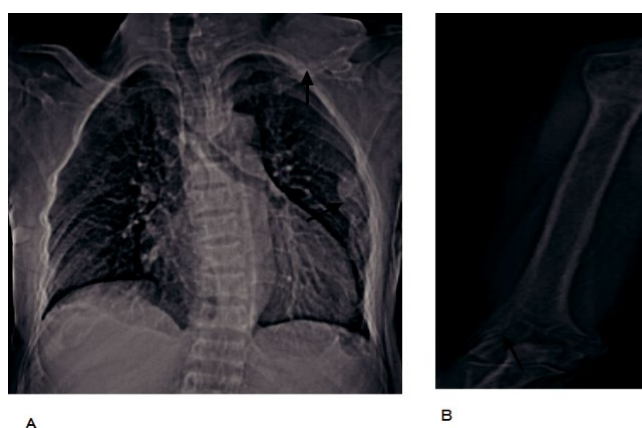


Figure 1. X-ray chest P/A view showed expansile lucent lesions in left lateral clavicle and multiple ribs (A) and fracture lower end of right humerus (B).

Computed tomography (CT) of chest and abdomen showed no tumor except multiple expansile radiolucent bony lesions in ribs and clavicle (Figure 2).

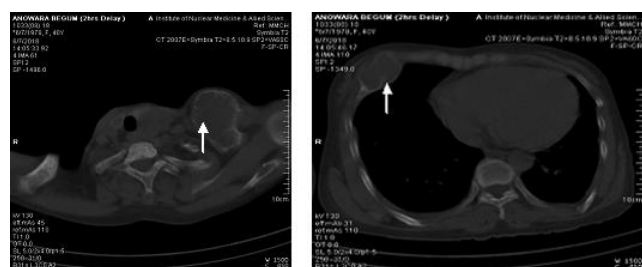


Figure 2: CT chest and abdomen shows multiple expansile lucent lesions in left clavicle (A), ribs (B) (white arrow marks).

Even though, these findings suggested metastatic bone lesions, the levels of tumor markers such as CEA, CA-125 and ALP were all within normal limits. Repeat laboratory studies, however, unveiled the differential diagnosis of metabolic bone disease (brown tumor). Blood counts and routine biochemical analysis were normal except for an

elevated serum PTH level (112 ng/dl, normal <20 ng/dl), which led to the consideration of underlying hyperparathyroidism. Thyroid function tests were within normal limits. For the purposes of ruling out the cause of hyperparathyroidism, high resolution ultrasound of neck was performed and revealed a solid hypoechoic nodular mass (~ 2.7 X 2.1 cm) in left side of neck adjoining left lobe of thyroid (Figure 3).

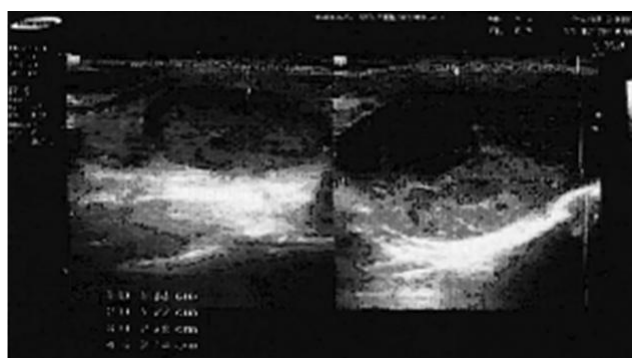


Figure 3: HRUS showed a large solid heterogeneous mass in left side of neck adjoining the left lobe of thyroid.

A dual phase ^{99m}Tc Sestamibi (MIBI) parathyroid SPECT/CT scan showed intense radiotracer uptake in the left upper neck consistent with parathyroid tumor and uptake of ^{99m}Tc-MIBI in the left clavicular swelling, ribs and skull bones (Figure 4).

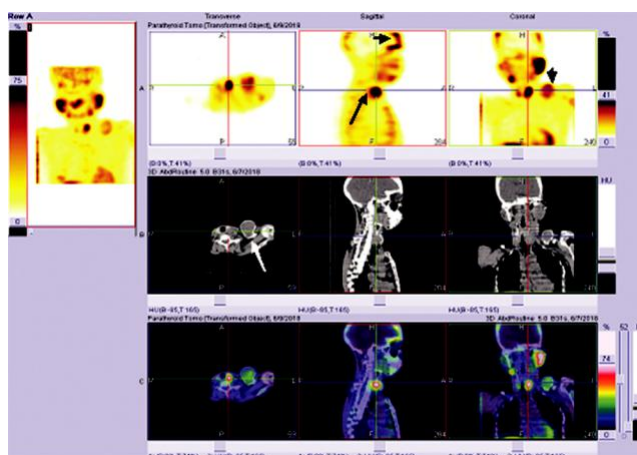


Figure 4: Hybrid SPECT/CT ^{99m}Tc-MIBI parathyroid scan showed increased uptake of radiotracer in left thyroid region (arrow in upper row) corresponds to the isodense soft tissue mass suggesting parathyroid mass. Increased uptake is also seen in the left clavicle, ribs and skull (arrow head) corresponds to expansile lytic bone lesions (white arrows).

CT portion of SPECT/CT showed hypodense soft tissue mass measuring ~ 3.1X 1.9 cm in left side of neck adjoining the left lobe of thyroid gland suggesting a parathyroid tumor and multiple expansile bone lesions. As parathyroid cancer can metastasized to bone, it can be unclear in parathyroid carcinoma whether the bony lesions are from brown tumors or metastatic parathyroid cancer.

Left sided parathyroidectomy was done and histopathology reported parathyroid adenoma (Figure 5), rather than carcinoma.

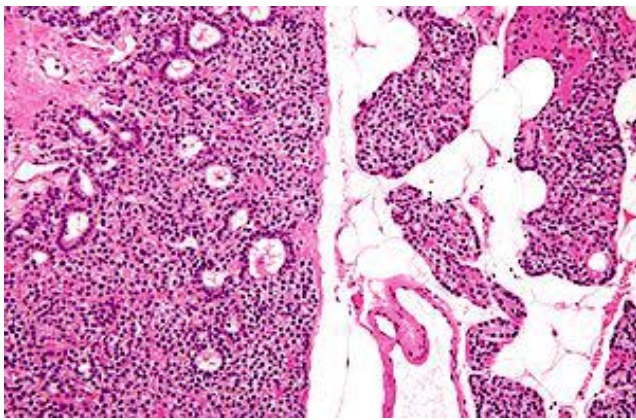


Figure 5: Histopathological examination demonstrates the presence of hypercellular nodules with chief cell hyperplasia and surrounded by a thin capsule suggesting parathyroid adenoma.

Biopsy of the clavicular lesion revealed a dense infiltration of the marrow by a reactive fibroblastic tissue with scattered multinucleated giant cells; hemorrhage and increased osteoblastic activity consistent with brown tumor (Figure 6). There were no malignant cell indicating metastasis. Calcium and vitamin D supplementations were ensured.

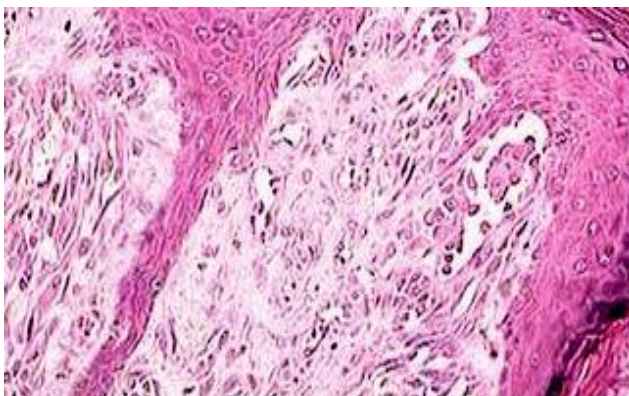


Figure 6: Biopsy of the clavicular lesion revealed a dense infiltration of the marrow by a reactive

fibroblastic tissue with scattered multinucleated giant cells, hemorrhage and increased osteoblastic activity

Follow up after 1.5 years revealed normal serum PTH level with no significant complaints.

DISCUSSION

Brown tumor comprises only a small percentage of bone expanding or osteolytic bony pathologies (6). It is caused by hyperparathyroidism, which may be primary or secondary or tertiary. Primary hyperparathyroidism due to parathyroid adenoma is one of the leading causes of Brown tumour. In our case, the increase secretion of PTH from the parathyroid adenoma triggered high osteoclast turnover activity, leading to multiple bone expanding lytic lesions (7). Initially, radiography, CT and MIBI of multiple osteolytic mass in the ribs, clavicle and humerus suggested that the bone lesions were brown tumor or metastases from a malignant parathyroid tumor. The high level of intact PTH in the serum; and MIBI positive lesions in the neck indicated that the patient might have the primary hyperparathyroidism and multiple bone metastases caused by carcinoma of the parathyroid gland rather than a benign tumor. However, after surgery, the parathyroid tumor was diagnosed as a parathyroid adenoma by histopathology rather than carcinoma. The biopsy from the lesion of left clavicle revealed brown tumor. At one and half years after tumor resection, there has been no recurrence of either the hyperparathyroidism or the metastases. These findings indicate that the patient did not have parathyroid carcinoma. Brown tumors are considered as the advanced stage of complication of HPT and are mainly the first presentation of the disease. They are relatively rare nowadays due to early diagnosis and prompt treatment of HPT. Inspite of this, Dilip et al. reported a series of 40 cases that all had generalized skeletal involvement (8). Within the skeletal manifestations of hyperparathyroidism are brown tumors that appear in approximately 10% of cases and in advanced stages of the disease. They may appear in any part of skeleton most commonly seen on the ribs, clavicle and pelvis. Involvement of the long bone is considered rarely in

patient with primary HPT. Our patient brings the number of long bone brown tumor in primary HPT to a few cases of literature (9). Only a few cases are occurred with normocalcemic primary HPT.

The tumors are usually soft, painless, minimally tender and appears elastic on palpation (10). Occasionally the lesions are painful (11), as was seen in our patient. The tumors are called 'brown' because of its color, which is a result of vascularity, hemorrhage and deposits of hemosiderin (10, 11). Since the major action of PTH is to raise serum calcium level, the main biochemical abnormality in primary HPT is an increase in the circulating concentrations of both PTH and calcium (12). Some patients with proven parathyroid adenoma have normal serum calcium level or the hypercalcemia (13). Approximately 20% of patient with normocalcemic primary hyperparathyroidism are true normocalcemic (12, 13), as in our case.

The diagnosis of HPT should be established by determination of the serum calcium, phosphate, alkaline phosphatase and PTH level rather than histopathological examination of focal lesion. The main challenge in diagnosing brown tumor is that it can be seen in normocalcemic patient as well (10), as in our patient. On CT scan brown tumor appears as a lytic lesion with associated soft tissue mass. However the appearance on CT is not specific, and metastases or multiple myeloma may have a similar appearance (14). Tc-99m MIBI might be taken up by brown tumors along with the parathyroid tumor, mimicking metastatic parathyroid carcinoma (15). The case reported here and few others reported in literature introduced an important caution in the interpretation of skeletal lesions taken up by Tc-99m MIBI. In patient suspected of harboring parathyroid carcinoma. A complete tumor survey including bone scan; abdominothoracic imaging and relevant laboratory study including cell counts, biochemical analysis, serum protein and electrophoresis and tumor marker are the rational workup of diagnosis of malignant bone

disease. When a osteolytic lesion of the bone is detected, especially when it is giant cell tumor, even with normal calcium level, PTH assay is necessary to exclude HPT. Treatment of the brown tumor should start with treatment of HPT (parathyroid adenoma) and if persistent after the primary treatment, enucleation and curettage should be added. Compressive lesions with normal compression, functional problem and fracture may regain early surgical intervention (10, 16). When parathyroid adenoma is removed and consecutively serum parathyroid hormone level decreased brown tumor really progress (17).

CONCLUSION

Brown tumors are extremely rare in normocalcemic primary hyperparathyroidism. We have reported a case of rarely seen metabolic bone disease mimicking the presentation of bone metastases. The point in reporting this case is that accurate diagnosis enables the proper treatment to be carried out, avoiding unnecessary harm to the patient.

REFERENCES

1. Yilmazlar S, Arslan E, Aksoy K, Tolunay S. Sellar-parasellar brown tumor: case report and review of literature. *Skull Base*. 2004 Aug;14(3):163-8; discussion168. PubMed PMID: 16145600; PubMed Central PMCID: PMC1151687.
2. Keyser JS, Postma GN. Brown tumor of the mandible. *Am J Otolaryngol*. 1996 Nov-Dec;17(6):407-10. Review. PubMed PMID: 8944301.
3. Mohan M, Neelakandan RS, D Siddharth and Sharma R. An unusual case of brown tumor of hyperparathyroidism associated with ectopic parathyroid adenoma. *Eur J Dent*. 2013; 7(4): 500–503 doi: 10.4103/1305-7456.120657
4. Khalatbari MR, Hamidi M, Moharamzad Y, Setayesh A, Amirjamsh A. Brown Tumors of the Anterior Skull Base as the Initial Manifestation of True Normocalcemic Primary Hyperparathyroidism: Report of Three Cases and Review of the Literature. *Id3*. DOI: 10.5137/1019-5149.JTN.4504-11.2.
5. Naderi N, Alamdari A, Edalatifard M, Allameh SF. A Brown Tumor Simulating Bone Metastases. *Case Reports in Clinical Practice*. 2016 Jan 20;1(1):7-10.
6. Khalil PN, Heining SM, Hum R, et al. Normal history and surgical treatment of brown tumor lesions at various sites in refractory primary hyperparathyroidism. *Eur j Med Res* 2007; 12: 222-230.

7. Syed Z, Khan A. Skeletal effect of primary hyperparathyroidism. *Endocr Pract* 2000; 6: 385-388.
8. Dilip K, Smsnil K, Amic A. Brown tumor of the palate and mandible in association with primary hyperparathyroidism. *J Oral Maxillary Surg* 2001; 59: 1252-1354.
9. Baig MN, Dhaibheid CM, Shannon FJ. Hip fracture in a patient with primary hyperparathyroidism: Medical and surgical lesions. *Cureus* 2018; 10(1) 2104. Doi 10. 7759/cureus 2104.
10. Cebesoy O, Karakok M, Arpacioğlu O, Baltacı ET. Brown tumor with atypical localization in a normocalcemic patient. *Arch Orthop Trauma Surg*. 2007 Sep;127(7):577-80. Epub 2007 Mar 22. PubMed PMID: 17377798.
11. Emin AH, Suoğlu Y, Demir D, Karatay MC. normocalcemic hyperparathyroidism presented with mandibular brown tumor. Report of a case . *Auris Nasus larynx*; 2004; 31; 299-364.
12. Marunia G, Herig A, Paillard M, Mouiller P. Normocalcemic primary hyperparathyroidism; Evidence for a generalized target tissue resistance to parathyroid tumor. *J Clin Endocrinol. Metab* 2003; 88: 4641-4648.
13. Leare H, Memahon DJ, Rubn MR, Bilezikian JP, Silverberg SJ. Normocalcemic primary hyperparathyroidism; Further characterization of a new clinical phenotype. *J Clin Endocrinol Metab* 2007; 92: 3001-3005.
14. Zharg HL, Multiple brown tumor. A diagnostic dilemma. *The Endocrinologist* 2010; 20: 152-154.
15. Lu G, Shih WJ, Xiu JW. Technetium 99m MIBI uptake in recurrent parathyroid carcinoma and brown tumors. *J Nucl Med* 1995;36:811-813.
16. Jebasingh F, Jacob JJ, Shah A, Paul TV, Seshadri MS. Bilateral maxillary brown tumor is the first presentation of primary hyperparathyroidism. *Oral Maxillary Surg* 2008;12:97-100.
17. Al-Gahtany M, Cusimano M, Singer W, Bilbao J, Koracs K, Marotta T. Brown tumor of the skull base; case report and review of the literature. *J Neurosurg* 2003;98:417-420.