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Case Study

Tertiary Hyperparathyroidism Presenting as Multifocal Brown Tumors: A Case Report

Mahmoud Karaki[1], Roy A Raad[2], Carole Saade Riachy[3], Fatima Yasmin[4], Layal Akl[5], Najat Joubran Fares[6], Roula Bou Khalil[7*]

Abstract

Brown Tumor (BT) of the bone is a rare manifestation of hyperparathyroidism (HPTH), an unusual reactive bone lesion attributed to disturbed bone remodeling, from long-standing increase in parathyroid hormone level (PTH). Historically, BTs were described with primary HPTH but due to early diagnosis of this entity, and improved survival in patients with end-stage renal disease (ESRD) especially those on renal replacement therapy (RRT), more cases of BT are now described in this population, and less in PHPTH. Thus, it is mostly the consequence of untreated secondary or tertiary HPTH whose major culprits are chronic kidney disease (CKD) and ESRD. The management of brown tumors related to chronic renal failure consists primarily of its prevention through the use of phosphate binders, vitamin D analogues, and calcimimetics with surgical parathyroidectomy reserved as the final resort in refractory cases. Herein, we present the case of a 24-year-old female patient with ESRD on intermittent hemodialysis (IHD) who developed recent onset facial tumefaction. Blood work revealed markedly elevated PTH at more than 5000 pg/ml, upper borderline hypercalcemia, and hyperphosphatemia. Further investigations with chest computed tomography (CT) and Technetium-99m (99mTc)- Sestamibi scan nuclear imaging showed multiple ribs lytic lesions as well as features of extensive BT and parathyroid adenomas.

[1]Diabetes and Endocrinology, University of Balamand, Beirut, Lebanon

[2]Clinical Assistant Professor, Department of Radiology, New York University (NYU) Grossman School of Medicine, USA

[3]Senior Lecturer, Faculty of Medicine and Pharmacy, Saint Joseph University, Beirut, Lebanon

[4]Diabetes and Endocrinology, University of Balamand, Beirut, Lebanon

[5]Diabetes and Endocrinology, University of Balamand, Beirut, Lebanon

[6]Head of Nephrology division, Saint Georges Hospital University Medical Center, Beirut, Lebanon

[7]Assistant Professor of Clinical Medicine, Diabetes and Endocrinology, Saint Georges Hospital University Medical Center, Beirut, Lebanon

[*]**Corresponding Author:** Roula Bou Khalil, Assistant Professor of Clinical Medicine, Diabetes and Endocrinology, Saint Georges Hospital University Medical Center, Beirut, Lebanon.

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Thereafter, the patient was sent for parathyroidectomy after which the patient developed hungry bone syndrome.

Keywords: Brown tumor; Hyperparathyroidism; Parathyroid hormone level; Renal osteodystrophy; End stage renal disease; Chronic kidney disease.

Introduction

Chronic kidney disease-mineral and bone disorder (CKD-MBD) describes a systemic disorder that incorporates either one or a combination of: abnormalities in calcium, phosphorous, PTH, and vitamin D metabolism, abnormalities in bone turnover as well as in extraskeletal calcification [1]. Renal osteodystrophy (ROD) exclusively defines the morphologic bone changes associated with CKD comprising high and low turnover spectrum of diseases [1,2]. The interplay of phosphate retention, decreased vitamin D (including calcitriol) and calcium related to CKD leads to secondary HPTH [3]. As a result, persistently elevated PTH stimulates osteoclastic activity and bone resorption leading to BT, a form of osteitis fibrosa cystica (OFC) [4]. Here, we describe a case of brown tumor involving the maxillo-facial and ribs regions in a patient on IHD for ESRD.

Case presentation

A 24- year-old female patient was referred to the hospital for weight loss of 12 kg in 1 year despite a stable appetite. The patient had only heat intolerance, denying any history of palpitation and tremor. The patient's medical history is relevant for chronic renal insufficiency for which the patient had been undergoing dialysis three times per week for 18 years. A mass was protruding through the patient face (Figure 1) that appeared around 6 months ago interfering with the patient's mastication and speech along with right sub-axillary tumefaction for 2 years. Serum chemistry revealed an elevated parathyroid hormone PTH level of more than 5000 pg/ml (normal range: 10-55 pg/ml), serum calcium 10 mg/dl (normal range:8.6-10.3 mg/dl), phosphorus 8.3 mg/dl (normal range: 2.8-4.5 mg/dl), serum albumin 4.4 g/dl (normal range:3.4-5.4),thyroid hormone level TSH 1.6 mUI/ml (normal range:0.35-4.5). Further investigations included a computed tomography (CT) scan of the chest that showed multiple lytic lesions in the ribs with large calcified lesion in the soft tissue of the left axilla. Complementary ultrasonography (US) of the neck revealed a 1.5 x 1.1 cm hypoechoic nodule in close contact with the left posterior aspect of the thyroid raising possibility of a parathyroid adenoma. Based on the medical history, clinical manifestations and paraclinical investigations, the most likely diagnosis was Brown Tumor with HPT. To complete the workup, a 99mTc Sestamibi whole-body scan was performed revealing the following findings: right and left inferior parathyroid adenomas with ectopic parathyroid adenoma in the superior mediastinum, extensive foci of intense uptake in the head/neck and chest regions, subsequently localizing to multiple expansile lytic lesions on complimentary SPECT-CT, consistent with extensive Brown Tumors. Dominant lesions include a 4.4 cm right maxillary/cheek mass (Figure 2 and 3) and a 6.7 cm soft tissue mass arising from the

right 11th rib, corresponding to the clinically palpable abnormalities (Figure 4), in addition to multiple expansile osseous lesions within the ribs bilaterally (Figure 5).

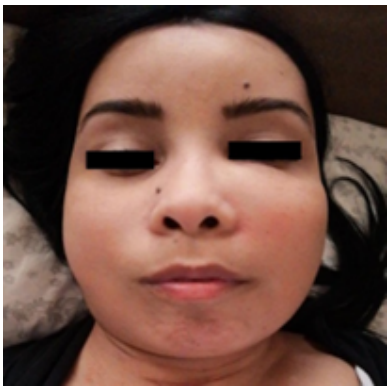

Figure 1: Left cheek tumefaction.

Figure 2: 99m Tc-sestamibi scan showing dominant right maxillary mass compatible with brown tumor.

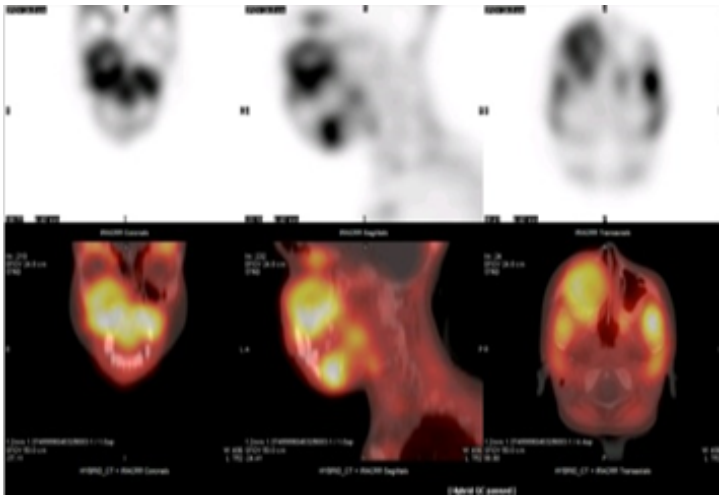

Figure 3: 99mTc-sestamibi scan showing intensely avid well-circumscribed right maxillary mass compatible with brown tumor.

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Patient underwent parathyroidectomy of right and left inferior parathyroid nodules as well as resection of a suspicious superior thyroid nodule in the right lobe with histological examination revealing benign parathyroid adenomas ad papillary carcinoma of the thyroid respectively. Total thyroidectomy was performed 1 month later with pathology showing papillary microcarcinoma 0.2 cm at right lobe. On day 2 post-operation, the patient developed hungry bone syndrome with calcium level reaching 5.6 mg/dl (normal range: 8.8–10.2).

The patient started on one alpha and calcium supplementation. Follow-up US of the neck 4 months later confirmed the absence of parathyroid adenoma. Periodic checks of the patient's PTH and calcium levels are shown in (Table 2).

Test	PTH	Ca
4 months postop	185 pg /ml	7.6 mg / dl
1 year post op	4.8 pg /ml	10.8 mg / dl
1.5 years post op	6.6 pg/ ml	11.6 mg / dl
2 years post op	2 pg / ml	8.8 mg / dl

Table 1: PTH and calcium levels during post-operative period.

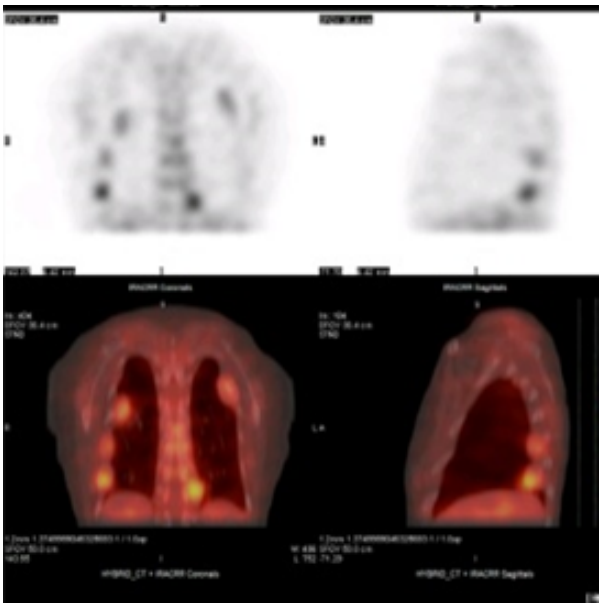

Figure 4: Sestamibi scan showing multiple intense brown tumors in ribs bilaterally.

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Discussion

Chronic renal failure, one of the most common causes of secondary and hence tertiary HPTH, leads to morphologic bone changes, known as renal osteodystrophy including: high bone turnover (OFC), low bone turnover (adynamic bone disease, osteomalacia), and mixed forms (mixed uremic osteodystrophy) [3,5]. Indeed, OFC is a severe entity of skeletal loss manifesting as bone erosions, resorption, cysts, BT and presenting clinically as fractures, bone pain and deformities [6,7].

Brown tumor is a benign lesion resulting from alteration in bone remodeling under the influence of persistently high PTH level over a prolonged period of time [8]. This leads to enhanced osteoclastic activity, along with reactive fibroblastic proliferation resulting in loss of bone trabecular pattern [9].

BT is a rare condition, first described by Friedrich Daniel von Recklinghausen in 1891 [10]. It is well documented in both primary and secondary/tertiary HPTH with a prevalence of 1.5%-1.7% in secondary form as opposed to primary form (3%) and more common among women (threefold) than men [11,12]. However, BT is being increasingly reported in HPTH secondary to renal failure as a result of increased survival of patients on dialysis [11]. The presentation can be either unilocular or multilocular [13]. Moreover, BT may involve maxillo-facial bones, jaw bones with important lesions being rare (0.1%) [14], skull, ribs, femur and rarely the spine with clinical manifestations ranging from asymptomatic to symptoms related to the affected anatomical locations [11,15]. For instance, such tumors can provoke disfigurement, macrognathia with subsequent chewing impairment, compressive symptoms including breathing/speaking difficulty as well as headache and visual disturbances, in addition to oral cavity disorders such as dental displacement and oro-nasal bleeding [16].

Histologically, the characteristic brown color of BT is attributed to the presence of high level of hemosiderin from the agglomerate of osteoclasts and macrophages, with loose connective tissue and focal hemorrhage that replace normal bone tissue [17].

From the radiological point of view, BT can present as incidental findings in many cases. On X-ray, brown tumor appears as well defined radiolucent lytic lesions with thinning of the cortex [18]. CT scans may reveal expansive soft tissue masses and irregular lytic lesions with ground-glass or “salt and pepper” appearance, as in this case, and contrast media uptake [19].

Given that a patient, having undiagnosed BT, may present with weight loss and skin tumefaction, like the patient, along with radiographic lytic lesions, it can be easily mistaken with underlying neoplastic process. In fact, BT mimics multiple myeloma, giant cell granulomas and metastatic lesions mainly from breast cancer or prostate cancer [20].

As a result, it is important to make a prompt differential diagnosis, usually through histological examination, in order to catch malignant diseases at early stages and treat

accordingly, as well as to prevent BT progression and neurologic complications despite its slow growth and non-neoplastic behavior.

The appropriate management of BT is often challenging, as there are no international recommendations to help guide treatment. The focus in management consists primarily of preventive measures and symptomatic control targeting the underlying HPTH in CKD/ESRD. It includes the use of low phosphate diet, meticulous usage of phosphate binders, the addition of native/active vitamin D analogues (i.e.calcitriol), and most importantly calcimimetics in the appropriate setting [21].

However, when conventional and pharmacologic interventions fail or provide minimal benefit, parathyroidectomy (PTX) is recommended and considered as gold standard treatment of secondary/tertiary HPTH in ESRD given that most of BT result from parathyroid adenoma [1].

Furthermore, PTX is especially considered in severe HPTH associated with refractory hypercalcemia, calciphylaxis, debilitating bone disease or unexplained myopathy [22].

sWith the fall in PTH levels, cessation of tumor growth and reduction in lesion size is observed. Nevertheless, surgical excision of BT mass might be required even after PTX [23], especially when the lesions are causing neurological deficits, pathological fractures, deformities interfering with essential one's function and persistent pain or other symptoms despite hyperparathyroidism control [24].

Although PTX is the optimal management of CKD HPTH, it can be complicated by severe hypocalcemia, known as hungry bone syndrome (HBS), as it happened with the patient. HBS is one of the causes of post parathyroidectomy hypocalcemia, attributed to massive transfer of calcium to bone tissue. It is accompanied by normal-high PTH level, low serum phosphate, low magnesium concentration and low 24 hours urinary calcium excretion despite aggressive parental calcium replacement [25].

HBS typically develops between third to fifth postoperative day [25]. Indeed, several risk factors can predict the occurrence of HBS including high preoperative PTH and calcium levels, radiological evidence of bone disease, in addition to large volume of parathyroid adenoma and low vitamin D level [25,26].

Conclusion

Mineral and bone disorders, as well as renal osteodystrophy are complex abnormalities causing morbidity and impaired quality of life in patients with chronic renal failure. BTs, a relevant differential diagnosis in the setting of HPTH and skeletal manifestations, are still overlooked. Early recognition is crucial, along with the exclusion of more serious conditions such as malignancy. Prompt intervention with medical or surgical options may have a better prognosis. Otherwise, untreated BTs lead to debilitated consequences such as bone destruction and compression of surrounding structures.

References

1. Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, et al. Definition, Evaluation, and Classification of Renal Osteodystrophy: A Position Statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2006;69(11):1945-53. PubMed | CrossRef
2. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. 2017;7:1-59. PubMed | CrossRef
3. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. Am J Kidney Dis. 2003;42(4 Suppl 3):S1-201. PubMed
4. Khan A, Bilezikian J. Primary Hyperparathyroidism: Pathophysiology and Impact on Bone. Cmaj. 2000;163(2):184-7. PubMed
5. Waziri B, Duarte R, Naicker S. Chronic Kidney Disease Mineral and Bone Disorder (CKD-MBD): Current Perspectives. Int J Nephrol Renovasc Dis. 2019;12:263-76. PubMed | CrossRef
6. Jervis L, James M, Howe W, Richards S. Osteolytic Lesions: Osteitis Fibrosa Cystica in the Setting of Severe Primary Hyperparathyroidism. BMJ Case Rep. 2017;2017:bcr-2017. PubMed | CrossRef
7. Bandeira F, Cusano NE, Silva BC, Cassibba S, Almeida CB, Machado VCC, et al. Bone Disease in Primary Hyperparathyroidism. Arq Bras Endocrinol Metabol. 2014;58(5):553–61. PubMed | CrossRef
8. Di Daniele N, Condò S, Ferrannini M, Bertoli M, Rovella V, Di Renzo L, et al. Brown Tumour in a Patient with Secondary Hyperparathyroidism Resistant to Medical Therapy: Case Report on Successful Treatment after Subtotal Parathyroidectomy. Int J Endocrinol. 2009;2009. PubMed | CrossRef
9. Marx SJ. Hyperparathyroid and Hypoparathyroid Disorders. N Engl J Med. 2000;343(25):1863-75. PubMed | CrossRef
10. Buchanan WW, Kraag GR, Palmer DG, Cockshott WP. The First Recorded Case of Osteitis Fibrosa Cystica. Can Med Assoc J. 1981;124(6):812. PubMed
11. Baracaldo RM, Bao D, Iampornpipopchai P, Fogel J, Rubinstein S. Facial Disfigurement Due to Osteitis Fibrosa Cystica or Brown Tumor from Secondary Hyperparathyroidism in Patients on Dialysis: A Systematic Review and An Illustrative Case Report. Hemodial Int. 2015;19(4):583-92. PubMed | CrossRef
12. Karagoz A, Turkmen K, Yazici R, Arslan S, Baktık S, Karanis MI, et al. An Exceedingly Rare Localization of a Brown Tumor in a Hemodialysis Patient. Hemodialysis International. 2013;17(4):660-3. PubMed | CrossRef
13. Tayfun H, Metin O, Hakan S, Zafer B, Vardar A. Brown Tumor as an Unusual but Preventable Cause of Spinal Cord Compression: Case Report and Review of the Literature. Asian J Neurosurg. 2014;9(01):40-4. PubMed | CrossRef
14. Pechalova PF, Poriazova EG. Brown Tumor at the Jaw in Patients with Secondary Hyperparathyroidism Due to Chronic Renal Failure. Acta Medica (Hradec Kralove, Czech Republic). 2013;56(2):83-6. PubMed | CrossRef
15. Altan L, Kurtoğlu Z, Yalçınkaya U, Aydınlı U, Ertürk E. Brown Tumor of The Sacral Spine in a Patient with Low-Back Pain. Rheumatol Int. 2007;28:77-81. PubMed | CrossRef
16. Can Ö, Boynueğri B, Gökçe AM, Özdemir E, Ferhatoğlu F, Canbakan M, et al. Brown Tumors: A Case Report and Review of The Literature. Case Rep Nephrol Dial. 2016;6(1):46-52. PubMed | CrossRef
17. Graf C, Huellner M, Tschopp O, Bode-Lesniewska B, Schmid C. 18 F-NaF-PET/CT in Patients with Primary Hyperparathyroidism and Brown Tumors. J Bone Miner Metab. 2020;38:299-309. PubMed | CrossRef
18. Rossi B, Ferraresi V, Appetecchia ML, Novello M, Zoccali C. Giant Cell Tumor of Bone in a Patient with Diagnosis of Primary Hyperparathyroidism: A Challenge in Differential Diagnosis with Brown Tumor. Skeletal Radiol. 2014;43:693-7. PubMed | CrossRef
19. Takeshita T, Takeshita K, Abe S, Takami H, Imamura T, Furui S. Brown Tumor with Fluid-Fluid Levels in A Patient with Primary Hyperparathyroidism: Radiological Findings. Radiat Med. 2006;24:631-4. PubMed | CrossRef
20. Resic H, Masnic F, Kukavica N, Spasovski G. Unusual Clinical Presentation of Brown Tumor in Hemodialysis Patients: Two Case Reports. Int Urol Nephrol. 2011;43:575-80. PubMed | CrossRef

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DOI: https://doi.org/10.37191/Mapsci-2582-7960-4(1)-034

21. Wiederkehr M. Brown Tumor Complicating End-Stage Kidney Disease. Clin Nephrol Case Stud. 2020;8:72. PubMed | CrossRef
22. Rodrigues N, Godinho I, Nogueira EL, Sofia J, López-Presa D, et al. Multiple Brown Tumors-A Rare Presentation in the Modern Era. Clin Nephrol. 2018;89(1):57. PubMed | CrossRef
23. Fatma LB, Barbouch S, Fethi BH, Imen BA, Karima K, Imed H, et al. Brown Tumors in Patients with Chronic Renal Failure and Secondary Hyperparathyroidism: Report of 12 Cases. Saudi J Kidney Dis Transpl. 2010;21(4):772-7. PubMed
24. Cardoso FN, Yanaguizawa M, Taberner GS, Kubota ÉS, Fernandes AD, Natour J. Radiology Contribution for The Evaluation of Secondary Hyperparathryroidism. Revista Brasileira de Reumatologia. 2007;47(3):207-11. CrossRef
25. Witteveen JE, Van Thiel S, Romijn JA, Hamdy NA. Hungry Bone Syndrome: Still A Challenge in The Post-Operative Management of Primary Hyperparathyroidism: A Systematic Review of the Literature. Eur J Endocrinol. 2013;168(3):R45-53. PubMed | CrossRef
26. Kaderli RM, Riss P, Dunkler D, Pietschmann P, Selberherr A, Scheuba C, et al. The Impact of Vitamin D Status on Hungry Bone Syndrome after Surgery for Primary Hyperparathyroidism. Eur J Endocrinol. 2018;178(1):1-9. PubMed | CrossRef