Case Report

Brown tumor of the femur associated with double parathyroid adenomas

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ABSTRACT

Severe parathyroid bone disease is a rare clinical presentation of primary hyperparathyroidism. Double parathyroid adenomas are even more rare cause of primary hyperparathyroidism. The authors present a case of double parathyroid adenomas in a 48-year-old man, who presented with painful left lower limb swelling, which was slowly growing in size in the last 20 years. Magnetic resonance imaging revealed a cystic bony lesion and coincidentally, a urinary bladder calculus. Biopsy of the mass revealed giant cell lesion. Laboratory investigations showed hypercalcemia and hypophosphatemia with elevated parathyroid hormone level. A computerized tomography scan of the neck delineated an adenoma of the left superior parathyroid gland, which was surgically removed. The left inferior parathyroid was also enlarged and was removed. Histological diagnosis confirmed double parathyroid adenomas. The rarity and the interesting clinical presentation of such association are discussed.

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Brown tumors of the bones are benign, slow growing and locally destructive lesions usually involve the ribs, clavicles, pelvic bones and mandible. Pathologically, the lesion is characterized by excessive osteoclast resorption with destruction of the cortical bone and creation of fibrous cysts.[1,2] Bone pain, fragility fractures causing skeletal deformation and altered body stature are the usual sequelae of brown tumors. This severe form of bone disease has been replaced today by characteristic findings of increased bone turnover, which mostly seems to reduce the amount of cortical bone in the appendicular skeleton.[2,3] In the majority of patients with primary hyperparathyroidism (pHPT) (85%) it is caused by solitary parathyroid adenoma (single gland disease), whereas 13% have hyperplasia (multiple gland disease), 1-2% have double adenoma and 1% have carcinoma.[4,5] The severity of hypercalcemia and bone disease in primary hyperparathyroidism are usually related to the serum levels of parathyroid hormone (PTH). As a consequence of hypercalcemia, weakness, weight loss, anorexia, nausea, vomiting, polyurea, polydepsia, recurrent stone formation, bone pain and recurrent fractures frequently occur.[5,6]

Surgery is the treatment of choice for most patients with primary hyperparathyroidism. If performed by an experienced surgeon, the long-term cure rate for initial exploration for non-familial disease is about 98%.[2,5,7] Brown tumor of the femur resulting in multiple fractures and deformities is a rare presentation of a pHPT. In this study, we describe a patient with double parathyroid adenomas causing brown tumors of the left femur and subsequent fractures and review of the literature.

Case Report. A 48-year-old man presented with a slow growing painful swelling of the left femur above the knee joint of 20 years duration. There was a history of repeated fractures during the same period. The patient also gave a history of renal problems in the form of dysuria, hematuria and

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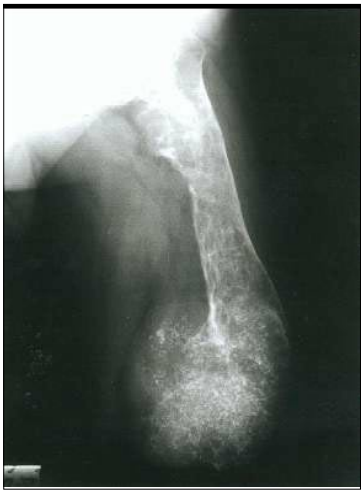

Figure 1 - X-ray of the left femur showing multiple cystic lesions of the entire femur with an expanding bony lesion and amorphous calcifications above the knee joint.

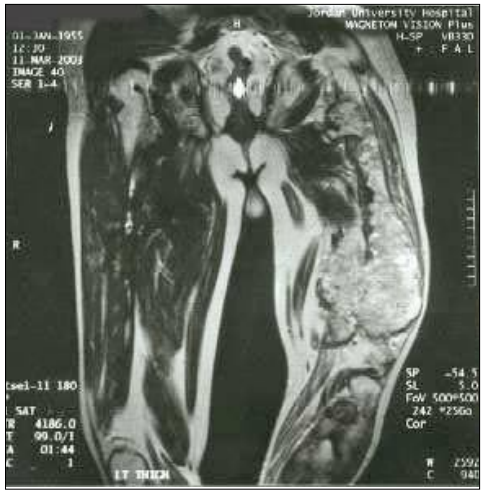

Figure 2 - Coronal T2 weighted image showing multiloculated high signal intensity expansile lesion of the metaphysis and diaphysis of the left femur.

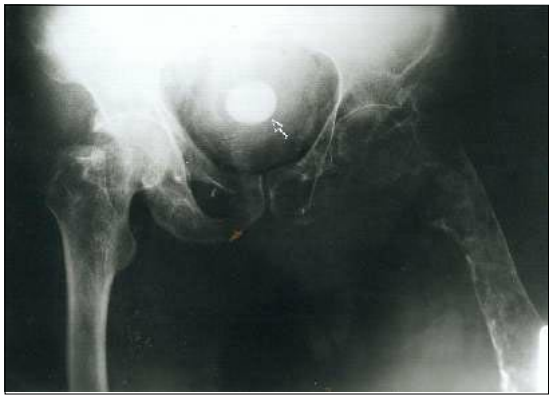

Figure 3 - Plain abdomen x-ray showing an incidental large urinary bladder calculus.

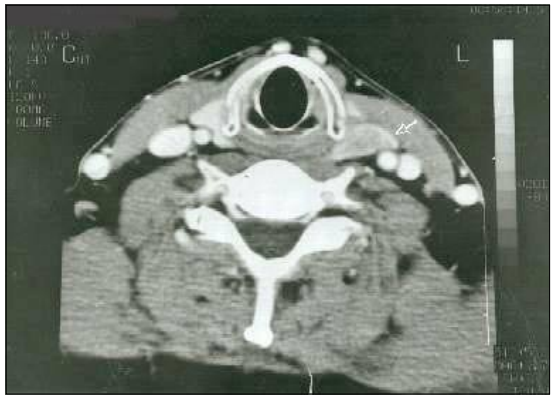

Figure 4 - Neck computed tomogram showing a giant left parathyroid adenoma (small arrow).

frequency. Physical examination of the lesion showed a tender swelling approximately 10x8cm in size above the left knee joint with shortening of the left limb.

Radiography of the lower limb **(Figure 1)** revealed cystic bone lesions involving the entire left femur with bony expansion above the knee joint. Magnetic resonance imaging of the left lower limb confirmed multiloculated cystic bony masses of the left femur **(Figure 2)**. Incisional biopsy of the mass revealed giant cell lesion. The serum levels of calcium was 11.9mg/dl (normal <10.5mg/dl), phosphorus level was 1.9mg/dl (normal 2.4-4.5mg/dl). Parathyroid hormone was 490pg/ml (Normal <54pg/ml) serum alkaline phosphatase was 349U/l (normal up to 100U/l). The patient also had a coincidental large urinary bladder stone on abdominal x-rays **(Figure 3)**.

Computed tomography (CT) of the neck revealed the presence of left parathyroid adenoma measuring 5x3x2cm **(Figure 4)**. Neck exploration with excision of the left superior and left inferior parathyroid adenomas was performed and a second biopsy of the left thigh mass was performed. Macroscopically, the left superior gland was 15gm in weight and the left inferior gland was 920mg in weight. Microscopic examination revealed the presence of double parathyroid adenomas and benign cystic bone lesion containing multinucleated giant cells. The patient had uneventful post-surgical course and his serum calcium was normal on the second postoperative day.

Discussion. The presence of double parathyroid adenoma as a cause of primary hyperparathyroidism is rare, it occurs in 1-2% and is reported to occur in sporadic or familial forms of primary hyperparathyroidism.[5,8,9] Severe parathyroid bone disease is rare today, however, occasional cases of ostitis fibrosa cystica are still reported.[10,11]

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. Brown tumors are benign lesions related to disturbed bone metabolism in patients with hyperparathyroidism; was commonly seen in 1925-1950, as many as 50% of patients presented with severe form of bone disease. Today this figure has fallen to below 10%.[5,12] Brown tumors of the bone typically involve the ribs, pelvic bones and the clavicle and very rarely the long bones such as the femur. There have been occasional reports of involvement of the cricoid,[10] the iliac bone,[13] the tibia,[14] the elbow[15] and the maxilla.[16] A medline review of the literature to May 2003 did not reveal any case of diffuse involvement of the femur with brown tumors resulting from double parathyroid adenoma. Due to its rarity, brown tumors are often mistaken with disseminated malignancy such as multiple myeloma or metastatic cancer.[2] In addition, they have similar radiologic features seen in other cystic bony lesions such as giant cell tumor, giant cell granuloma and aneurysmal bone cyst. However, the multiplicity of these lesions in combination with high serum calcium and low phosphorous should suggest primary hyperparathyroidism. An elevated serum level of PTH confirms the diagnosis.

Both ultrasound (U/S) 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.[17,18] Sestamibi scan, however, is indicated if ectopic PTH producing adenoma is suspected or if the CT scan and the U/S failed in localizing the PTH producing lesion.[19] In hyperparathyroid bone disease and hypercalcemia surgical exploration of the neck is recommended.[2,5,20] Several approaches are described ranging from minimally invasive parathyroidectomy to standard bilateral neck exploration with a success rate of curing hypercalcemia approaching 98%.[2,5,7] Many reports have confirmed dramatic improvement of these patients after parathyroidectomy with significant regression of their bone disease and spontaneous disappearance of brown tumors.[5,7]

In conclusion, primary hyperparathyroidism should be kept in mind in all patients presenting with longstanding history of severe bone disease and hypercalcemia. Finding an elevated serum level of PTH confirms the diagnosis. Surgical excision of the PTH producing lesion is associated with high success rate.

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References

1. Chapman S, Nakielny R. In: Chapman S, Nakielny R, editors. Aid to radiological differential diagnosis. 3rd ed. Edinburgh (UK): Harcourt publishers limited; 2000. p. 25-548.
2. Younes NA, Al-Trawneh IS, Albesoul NM, Hamdan BR, Sroujieh AS. Clinical spectrum of primary hyperparathyroidism. ***Saudi Med J*** 2003; 24: 179-183.
3. Silverberg SJ, Shane E, Jacobs TP, Siris E, Bilezikian JP. A 10 year prospective study of primary hyperparathyroidism with or without parathyroid surgery. ***N Engl J Med*** 1999; 341: 1249-1255.
4. Thompson NW, Eckhauser F, Harness J. The anatomy of primary hyperparathyroidism. ***Surgery*** 1982; 92: 814-821.
5. Delbridge LW, Younes NA, Guinea AI, Reeve TS, Clifton-Bligh P, Robinson BG. Surgery for primary hyperparathyroidism 1962-1996: indications and outcomes. ***Med J Aust*** 1998; 168: 153-156.
6. Heath H. Clinical spectrum of primary hyperparathyroidism: Evolution with changes in medical practice and technology. ***J Bone Miner Res*** 1991; 6: S63-S70.
7. Clark OH, Wilkes W, Siperstein AE, Duh QY. Diagnosis and management of primary hyperparathyroidism: safety, efficacy and deficiencies in our knowledge. ***J Bone Miner Res*** 1991; 6 (Suppl 2): 135-142.
8. Attie JN, Bock G, Augeste LJ. Multiple parathyroid adenomas: report of thirty-three cases. ***Surgery*** 1990; 108: 1014-1019.
9. Roses DF, Karp NS, Sudarsky LA, Valensi QJ, Rosen RJ, Blum M. Primary hyperparathyroidism associated with two enlarged parathyroid glands. ***Arch Surg*** 1989; 124: 1261-1265.
10. Blinder G, Hiller N, Matas M. Gail N, Shilo S. Brown tumour in the cricoid cartilage: an unusual manifestation of primary hyperparathyroidism. ***Ann Otol Rhinol Laryngol*** 1997; 106: 253-254.
11. Case records of The Massachusetts General Hospital Weekly clinics pathological exercises. Case 14-1993. A 74-year-old woman with hyperpara-thyroidism and osteolytic lesion in the humerus. ***N Engl J Med*** 1993; 328: 1031-1035.
12. Silverberg SJ, Bilezikian JP. Evaluation and management of primary hyperparathyroidism. ***J Clin Endocrinol Metab*** 1996; 81: 2036-2040.
13. Ishikawa S, Ozaki T, Kawai A, Inoue H, Doihara H. Hyperparathyroid crises in a patient with a giant brown tumor of the iliac bone: a case report. ***Hiroshima J Med Sci*** 1998; 47: 27-30.
14. Chuang TC, Chang JM, Hwang SJ, Hsiao PJ, Lai YH. A patient with primary hyperparathyroidism with full-blown bone changes simulating malignancy. ***Kaohsiung J Med Sci*** 1998; 14: 584-589.
15. Jap TS, Ho LT, Chang CY. Hyperparathyroidism presenting as a large bone tumor. A case report. ***S Afr Med J*** 1989; 75: 393-394.
16. Merz MN, Massich DD, Marsh W, Schuller DE. Hyperparathyroidism presenting as brown tumor of the maxilla. ***Am J Otolaryngol*** 2002; 23: 173-176.
17. Scheible W, Deutsch AL, Leopold GR. Parathyroid adenoma: accuracy of preoperative localization by high resolution real time sonography. ***J Clin Ultrasound*** 1981; 9: 325-330.
18. Krubsack AJ, Wilson SD, Lawson TL, Collier BD, Hellman RS, Isitman AT. Prospective comparison of radionuclide, computed tomographic and sonographic localization of parathyroid tumors. ***World J Surg*** 1986; 10: 579-585.
19. McBiles M, Lambert AT, Cote MG, Kim SY. Sestamibi parathyroid imaging. ***Semin Nucl Med*** 1995; 25: 221-234.
20. Eigelberger MS, Clark OH. Surgical approaches to primary hyperparathyroidism. ***Endocrinol Metab Clinics*** 2000; 29: 479-502.