VIA MEDICA

CASE REPORT

Konrad Tałasiewicz, Aleksandra Czachowska, Katarzyna Śmiałek-Kania, Beata Jagielska

Department of Oncology Diagnostics, Cardioncology and Palliative Medicine, Maria Sklodowska-Curie Institute — Oncology Center in Warsaw

Multiple brown tumours in the course of primary hyperparathyroidism mimicking bone metastases — case report

Address for correspondence:
Lek. Konrad Tałasiewicz
Klinika Diagnostyki Onkologicznej,
Kardioonkologii i Medycyny Paliatywnej
Centrum Onkologii — Instytut
im. Marii Skłodowskiej-Curie
ul. Roentgena 5, 02–781 Warszawa
e-mail: ktalasiewicz@gmail.com

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ABSTRACT

Brown tumours (especially multiple) are uncommon manifestations of primary hyperparathyroidism (PHPT) in developed countries. Although PHTP can cause various symptoms, it can often be mistaken for malignancy. The disease itself (although curable) can lead to disabilities and other serious complications. Herein we report the case of a 65-year-old patient with multiple brown tumours as a very rare first manifestation of normocalcaemic form of primary hyperparathyroidism caused by a giant parathyroid adenoma.

Key words: brown tumours, giant parathyroid adenoma, primary hyperparathyroidism

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Introduction

Primary hyperparathyroidism (PHPT) relates to excessive production of parathormone (PTH) in the parathyroid glands. The most common cause of the disease is a sporadic adenoma (85–95%). Less frequently, parathyroid carcinomas, multiple endocrine neoplasia, genetic syndromes, or metabolic diseases can explain a new diagnosis of PHPT [1, 2].

The persistent elevated level of PTH relates to the activation of calcitriol receptors in various peripheral target organs like the kidney, small intestine, and bones. An elevated level of calcium leads to typical symptoms like renal lithiasis, nephrocalcinosis, calcification of vascular and heart valve-cusps, acute or chronic pancreatitis, and chondrocalcinosis. Sometimes a single bone lesion, multiple bone lesions, or even parathyroid crisis may be the first sign of newly diagnosed PHTP [2].

Although many patients are asymptomatic (up to 70–80%), elevated ionised calcium plasma levels are commonly observed in these cases [3].

Primary hyperparathyroidism is the only cause of hypercalcaemia associated with high concentrations of serum PTH (> 55 pg/mL) [2].

Case description

A 65-year-old male was admitted to a regional trauma centre because of significant pain in his right arm, which materialised while exiting a car. An X-ray of the upper right limb confirmed a pathological humerus fracture (Fig. 1). Because of pain in both knees an additional X-ray of this area was done, which confirmed multiple pathological lytic lesions in both femoral bones (Fig. 2).

The arm fracture was treated non-operatively by shoulder immobilisation. The patient was referred to a specialised oncology centre because of the probable metastatic nature of the lesions in his bones, suspected to be the cause of the pathological fracture.

Three years before this incident, the patient was hospitalised because of a rupture of both quadriceps

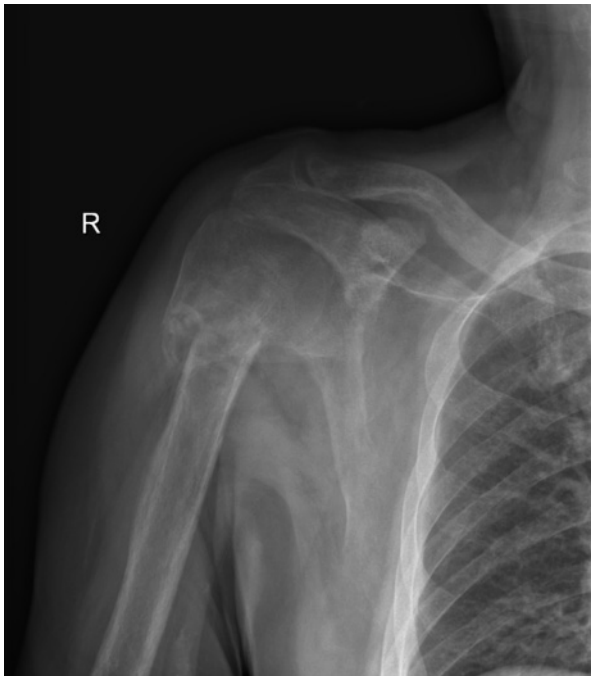

Figure 1. Pathologic humerus fracture

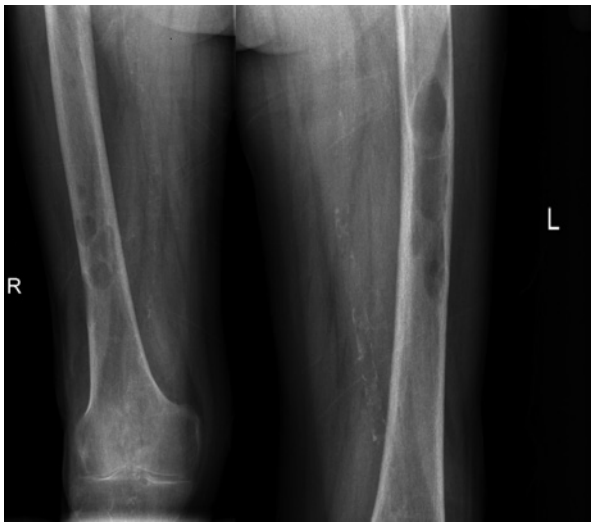

Figure 2. Multiple brown tumors in femurs

tendons, which resulted in persistent pain and permanent disability. At the same time, the patient experienced acute coronary syndrome, after which a multivessel coronary disease (MCD) was found. After a coronary percutaneous intervention, the patient eventually required a coronary artery grafting bypass. Subsequently, contrast-induced chronic kidney disease (stage 3B) was diagnosed. The patient was under constant ambulatory supervision by his general practitioner, as well as a nephrologist, a cardiologist, an orthopaedic surgeon, and a physical medicine and rehabilitation physician.

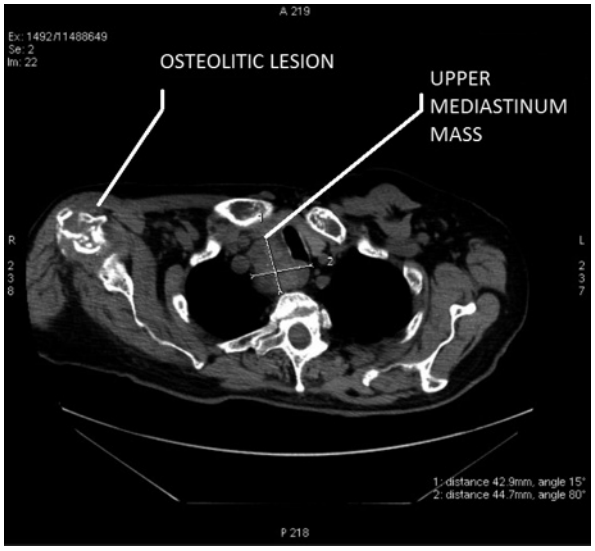

Figure 3. Upper mediastinum mass and osteolytic lesions (brown tumors)

The patient was in poor physical and psychological condition during the admission to the hospital due to the disability caused by the patient's history and the metastatic cancer disease diagnosis. Laboratory analysis showed that alkaline phosphatase was 1069 IU/l (5–136), beta-2-microglobulin was 8.18 mg/L (0.70–1.80), calcium level was 2.49 mmol/l (2.10–2.60), albumins were 39.6 g/l (38.3–46.9), creatinine was 2.85 mg/dl (0.6–1.3), and LDH was 122 IU/l (85–227).

A CT full body scan (without contrast) revealed multiple metastatic bone lesions in all the examined bones with various regions noted for a risk of fracture. Chest scans showed a heterogeneous tumour sized 45 × 43 mm in the upper mediastinum (behind the right thyroid lobe) (Fig. 3). Bone scintigraphy revealed increased uptake of ^{99m}Tc-MDP in all bones — suggesting multiple bone metastases.

To exclude multiple myeloma, a bone marrow biopsy and other serum tests were performed, and the results were negative. Due to the localisation of the tumour, we decided to perform an endoscopic ultrasound with fine-needle aspiration and a core biopsy of the lesion. Unfortunately, the results were inconclusive (thyroglobulin staining was negative) — a pathologist could only suggest the possible differentiation between ectopic thyroid gland/thyroid adenoma/thyroid carcinoma.

After a multidisciplinary team meeting, the patient was qualified for palliative treatment of thyroidectomy and external beam radiotherapy for bone metastases ± radioiodine therapy (due to possible thyroid malignancy).

After our request, further documentation from prior hospitalisations and out-patient clinics was delivered, which showed highly-elevated calcium levels and a decreased level of inorganic phosphor over the course of various patient visits. Due to this fact, we decided to test

the parathormone (PTH) level, which was unsurprisingly high 1528 pg/ml (14–72).

These results led us to the conclusion that the most probable cause of all the symptoms presented by our patient were caused by primary hyperparathyroidism (PHPT) due to the parathyroid adenoma (or less probably by parathyroid cancer or other less probable causes of PHPT).

These results were confirmed during the surgery, when the 6-cm tumour was removed. After the procedure, we observed "hungry bones syndrome", which needed calcium and vitamin D supplementation. After the procedure, PTH levels dropped. After a few months of rehabilitation and further treatment in the endocrinology unit the patient was cured from the disease.

Discussion

Osteitis fibrosis cystica (or osteodystrophia fibrosa, von Recklinhausen disease of the bone) is a benign bone disease caused by elevated levels of PTH due to primary hyperparathyroidism, which leads to an excessive osteoclast reaction. Osteoclasts cause lytic bone lesions, which can be seen on bone scintigraphy (with increased uptake of ^{99m}Tc-MDP) [4], X-rays, or CT scans [5]. Unfortunately, these lytic lesions can be mistakenly taken as a giant cell tumour, multiple bone metastases or multiple myeloma [4, 6–8]. It should be emphasised that today hyperparathyroidism bone disease or nephrolithiasis are rarely seen as a first manifestation of the disease, due to the common evaluation of serum calcium level for various reasons. At present, in western countries, the disease is mainly "asymptomatic", causing mostly psychological and psychiatric disorders [9, 10].

In the case report above, achieving the right diagnosis was difficult because we found calcium levels to be normal during the diagnostic process. This can be explained by a concurrent low level of vitamin D — our patient's vitamin D level was 3.67 ng/ml (> 20). Although the problem of vitamin D deficiency in PHPT is a well-known problem [11], recently it has been highlighted that it can be related to the normocalcaemic form of PHPT [12]. However, in most of the cases of PHPT patients might have a normal calcium level at some point during the course of the disease, which is probably what happened in this case [13]. Another difficulty was the misleading pathologic report and the fact that parathyroid adenomas are usually very small (weight between 70 mg and 1 g). There are only sporadic reports of giant adenomas [14]. Brown tumours (especially multiple) are also a very uncommon manifestation of PHPT in developed countries (< 1%) [15], so the case reported herein is an extremely rare example of such a severe disorder caused by prolonged PTH stimulation.

Finally, the presented patient suffered with typical symptoms of PHPT, like tendon ruptures (in cases of persistent ruptures, PHPT always should be taken into consideration), renal insufficiency, lytic bone lesions, cardiovascular disease, and psychological disorders because they went unrecognised as a PHPT manifestation over several years.

Conclusions

Although PHTP can cause various symptoms, it can often be mistaken for malignancy. The disease itself (although curable) can lead to disabilities and other serious complications. An early diagnosis appears to be crucial in avoiding complete manifestation of the disease. PHTP should always be considered in patients presenting multiple lytic bone lesions even with normal calcaemic levels. This can save time and resources and ultimately lead to proper patient treatment.

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Conflicts of interest disclosures

The authors declare that they have no competing interest.

References

1. Mackenzie-Feder J, Sirrs S, Anderson D, et al. Primary hyperparathyroidism: an overview. Int J Endocrinol. 2011; 2011: 251410, doi: 10.1155/2011/251410, indexed in Pubmed: 21747852.
2. Sitges-Serra A, Bergenfelz A. Clinical update: sporadic primary hyperparathyroidism. Lancet. 2007; 370(9586): 468–470, doi: 10.1016/S0140-6736(07)61213-6, indexed in Pubmed: 17693163.
3. Fraser W. Hyperparathyroidism. Lancet. 2009; 374(9684): 145–158, doi: 10.1016/s0140-6736(09)60507-9, indexed in Pubmed: 19595349.
4. Rubin MR, Livolsi VA, Bandeira F, et al. Tc99m-sestamibi uptake in osteitis fibrosa cystica simulating metastatic bone disease. J Clin Endocrinol Metab. 2001; 86(11): 5138–5141, doi: 10.1210/jcem.86.11.7994, indexed in Pubmed: 11701666.
5. Sandoval MA, Paz-Pacheco E. Primary hyperparathyroidism with classic and severe skeletal involvement. BMJ Case Rep. 2010; 2010, doi: 10.1136/bcr.04.2010.2929, indexed in Pubmed: 22767476.
6. Lee JaH, Chung SM, Kim HSu. Osteitis fibrosa cystica mistaken for malignant disease. Clin Exp Otorhinolaryngol. 2013; 6(2): 110–113, doi: 10.3342/ceo.2013.6.2.110, indexed in Pubmed: 23799171.
7. Hsieh MC, Ko JY, Eng HL. Pathologic fracture of the distal femur in osteitis fibrosa cystica simulating metastatic disease. Arch Orthop Trauma Surg. 2004; 124(7): 498–501, doi: 10.1007/s00402-004-0697-y, indexed in Pubmed: 15168133.

8. Ullah E, Ahmad M, Ali SA, et al. Primary hyperparathyroidism having multiple Brown tumors mimicking malignancy. Indian J Endocrinol Metab. 2012; 16(6): 1040–1042, doi: 10.4103/2230-8210.103037, indexed in Pubmed: 23226663.
9. Walker MD, Rubin M, Silverberg SJ. Nontraditional manifestations of primary hyperparathyroidism. J Clin Densitom. 2013; 16(1): 40–47, doi: 10.1016/j.jocd.2012.11.008, indexed in Pubmed: 23374740.
10. Bilezikian JP, Khan AA, Potts JT, et al. Third International Workshop on the Management of Asymptomatic Primary Hyperthyroidism. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the third international workshop. J Clin Endocrinol Metab. 2009; 94(2): 335–339, doi: 10.1210/jc.2008-1763, indexed in Pubmed: 19193908.
11. Silverberg SJ, Shane E, Dempster DW, et al. The effects of vitamin D insufficiency in patients with primary hyperparathyroidism. Am J Med. 1999; 107(6): 561–567, doi: 10.1016/s0002-9343(99)00294-6, indexed in Pubmed: 10625024.
12. Souberbielle JC, Friedlander G, Cormier C. Practical considerations in PTH testing. Clin Chim Acta. 2006; 366(1-2): 81–89, doi: 10.1016/j.cca.2005.10.010, indexed in Pubmed: 16310759.
13. Cusano NE, Silverberg SJ, Bilezikian JP. Normocalcemic primary hyperparathyroidism. J Clin Densitom. 2013; 16(1): 33–39, doi: 10.1016/j.jocd.2012.12.001, indexed in Pubmed: 23374739.
14. Power C, Kavanagh D, Hill ADK, et al. Unusual presentation of a giant parathyroid adenoma: report of a case. Surg Today. 2005; 35(3): 235–237, doi: 10.1007/s00595-004-2902-6, indexed in Pubmed: 15772795.
15. De Crea C, Traini E, Oragano L, et al. Are brown tumours a forgotten disease in developed countries? Acta Otorhinolaryngol Ital. 2012; 32(6): 410–415, indexed in Pubmed: 23349562.