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Case Report

CASE REPORT

A case of oncogenic osteomalacia owing to inguinal tumor

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Abstract

The oncogenic hypophosphatemic osteomalacia is a very incapacitating disease and the mortality rate, mainly due to metabolic disorder, depends on the early diagnosis, since the surgery is curative. The major difficulty is to consider this kind of disease in patients with complex clinical presentation. Moreover, medical centers have to provide a good diagnostic infrastructure because these tumors, in most cases, are small and do not have an obvious site. This case report is about a man with a rapid loss of strength and muscle mass, which had his diagnosis in a late, culminating in significant deformities and organic dysfunctions with clinical repercussions. However, the fast diagnosis with appropriate tests determined the stop point of the evolution of disease and marked the beginning of metabolic recovery. This case reinforces the global problem health care infrastructure and the access to diagnostic equipment, demonstrating the impact on the patient's health of our service.

INTRODUCTION

Oncogenic hypophosphatemic osteomalacia (OHO) is a rare paraneoplastic syndrome, in most cases induced by small benign mesenchymal tumors in any location [1, 2]. The structural deformations are induced by bone demineralization, presenting hypophosphatemia and 1,25-dihydroxy-vitamin D, hyperphosphaturia and initial normal serum parathyroid hormone (PTH), calcium and 25-hydroxy-vitamin-D levels.

These structural and laboratory changes are consequences of excessive fibroblast growth factor 23 (FGF 23) secreted by the tumor, that causes low tubular phosphorus absorption and modify the renal hydroxylation of vitamin D [3, 4]. Gradually, the patient develop pain on walking and during routine activities, associated to body moves limitations, multiple fractures, renal and cardiac dysfunction and death. Nevertheless, a simply resection of this tumor stops the evolution [5].

CASE REPORT

A 40-year-old patient, male, was referred to the General Surgery Unit of Complexo Hospitalar Santa Casa with several structural deformities (fractures with poor bone healing, vertebral and limb shortening) that have evolved over the last three years. Bone destruction, fractures, salt and pepper skull effect was demonstrated. These fractures generated a thoracic architecture deformity by spine and ribs alterations. This condition

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Table 1: Preoperative laboratory exams.

Exams	Values
Total proteins (serum) (NR: 6.0–8.5 g/dl)	7.2 g/dl
Albumin (NR: 3.5–4.8 g/dl)	4.41 g/dl
Alpha-1 globulin (NR: 0.1–0.3 g/dl)	0.27 g/dl
Alpha-2 globulin (NR: 0.5–1.1 g/dl)	0.76 g/dl
Beta-1 globulin (NR: 0.36–0.52 g/dl)	0.36 g/dl
Beta-2 globulin (NR: 1.21–2.70 μg/ml)	0.40 μg/dl
Gamma globulin (NR: 0.5–1.4 g/dl)	1.00 g/dl
Thyroid stimulating hormone (TSH) (NR: 0.5–6,0 μU/ml)	4.88 μU/ml
PTH (NR: 10–65 pg/ml)	189.2 pg/ml
Urinary protein (NR: 0–20 mg/dl)	0.45 g/dl
Anti-nuclear antibody (NR: negative)	Negative
Calcium (serum) (NR: 4.4–5.4 mg/dl)	9.8 mg/dl
Inorganic phosphorus (serum) (NR: 3.4–4.5 mg/dl)	1.7 mg/dl
Inorganic phosphorus (urinary) (NR: 400–1.300 mg/24 h)	681 mg/24 h
25-Hydroxy-vitamin-D (NR: >30.0 ng/ml)	30 ng/ml

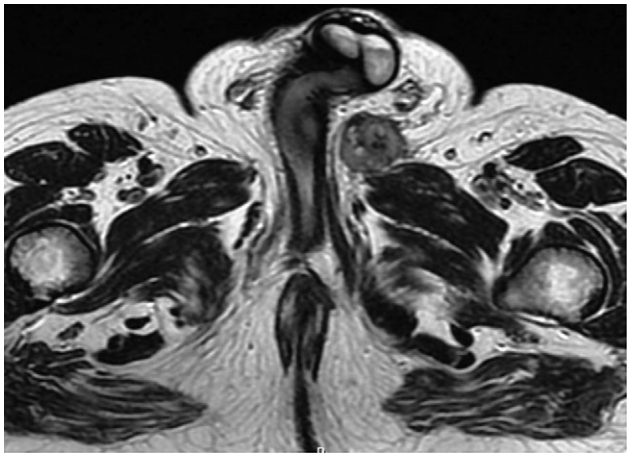

Figure 1: MRI (inguinal view).

started with pain to walk that progressed to walking disability without aid.

In one year, he suffered an acute myocardial infarction without known primary risk factors. The heart evaluation by a transthoracic echocardiogram has shown a left ventricular dysfunction—grade 2, diffuse hypokinesia, diastolic dysfunction—grade 2, minimal mitral regurgitation and a 35% ejection fraction. Due to the volumetric decrease of the thorax, the pulmonary function deteriorated.

The investigation started with some laboratory exams in an attempt to elucidate the cause of the structural deformities (osteomalacia) (Table 1).

He had some radiographic exams that showed multiple fractures in limbs, decreased axial skeleton and loss of bone mass. The computer tomography (CT) revealed a diffuse reduction of bone attenuation coefficient and vertebral depression, suggesting osteoporosis. However, no visceral abnormality was found. At the clinical examination, no additional anatomical changes were found to detect the initial site of the disease. A whole-body magnetic resonance imaging (MRI) (Fig. 1) found a nodular image in left inguinoscrotal area ($2.5 \times 2.1 \times 30\,cm^3$), with heterogeneous signal intensity in T1 and T2 and high contrast impregnation near the left Long Adductor Muscle, without invasion, followed by lymph nodes. It was also found fracture

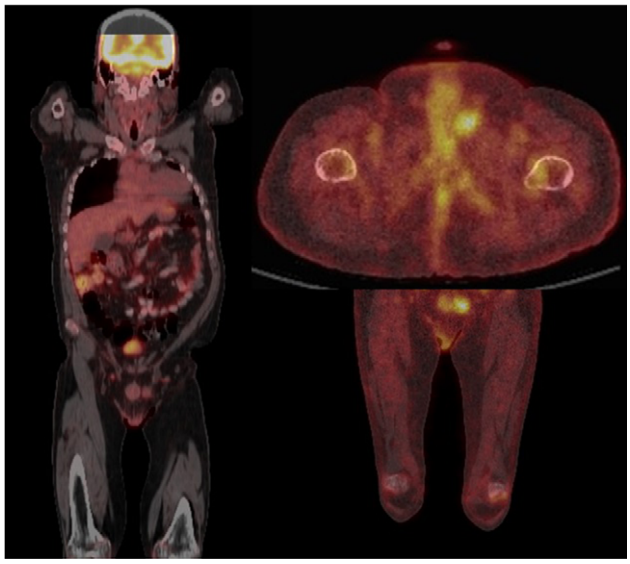

Figure 2: PET-CT.

signs in inferior ischiopubic area, bilateral, pubic and femur, suggesting pathologic fractures.

Due to the high suspicion of a secretive tumor, the surgical team decided to investigate with a whole-body positron emission tomography (PET/CT) (Fig. 2) that found several bone deformities by metabolic disorder and a nodular lesion (soft part aspect on acral site) located on the subcutaneous tissue, left inguinal region at the base of the scrotum, prior to the medial margin of the pectineus muscle, measuring $2.5 \times 1.6\,cm^2$ (SUV 3.8).

The bone scintigraphy with technetium (Figs 3 and 4), that can be performed to study the degree of loss of bone mass and other structural abnormalities, found a diffuse capitation in multiple articulations (arms, legs, ribs, spine, head and pelvis) compatible with bone wear and the same scrotal injury.

The final diagnosis was confirmed after a surgical resection with free margins, that presented to histopathological and immunohistochemical analysis, a mesenchymal phosphaturic tumor with $3.5 \times 3.0 \times 2.0\,cm^3$ without invasion, known as OHO (Table 2). Our service could not afford the necessary kit for FGF-23 testing.

After seventh postoperative day and continuous multivitamin and mineral supplementation (indicated by our Nutrition Team), the patient underwent a second transesophageal echocardiogram, presenting a great improve of cardiac parameters, with normal chamber function and a 66% ejection function (much more than we expected). No cardiovascular intervention was performed, except respiratory physiotherapy. Postoperative laboratory exams improved drastically (Table 3). After three months, the pain almost disappeared with low levels of analgesics, physiotherapy two times a week, walking without aid and normal lung function.

DISCUSSION

Disabling diseases are common, like trauma consequences, some kind of cancers or congenital malformations. Nevertheless, some diseases that causes such damage to the patient, society and costs to government could be treated since the first signals and have a better upshot. In case of OHO, this kind of tumor, when simply resected with free margin, determinate the cure of this disease and stop the evaluation to

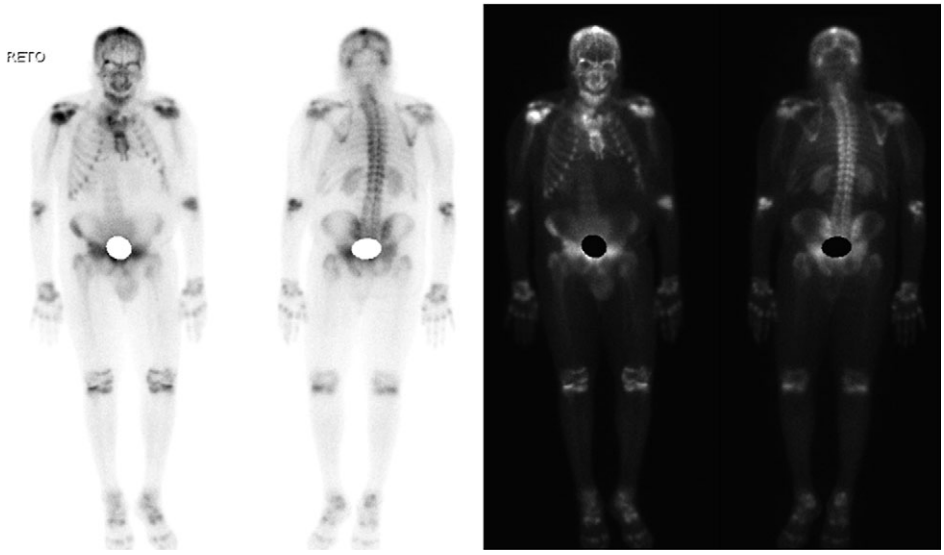

Figure 3: bone scintigraphy with technetium.

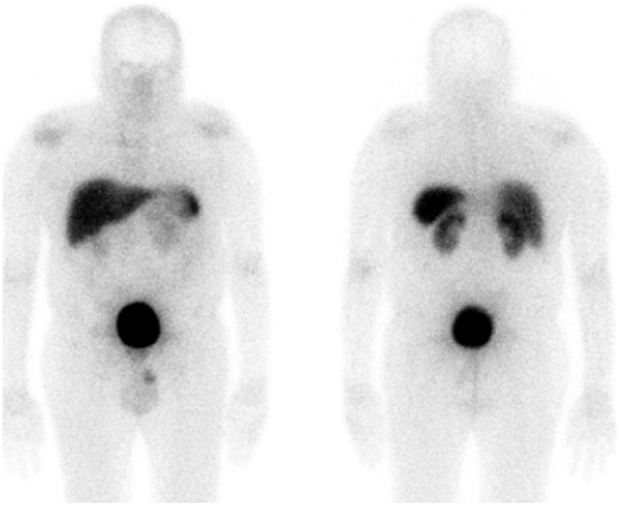

Figure 4: bone scintigraphy with technetium (focus).

Table 2: Immunohistochemical analysis.

Antibody	Results
Vimentin (V9)	Positive
CD 56 (123C3)	Positive
CD 99 (12-E7)	Positive
CD 34 (QBEnd-10)	Negative
CD 57 (TB 01)	Negative
S100 automated (p)	Negative
Actine ML (1A4)	Negative
CKM automated (AE1/AE3/PCK26)	Negative
CK 7 automated (SP52)	Negative
GFAP (6F2)	Negative
NSE (BBS/NC/V I-H14)	Negative
Sinaptophisine automated (Sp11)	Negative
Ki 67 automated (30–9)	3%

Table 3: Postoperative laboratory exams.

Exams	Values
Total proteins (serum) (NR: 6,0–8.5 g/dl)	7.4 g/dl
Albumin (NR: 3.5–4.8 g/dl)	4.02 g/dl
Alpha-1 globulin (NR: 0.1–0.3 g/dl)	0.29 g/dl
Alpha-2 globulin (NR: 0.5–1.1 g/dl)	0.93 g/dl
Beta-1 globulin (NR: 0.36–0.52 g/dl)	0.31 g/dl
Beta-2 globulin (NR: 1.21–2.70 μg/ml)	0.67 μg/dl
Gamma globulin (NR: 0.5–1.4 g/dl)	1.18 g/dl
Thyroid stimulating hormone (TSH) (NR: 0.5–6,0 μU/ml)	4.65μU/ml
PTH (NR: 10–65 pg/ml)	59 pg/ml
Urinary protein (NR: 0–20 mg/dl)	4.56 g/dl
Anti-nuclear antibody (NR: negative)	Negative
Calcium (serum) (NR: 4.4–5.4 mg/dl)	5.2 mg/dl
Inorganic phosphorus (serum) (NR: 3.4–4.5 mg/dl)	3.8 mg/dl
Inorganic phosphorus (urinary) (NR: 400–1.300 mg/24 h)	729 mg/24 h
25-Hydroxy-vitamin-D (NR: > 30,0 ng/ml)	38 ng/ml

limited structural and organic dysfunction [6, 7]. There is no large review about OHO tumoral location (maybe because there is no specific site to this cancer grow up), but probably this is not the first one with inguinal location. One important aspect is to be secure that all tumoral lesion was removed (not just to prevent an uncommon recidive, but to cure the disease) and a perioperative analysis by pathologist can solve that question.

The early search for tertiary centers with expertise in OHO are the basis to have good results with no or minimum sequelae. The physician that takes into account some nonspecific points, like pain and difficult to walk, that many times could be confused with orthopedic diseases, is the key point to this patient life [8]. Simple laboratory tests (serum and urinary phosphorus, calcium, vitamin D varieties, PTH) and some radiographs could help the diagnosis without so much cost [7].

Several genetic and acquired diseases must be differentiated to OHO, once can be found elevated FGF-23 and clinical characteristics (OHO-like). Mesenchymal tumors can have

recurrences, but OHO does not need regular screening tests because of the low incidence of recurrences [7]. Our team proposes just a regular clinical review, following the recovery of motor function and clinical implications, only requesting some tests if there are complaints. In some services, radiological work up functional imaging is done before anatomical imaging, but that's not a reality of all medical centers because this exams are expensive and restrict to few centers.

The great challenge is how to locate exactly this mesenchymal tumor site. Nowadays, the main exams include CT, MRI and scintigraphy with some radioisotope (technetium is the most commonly used) [9]. These kinds of exams are very expensive and normally not easy to be found in the routine of the medical center radiology units around the world. There is no consensus on literature about the gold standard exam, but most services use MRI to screen the tumoral site.

The close follow up in rehabilitation to reintegrate this patient to family and society is crucial, once this disease starts, mostly, when this individual is economically active and has a family [10].

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

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ETHICAL APPROVAL

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CONSENT

Linked document.

GUARANTOR

Luiza Tonello and Arthur Paredes Gatti.

REFERENCES

1. Chong WH, Molinolo AA, Chen CC, Collins MT. Tumor induced osteomalacia. *Endocr Relat Cancer* 2011;**18**:53–77.
2. Folpe AL, Fanburg-Smith JC, Billings SD, Bisceglia M, Bertoni F, Cho JY, *et al.* Most osteomalacia-associated mesenchymal tumors are a single histopathologic entity. *Am J Surg Pathol* 2004;**28**:1–30.
3. Nelson AE, Robinson BG, Mason RS. Oncogenic osteomalacia: is there a new phosphate regulating hormone? *Clin Endocrinol (Oxf)* 1997;**47**:635–42.
4. Jerkovich F, Moncet D, Babini S, Zoppi JA, Graciolli F, Oliveri B. Osteomalacia oncogénica—presentación de dos casos. *Medicina* 2015;**75**(1):37–40.
5. Ray S, Chakraborty PP, Blswas K, Ghosh S, Mukhopadhyay S, Chowdhury S. A case of oncogenic osteomalacia due to occult nasal sinus tumor. Clinical cases in mineral and bone. *Metabolism* 2015;**12**(1):65–8.
6. Chang CV, Conde SJ, Luvizotto RAM, Nunes VS, Bonates MC, Felicio AC, *et al.* Oncogenic osteomalacia: loss of hypophosphatemia might be the key to avoid misdiagnosis. *Arq Bras Endocrinol Metab* 2012;**56**(8):570–3.
7. Jonsson KB, Zahradnik R, Larsson T, White KE, Sugimoto T, Imani shi Y, *et al.* Fibroblast growth factor 23 in oncogenic osteomalacia and Xlinked hypophosphatemia. *N Engl J Med* 2003;**348**:1656–63.
8. Radaideh ARM, Jaradat D, Abu-Kalaf MM, Nusier MK. Resolution of severe oncogenic hypophosphatemic osteomalacia after resection of a deeply located soft-tissue tumour. *Curr Oncol* 2009;**16**(5):87–90.
9. Serafini EM, Pisarevsky AA, Plumet Garrido J, Zamora RJ, Petrucci EA. Osteomalacia inducida por tumor: hemangiopericitoma rinosinusal. *Medicina* 2013;**73**:39–42.
10. Qari H, Hamao-Sakamoto A, Fuselier C, Cheng YL, Kessler H, Wright J. Phosphaturic mesenchymal tumor: 2 new oral cases and review of 53 cases in the head and neck. *Head Neck Pathol* 2015,1–9.