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Oncogenic hypophosphatemic osteomalacia: From the first signal of disease to the first signal of healthy

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ABSTRACT

INTRODUCTION: The physical incapacitation of the oncogenic hypophosphatemic osteomalacia (OHO) can be catastrophic and can lead to deformities, metabolic and organic instability and death. The only positive outcome is through early diagnosis by the clinical suspicion. At this moment, medical center infrastructure is also a keypoint.
PRESENTATION OF CASE: This case report is about a 60-year old woman with multiple fractures, gradual loss of strength and muscle mass and limiting deformities in two years of evolution until the diagnostic.
DISCUSSION: The lack of knowledge of this disease causes a delay in diagnosis that can bring deformities to the patient, as well as death. Is crucial that is hypothesized to carry out the necessary tests, since they are expensive and not always available.
CONCLUSION: This case reinforces the importance to understand the OHO and tumoral search, once this lesion is, in most cases, imperceptible to physical examination or several imaging studies.

1. Introduction

OHO is an uncommon paraneoplastic syndrome, mostly induced by small benign mesenchymal tumors that can be found in any location [1]. This syndrome causes structural deformations by demineralization of the bone owing to low levels of phosphatemia and 1,25-dihydroxy-vitamin D, hyperphosphaturia (with normal serum parathyroid hormone, calcium and 25-hydroxy-vitamin-D levels) [2,3].

Low tubular phosphorus absorption and some alterations on vitamin D metabolism are unleashed by excessive Fibroblast Growth Factor 23 (FGF 23) secreted by the tumor, resulting in structural changes. At the end of this cycle, the patient develops osteomalacia [3,4]. The first signals are pain to develop some activities, loses body mass, evolve to body moves limitations, multiple fractures, renal and heart dysfunctions that can lead to death [4].

A tumor resection is the only way to stop this event loop and, as sooner the diagnosis is made (and consequently the surgery), smaller will be the sequels [5].

2. Presentation of case

A 60-year old woman showed malnutrition, repeated cramps, general pain and multiples fractures after minimal traumas in two years of evolution. She used non-steroidal anti-inflammatory drugs and opioids to control the pain, but without great results. A year ago, she broke the left humerus after a minimal energy trauma, requiring the use of plaster cast for eight months. After ten months, she broke the right humerus, presented gradual loss of strength and muscle mass, especially in lower limbs, which led to the use of crutches and, posteriorly, confined to bed.

She had a long term diabetes-2, hard control hypertension and subclinical hypothyroidism, without familiar diseases compatible with her issues. Several fractures were found, when she was admitted in hospital, in ribs, right subtrochanteric area, bilateral coxarthrosis and right tibia. The laboratory analysis revealed normal levels of calcium and parathyroid hormone, high levels of alkaline phosphatase, hypokalemia and hypophosphatemia (Table 1). The hypothesis of osteomalacia induced by mesenchymal tumor phosphatonin producer was raised. The research of FGF-23 was not performed, since this test is quite expensive in Brazil, only being quantified in research protocols a few centers

The patient did a Photon Emission Computed Tomography/Computed Tomography (SPECT/CT) to locate the tumor (Fig. 1). The SPECT/CT reconstruction presented multiples fracture areas

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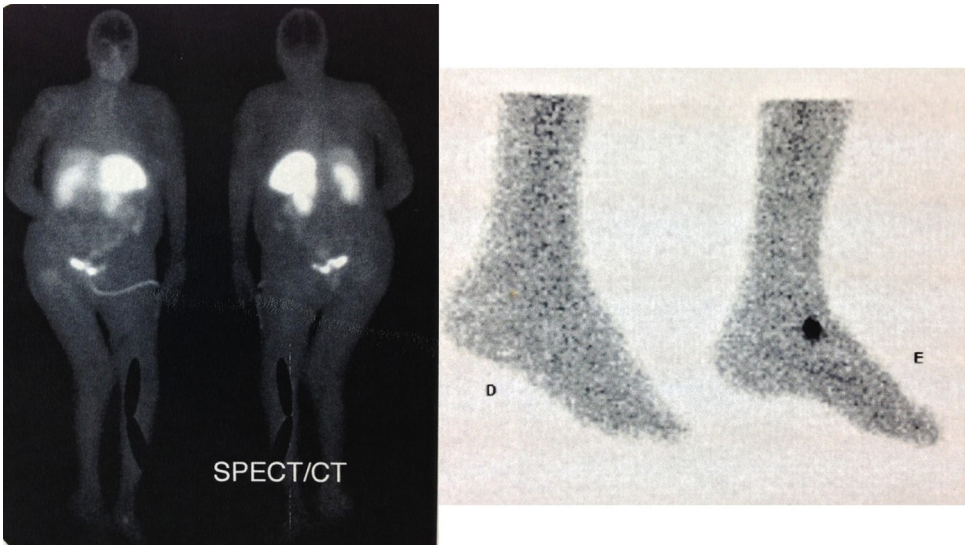

Fig. 1. SPECT/CT.

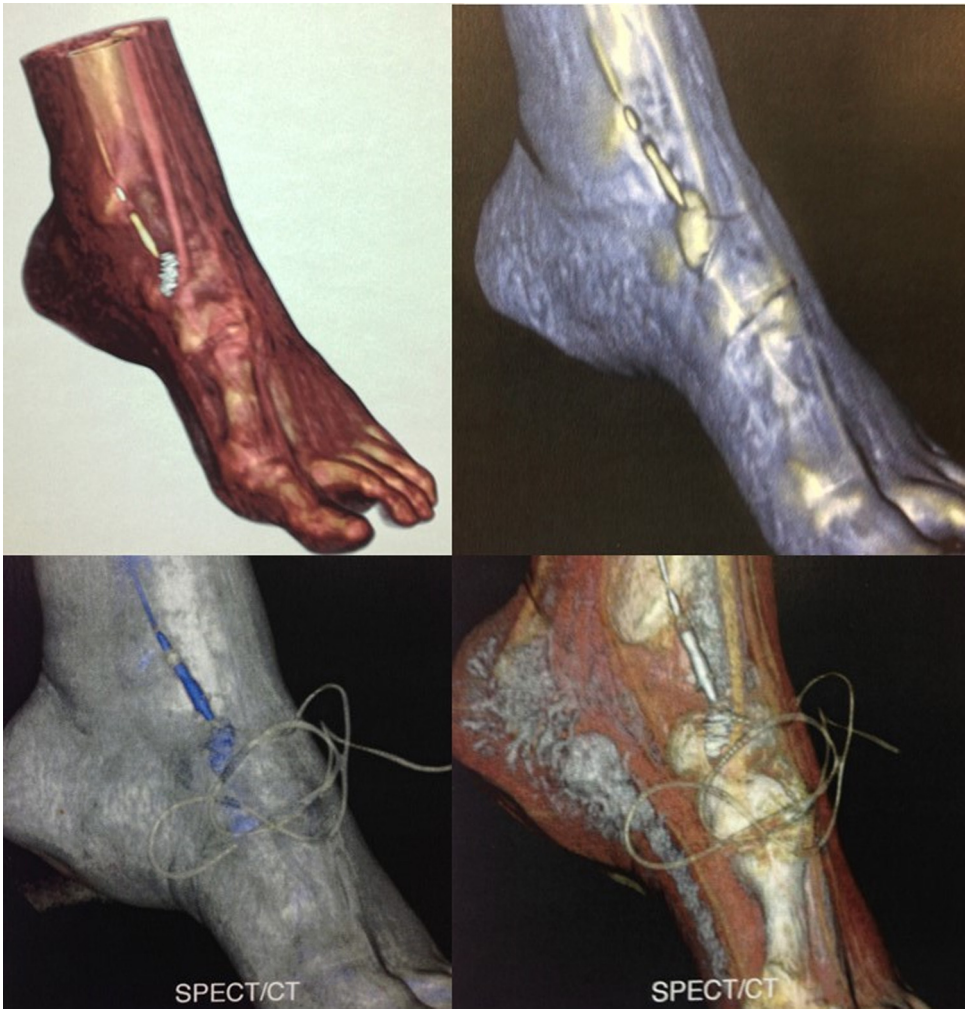

Fig. 2. SPECT/CT and Reconstruction.

and a hypercaptation in left tibial articular plateau, measuring about 0.8 cm (Fig. 2).

The tumor was surgically removed with free margins (Fig. 3), revealing a glandular aspect in macroscopy (Fig. 4) and mesenchymal aspect in microscopy pathology analysis, leading to the diagnosis of oncogenic hypophosphatemic osteomalacia. At any moment was measured calcitonin since have been no clinical decompensation of the patient.

Table 1
Laboratory Tests.

Exams	Values
Inorganic Phosphorus (Serum) (NR: 3.4–4.5 mg/dl)	0,8 mg/dl
Magnesium (Serum) (NR: 1.7–2.7 mg/dl)	1,8 mmol/l
Sodium (Serum) (NR: 135–145 mg/dl)	142 mg/dl
Potassium (Serum) (NR: 3.5–5.5 mg/dl)	3,1 mg/dl
Calcium (Serum) (NR: 4.4–5.4 mg/dl)	4,4 mg/dl
Creatinine (Serum) (NR: 0.5–1.2 mg/dl)	0,5 mg/dl
PTH (NR: 10–65 pg/ml) (NR: 16–87 pg/ml)	25 pg/ml
1,25-dihydroxy-vitamin D (NR: >19, 9–79, 3 pg/ml)	9,0 pg/ml

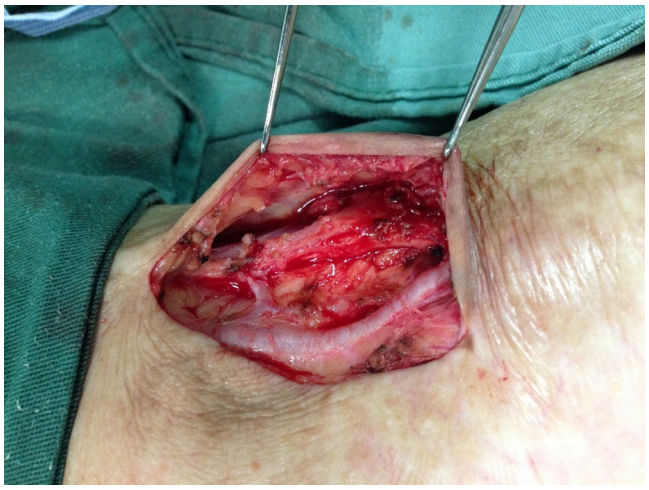

Fig. 3. Tumor Site.

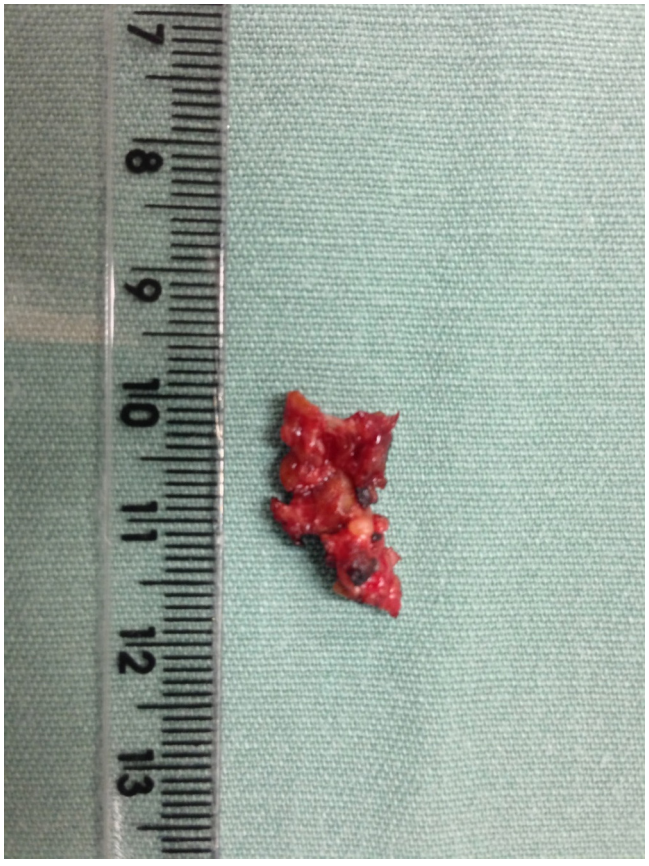

Fig. 4. Tumoral Exeresis.

After surgery, the laboratorial alterations become normal, nutritional parameters improved, the patient reported clinical improvement. However, the structural deformities, walk limitation and heart condition didn't change because the diagnosis was too late. Associating these sequels to the fact that the patient acquired sepsis by urinary infection on Intensive Care Unit, she evolved to an acute abdomen by hypomotility, without obstructive factor by CT. Even healed of the disease, this acute metabolic response and urinary sepsis lead her to death.

3. Discussion

Into deep universe of diseases, some kinds have a particularity: completely cure after treatment. This is the case of OHO; when resected with free margin, determinate the cure of this disease and stop the evaluation to limited structural and organic dysfunction. The great challenge is the early diagnosis and medical infrastructure to do that [6,7].

Some other diseases (genetic and acquired) must be differentiated to OHO, once can be found elevated FGF-23 and clinical characteristics OHO-like. X-linked Hypophosphatemic Rickets usually presents in childhood with rickets and dental disturbs; Autosomal-dominant Hypophosphatemic Rickets can spontaneous remit and recur; Autosomal-recessive Hypophosphatemic Rickets have consanguineous parent associated; Hereditary Hypophosphatemic Rickets with Hypercalciuria have high levels of 1,25-vitamin D and urinary calcium and low PTH; X-linked Recessive Hypophosphatemic Rickets have male predominance, hypercalciuria, kidney stones and renal failure; Inherited Fanconi have proximal renal tubular acidosis and Acquired Fanconi have the same characteristics, including history of exposure to chemotherapeutic agents and heavy metals [2].

When this kind of tumor is completely removed with free margins, the first signals of health improve are palpable. Lymph nodal resection didn't presented benefits once this tumor have low incidence of metastasis [1]. Quick normalization of laboratory results, better physiotherapeutic outcomes, improvement in heart function, but, when this diagnosis is delayed, structural malformation, heart sequels, bone dysfunction and metabolic disorders could lead to poor quality of life or death [8].

Several exams, like CT, NMR and Scintigraphy with some radioisotope (for example, technetium), could help to find exactly where the tumor is located and, consequently, guides the surgeon to resect the lesion [9]. Once having the disease suspect, the problem is the cost of these exams, apart from the fact that few medical center have this expansive technology, what gives to medical team a big responsibility to exclude other illnesses, make a brainstorm with patient relate and low cost exams and make the early diagnosis without seeing the tumor [2,10].

4. Conclusion

Mesenchymal tumors can have recurrences, but OHO doesn't need regular screening tests because of the low incidence of recurrences. Our service proposes just a regular clinical review, following the recovery of motor function and clinical implications, only requesting some tests if there are complaints.

A multidisciplinary care is crucial to rehabilitate as much as possible. The focus needs to be the patient reintegration to family and society and restarts life like an economically active individual, regardless of the sequel that the delay in diagnosis caused [8].

Conflict of interest

No conflicts of interest.

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Ethical approval

Consent form stating approves study. It was not necessary ethics committee.

Author contribution

Arthur Paredes Gatti: study concept; data analysis; writing the paper.
Luiza Tonello: study concept; data analysis; writing the paper.
João Diedrisch Neto: study concept; data analysis; writing the paper.
Uirá Fernandes Teixeira: data analysis; data collection.
Marcos Bertozzi Goldoni: data analysis; data collection.
Paulo Roberto Ott Fontes: data analysis; data collection.
José Artur Sampaio: data analysis; data collection.
Luiz Maraninchi Pereira Lima: data analysis; data collection.
Fábio Luiz Waechter: data analysis; data collection.

Consent

Consent form stating approves study.

Guarantor

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