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ONCOGENIC HYPOPHOSPHATEMIC OSTEOMALACIA: A DIFFERENTIAL DIAGNOSIS OF RHEUMATIC DISEASES

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BACKGROUND

Oncogenic osteomalacia is a rare disease caused by usually benign mesenchymal or endodermic tumors that secrete fibroblast growth factor 23 (FGF-23), leading to hypophosphatemia through hyperphosphaturia and low calcitriol levels.

Clinical manifestations include muscle, bone and joint pain, though the disease may be asymptomatic. In time, patients usually develop bone fractures due to inappropriate bone mineralization. Diagnosis is often delayed due to poor recognition of this entity and misdiagnosis as other rheumatic diseases such as rheumatoid arthritis (RA) or systemic lupus erythematosus.

Treatment consists in the replacement of phosphorus, normalization of vitamin D levels, discontinuing any inappropriate medication that might increase bone fragility (ex.: prednisone) and surgical excision of the tumor. Surgical treatment may be curative, but the disease often relapses. Novel treatments with FGF-23 targeted therapy have been promising.

CASE REPORT

A 42-year-old female presented with a 11-year history of widespread myalgia, bone pain and arthralgia of insidious instalment, with progressive loss of functionality. After 4 years of symptoms, she was diagnosed with RA and was started on methotrexate, hydroxychloroquine and low dose prednisone. Her pain and functionality worsened, and in the next years she developed multiple fractures, including right humerus, multiple metatarsals, ribs and vertebrae. At 10 years of symptoms, she was referred to our center, where a diagnostic workup found a serum phosphorus level of 1 mg/dL [reference value (RV): 2.7-4.5], high alkaline phosphatase (435 U/L, RV: 35-104), with normal levels of calcium (9.3 mg/dL, RV 8.4-10.2) and 25-hydroxyvitamin D (58 ng/mL). Her phosphaturia was inappropriately normal (709 mg/24 h, RV 400-1300). Bone mineral densitometry showed: lumbar spine Z-score of -4.3, Femoral neck Z-score of -2.4, total hip Z-score of -2.5. Bone biopsy with tetracycline confirmed osteomalacia. She was started on oral phosphorus solution with a satisfactory increase of her serum phosphorus levels.

Tumor investigation with ^{99m}Tc-sestamibi and ¹⁸F-FDG scans were negative, but a ⁶⁸Ga-DOTATATE positron emission tomography (PET) scan revealed a 0.3 × 0.8 cm mass in the right mastoid (Fig. 1), and total right mastoidectomy was performed. Histopathological analysis showed a mesenchymal tumor. Serum phosphorus levels normalized after surgery and oral phosphorus was discontinued (Fig. 2).

Unfortunately, the disease relapsed after 4 months of follow up. Due to the intracranial location of the original tumor, widening of the surgical margins was not considered, and oral phosphorus was restated. The patient has not had any new fractures since starting follow up in our center.

CONCLUSION

Osteomalacia may present with nonspecific symptoms that can be mistaken for other rheumatic diseases. In this case, the misdiagnosis of RA led to years of oral prednisone, which certainly worsened her bone disease. To prevent this scenario, we advocate for the screening of metabolic bone disease with serum dosage of calcium, phosphorous, alkaline phosphatase and vitamin D for patients manifesting common rheumatic symptoms.

We identified a small ^{99m}Tc-sestamibi and ¹⁸F-FDG negative, ⁶⁸Ga DOTATATE positive mass in her right mastoid bone. Surgical excision was successful in normalizing her serum phosphate levels, but after just 4 months there was recurrence of the hypophosphatemia and oral therapy had to be restarted.

Figure 1. A, B and C: ^{68}Ga DOTATATE PET scan showing an increased uptake in the right mastoid. D and E: CT scan showing a 0.3 x 0.8 cm needle-shaped mass in the right mastoid.

Figure 2. Serum phosphorus levels. Total right mastoidectomy was performed on May 13th of 2019. Oral phosphorus solution was interrupted on the day of the surgery.