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TEST YOURSELF: ANSWER

Test yourself answer: plantar soft tissue foot mass with insufficiency-type stress fractures

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Answer

Phosphaturic mesenchymal tumor (PMT) with tumor-induced osteomalacia (TIO) and insufficiency-type stress fractures.

Discussion

Phosphaturic mesenchymal tumors (PMTs) are rare, with about 450 reported cases in the medical literature [1]. They were first identified and named in 1987 by Weidner and Santa Cruz, who recognized them as a cause for osteomalacia and rickets [2]. PMTs are typically diagnosed in people aged 40–45 years, with no gender preference [3]. The incidence rate is low, at about 0.04 to 0.13 cases per 100,000 people per year [4, 5]. Most cases (95%) affect the extremities [6]. While PMTs are generally benign, rare malignant variants have also been reported [7].

The case presentation can be found at https://doi.org/10.1007/s00256-023-04469-3

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PMT cells secrete a hormone-like peptide called fibroblast growth factor-23 (FGF23)—a phosphotropic hormone produced by osteocytes that affect bone metabolism and mineralization on a few fronts [8]:

1. Suppresses expression of sodium-phosphate cotransporters in proximal renal tubules, which reduces serum phospate.
2. Hinders the activity of 1-α-hydroxylase, a crucial enzyme in synthesizing 1,25-dihydroxy vitamin D3, which affects calcium and phosphate reabsorption.
3. Demonstrates an inhibitory effect on parathyroid hormone (PTH) secretion.
4. Inhibits bone mineralization.

Cumulatively, FGF23 leads to the rare paraneoplastic syndrome of tumor-induced osteomalacia (TIO)/oncogenic osteomalacia, and patients may experience bone pain due to insufficient osteomalacic fractures.

Identifying PMTs can be difficult because of their vague symptoms, small size, slow growth, and location. Diagnostic latency can range from 2.9 to 28 years [9]; therefore, having a high level of clinical suspicion can be helpful in diagnosis.

Biochemically, individuals with PMTs may exhibit regular kidney function, higher levels of FGF23, elevated alkaline phosphatase, reduced levels of 1,25-dihydroxy Vitamin D3, and hypophosphatemia [10].

Radiographic findings of TIO include osteopenia, coarse trabeculae, thin cortices, and—most notably-- insufficiency-type stress fractures.

In more than 96% of cases, PET-CT with somatostatin analog can accurately identify the location of the tumor [11, 12]. A newer method called 68 Ga-DOTA-TOC-PET/CT-scan, uses an acid called DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) to bind with a derivative of octreotide called (Tyr3)-octreotate, has proven to be the most sensitive in detecting underlying PMTs [13, 14].

PMTs may present with a varied imaging appearance on MRI [15].

Histologically, PMTs typically comprise a variably cellular, cytologically bland, spindled, or stellate cellular proliferation, usually with a prominent vascular network. A distinctive smudgy basophilic myxoid or myxochondroid matrix with smudgy calcifications is usually present. Osteoclast-like giant cells, fibrohistiocytic spindled cells, microcystic changes, adipose tissue, or peripheral mature bone may be present. Rare cases display malignant histologic features [16].

Surgical resection typically has a good outcome; symptoms and serum phosphate levels should return to normal within 5 to 10 days, while bony healing time can vary [17]. Monitoring serum phosphate levels every six months and continuing with long-term follow-up is important to watch for potential recurrence [18].

At two-year follow-up, our patient's fractures healed.

In summary, PMTs are rare tumors that cause FGF23 overproduction, resulting in hypophosphatemia, TIO, and insufficiency-type stress fractures that can be corrected with complete excision. Most PMTs are benign, but malignant PMTs can also occur. While the appendicular skeleton is the most common site, PMTs may rarely occur in the axial skeleton and other locations. A practical stepwise diagnostic approach can be venous sampling for FGF23 levels for detection, 68 Ga-DOTA-TOC-PET/CT-scan for functional localization, and MRI for detailed anatomic characterization.

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Data availability The data is not publicly available due to containing sensitive information that could compromise research/case participant privacy.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Disclosures Informed consent was obtained from the subject described in this report.

References

1. Folpe AL. Phosphaturic mesenchymal tumors: a review and update. Semin Diagn Pathol. 2019;36(4):260–8. https://doi.org/10.1053/j.semdp.2019.07.002. ISSN 0740-2570.
2. Weidner N, Santa Cruz D. Phosphaturic mesenchymal tumors. A polymorphous group causing osteomalacia or rickets. Cancer. 1987;59:1442–54.
3. Hudairy RE, Meliti A, Mokhtar G, Alanazi M. Phosphaturic mesenchymal tumor: a case report of a rare entity. Cureus. 2022;14(2):e22712. https://doi.org/10.7759/cureus.22712.
4. Abrahamsen B, Smith CD, Minisola S. Epidemiology of tumor-induced osteomalacia in Denmark. Calcif Tissue Int. 2021;109(2):147–56. https://doi.org/10.1007/s00223-021-00843-2.
5. Endo I, Fukumoto S, Ozono K, Namba N, Inoue D, Okazaki R, ... Matsumoto T. Nationwide survey of fibroblast growth factor 23 (FGF23)-related hypophosphatemic diseases in Japan: prevalence, biochemical data and treatment. Endocr J. 2015;62(9):811–816
6. Pelo S, Gasparini G, Garagiola U, D'Amato G, Saponaro G, Doneddu P, Todaro M, Moro A. Phosphaturic mesenchymal tumor, an unusual localization in head and neck. J Surg Case Rep. 2018;2018(5):rjy091. https://doi.org/10.1093/jscr/rjy091.
7. Oyama N, Kojima-Ishii K, Toda N, Matsuo T, Tocan V, Ohkubo K, Oba U, Koga Y, Setsu N, Yamada Y, Kohashi K. Malignant transformation of phosphaturic mesenchymal tumor: a case report and literature review. Clin Pediatr Endocrinol. 2020;29(2):69–75.
8. Fukumoto S. FGF23-related hypophosphatemic rickets/osteomalacia: diagnosis and new treatment. Feb J Mol Endocrinol. 2021;66(2):R57–65. https://doi.org/10.1530/JME-20-0089.
9. Minisola S, Peacock M, Fukumoto S, Cipriani C, Pepe J, Tella SH, Collins MT. Tumour-induced osteomalacia Nat Rev Dis Primers. 2017;13(3):17044. https://doi.org/10.1038/nrdp.2017.44.
10. Ghorbani-Aghbolaghi A, Darrow MA, Wang T. Phosphaturic mesenchymal tumor (PMT): exceptionally rare disease, yet crucial not to miss. Autops Case Rep. 2017;7(3):32–7. https://doi.org/10.4322/acr.2017.031.
11. Moran M, Paul A. Octreide scanning in the detection of a mesenchymal tumour in the pubic symphysis causing hypophosphataemic osteomalacia. Int Orthop. 2002;26:61–2.
12. Hesse E, Moessinger E, Rosenthal H, et al. Oncogenic osteomalacia: exact tumor localization by co-registration of positron emission and computed tomography. J Bone Miner Res. 2007;22:158–62.
13. He Q, Zhang B, Zhang L, Chen Z, Shi X, Yi C, Wang X, Zhang X. Diagnostic efficiency of (68)Ga-DOTANOC PET/CT in patients with suspected tumourinduced osteomalacia. Eur Radiol. 2021;31(4):2414–21.
14. Agrawal K, Bhadada S, Mittal BR, Shukla J, Sood A, Bhattacharya A, Bhansali A. Comparison of 18F-FDG and 68Ga DOTATATE PET/CT in localization of tumor causing oncogenic osteomalacia. Clin Nucl Med. 2015;40(1):e6–10.
15. Frank FA, Gerber L, Cornelius A, Baumhoer D, Krieg AH. FGF-23 transmitted tumor-induced hypophosphatemic osteomalacia: a rare case of a young woman with recurrent fractures and review of the literature. J Bone Oncol. 2022;29:100413.
16. Shankar V, Pernick N. Phosphaturic Mesenchymal Tumor. Pathology Outlines - Phosphaturic Mesenchymal Tumor, 1 Nov. 2021. https://www.pathologyoutlines.com/topic/softtissuephosphaturic.html
17. Pal R, Bhadada SK, Singhare A, Bhansali A, Kamalanathan S, Chadha M, Chauhan P, Sood A, Dhiman V, Sharma DC, Saikia UN, Chatterjee D, Agashe V. Tumor-induced osteomalacia: experience from three tertiary care centers in India. Endocr Connect. 2019;8(3):266–76. https://doi.org/10.1530/EC-18-0552.
18. Brandi ML, Clunie GPR, Houillier P, Suzanne M, de Beur J, Minisola S, Oheim R, Seefried L. Challenges in the management of tumor-induced osteomalacia (TIO). Bone. 2021;152:116064. https://doi.org/10.1016/j.bone.2021.116064. ISSN 8756-3282.