

Tumor-induced osteomalacia caused by a phosphaturic mesenchymal tumor of the femur

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To the Editor: Tumor-induced osteomalacia (TIO) is an extremely rare paraneoplastic syndrome that is characterized by hypophosphatemia and hyperphosphaturia.^[1] Since TIO was first described in 1947, more than 500 cases have been reported worldwide.^[2,3] TIO is an acquired hypophosphatemic osteomalacia caused by decreased phosphorus reabsorption in the renal tubules and increased renal phosphorus excretion. The clinical manifestations of TIO are diverse and non-specific; the most common presentations are progressive bone pain, fracture, skeletal deformity, and movement dysfunction.^[1-3] To date, very few reported cases of TIO have presented with adjacent bone destruction caused by a phosphaturic mesenchymal tumor. Thus, clinicians lack knowledge and experience in prompt diagnosis and reasonable treatment of this rare condition. Herein, we present a case of TIO with substantial bone destruction that was successfully treated surgically [Figure 1].

A 15-year-old boy presented with a 3-year history of severe systemic multiple bone pain, hypophosphatemia, and mobility impairment. There were no other symptoms, no history of recent trauma or surgery, and no history of the underlying disease. Physical examination showed a decreased muscle strength of 5-/5 grade in the bilateral lower limbs, plus sternal tenderness and thoracic crushing pain. Laboratory tests demonstrated hypophosphatemia, elevated β -C-terminal telopeptide of type I collagen, normal parathyroid hormone level, elevated serum alkaline phosphatase level, and normal 1, 25-dihydroxy vitamin D level. Radiography showed substantial bone destruction in the right distal femur. Magnetic resonance imaging (MRI) revealed a tumor in the right distal femur with irregular hyperintense signals on T1- and T2-weighted imagery. ^{99m}Tc-Octreotide scanning and

⁶⁸Gallium(Ga)-DOTA-TATE positron emission tomography/computed tomography (PET/CT) identified high-intake space-occupying lesions in the right distal femur, which was highly suggestive of oncogenic osteomalacia. Analgesic therapy was administered, followed by tumor resection and reconstruction with a knee prosthesis in the right lower extremity. Post-operative radiography showed satisfactory positioning of the prosthesis. The tumor was successfully excised, and pathological results confirmed TIO with a phosphaturic mesenchymal tumor. The serum phosphate level returned to normal post-operatively, and the symptoms improved substantially compared with pre-operatively. Moreover, the visual analogue scale score for bone pain improved from 6 to 7 pre-operatively to 1 to 2 post-operatively. The patient declined adjuvant treatment but underwent rehabilitation and outpatient monitoring.

TIO is a paraneoplastic syndrome usually associated with mesenchymal tumors; phosphatonins decrease the renal resorption of phosphate, leading to hypophosphatemia, muscle weakness, and osteomalacia.^[1-3] However, it is extremely rare for a patient with TIO to present with a giant soft tissue mass and substantial destruction of adjacent bones. The methods used to detect TIO include ^{99m}Tc-Octreotide scanning and ⁶⁸Ga-DOTA-TATE PET/CT.^[2,3] Somatostatin receptor imaging utilizes the characteristics of the somatostatin receptor (SSTR) expression in phosphaturic mesenchymal tumors. The accuracy of ⁶⁸Ga-DOTA-TATE PET/CT in diagnosing TIO is 98.0%, which is significantly higher than other detection methods.^[2,3] The final diagnosis depends on the history, clinical manifestations, laboratory tests, imaging, pathological characteristics, and treatment effect. In the present case, the phosphaturic mesenchymal tumor had to be differentiated from neoplasms that commonly involve the femur in

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DOI:
10.1097/CM9.0000000000000458

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Chinese Medical Journal 2019;132(19)

Received: 25-07-2019 Edited by: Peng Lyu

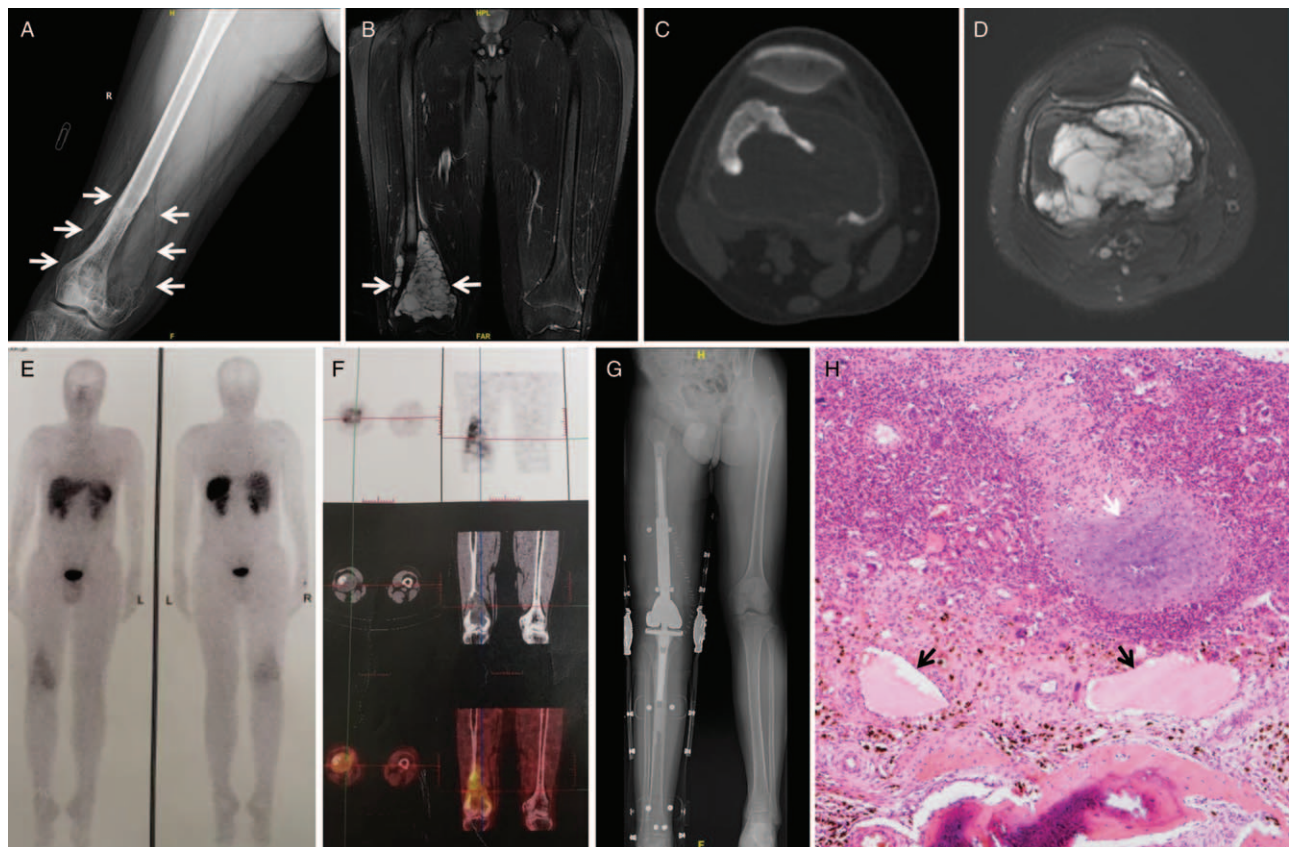


Figure 1: Tumor-induced osteomalacia with bone destruction in a 15-year-old boy. (A) Pre-operative radiograph showing substantial bone destruction in the right distal femur, and arrows pointing at the soft tissue tumor. (B–D) Computed tomography and magnetic resonance imaging reveal a soft tissue tumor with the destruction of the adjacent femur, and arrows pointing at the phosphaturic mesenchymal tumor. (E and F) The ^{99m}Tc -octreotide scanning and ^{68}Ga -DOTA-TATE positron emission tomography/computed tomography identify high-intake space-occupying lesions in the right distal femur, which is highly suggestive of oncogenic osteomalacia. (G) Post-operative radiograph showing satisfactory positioning of the prosthesis. (H) Histopathologic confirmation of tumor-induced osteomalacia with a phosphaturic mesenchymal tumor. Microphotography with arrows revealing characteristic nests of tumor cells separated by bland spindle cells with scattered nebulous calcification (white arrow), chondroid matrix production, and a rich vasculature (black arrows; hematoxylin-eosin staining, original magnification $\times 200$).

this age group, mostly osteosarcoma, and other malignant tumors. In imaging studies, although plain radiography might reflect the radiologic characteristics of the lesion, CT and MRI more accurately assess the extent of the mass within the bone and surrounding soft tissue. The ^{99m}Tc -Octreotide imaging and ^{68}Ga -DOTA-TATE PET/CT play a complementary role in obtaining an accurate diagnosis. Pathological results remain the “gold standard” to diagnose and definitively confirm the presence of a phosphaturic mesenchymal tumor.^[2,3] Surgical resection is the optimal treatment option to correct the biochemical abnormalities and remineralize the bone substance in patients with TIO.^[4,5] Surgical resection involves complete surgical excision to remove the pathogenic tumor, and pathological examination to confirm whether the tumor is a phosphaturic mesenchymal tumor. Improper selection of surgical procedures or incomplete resection can lead to the recurrence of the phosphaturic mesenchymal tumor and associated symptoms.^[4,5] The present case highlights the importance of accurate diagnosis and proper treatment for patients with a unique presentation of TIO.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient or his parents has or have given his or their consent for his images and other

clinical information to be reported in the journal. The patient or his parents understand(s) that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

References

- McCANCE RA. Osteomalacia with Looser's nodes (Milkman's syndrome) due to a raised resistance to vitamin D acquired about the age of 15 years. *Q J Med* 1947;16:33–46.
- Carpenter TO. Oncogenic osteomalacia - a complex dance of factors. *N Engl J Med* 2003;348:1705–1708. doi: 10.1056/NEJMe030037.
- Shi X, Jing H, Li F, Zhao Y, Wang Z, Huo L. ^{99m}Tc -HYNIC-TOC in the evaluation of recurrent tumor-induced osteomalacia. *Clin Nucl Med* 2019;44:209–213. doi: 10.1097/RLU.0000000000002458.
- Vollbrecht JE, Rao DS. Images in clinical medicine. Tumor-induced osteomalacia. *N Engl J Med* 2008;358:1282. doi: 10.1056/NEJ-Micm066066.
- Mumford E, Marks J, Wagner T, Gallimore A, Gane S, Walsh SB. Oncogenic osteomalacia: diagnosis, localisation, and cure. *Lancet Oncol* 2018;19:e365. doi: 10.1016/S1470-2045(18)30276-6.

How to cite this article: Liu SZ, Zhou X, Song A, Huo Z, Wang YP, Liu Y. Tumor-induced osteomalacia caused by a phosphaturic mesenchymal tumor of the femur. *Chin Med J* 2019;132:2380–2381. doi: 10.1097/CM9.0000000000000458