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REVIEW

- 1908** Bone alterations in inflammatory bowel diseases
Sgambato D, Gimigliano F, De Musis C, Moretti A, Toro G, Ferrante E, Miranda A, De Mauro D, Romano L, Iolascon G, Romano M

MINIREVIEWS

- 1926** Extrahepatic hepcidin production: The intriguing outcomes of recent years
Daher R, Lefebvre T, Puy H, Karim Z
- 1937** Neoadjuvant endocrine therapy: A potential strategy for ER-positive breast cancer
Yao LT, Wang MZ, Wang MS, Yu XT, Guo JY, Sun T, Li XY, Xu YY

ORIGINAL ARTICLE**Basic Study**

- 1954** Vestigial like family member 3 is a novel prognostic biomarker for gastric cancer
Zhang LH, Wang Z, Li LH, Liu YK, Jin LF, Qi XW, Zhang C, Wang T, Hua D

Retrospective Study

- 1964** HER2 heterogeneity is a poor prognosticator for HER2-positive gastric cancer
Kaito A, Kuwata T, Tokunaga M, Shitara K, Sato R, Akimoto T, Kinoshita T

Case Control Study

- 1978** Changes in corneal endothelial cell density in patients with primary open-angle glaucoma
Yu ZY, Wu L, Qu B

Observational Study

- 1986** Myocardial bridge-related coronary heart disease: Independent influencing factors and their predicting value
Zhao DH, Fan Q, Ning JX, Wang X, Tian JY
- 1996** Clinical significance and role of up-regulation of SERPINA3 expression in endometrial cancer
Zhou ML, Chen FS, Mao H
- 2003** Evaluation of right ventricular volume and systolic function in normal fetuses using intelligent spatiotemporal image correlation
Sun JX, Cai AL, Xie LM

- 2013** Correlation between intracoronary thrombus components and coronary blood flow after percutaneous coronary intervention for acute myocardial infarction at different onset time
Zhang MJ, Liu X, Liu LH, Li N, Zhang N, Wang YQ, Sun XJ, Huang PH, Yin HM, Liu YH, Zheng H

META-ANALYSIS

- 2022** Performance of common imaging techniques *vs* serum biomarkers in assessing fibrosis in patients with chronic hepatitis B: A systematic review and meta-analysis
Xu XY, Wang WS, Zhang QM, Li JL, Sun JB, Qin TT, Liu HB

CASE REPORT

- 2038** Acute bleeding after argon plasma coagulation for weight regain after gastric bypass: A case report
Moura DTHD, Sachdev AH, Lu PW, Ribeiro IB, Thompson CC
- 2044** Left colonic metastasis from primary hepatocellular carcinoma: A case report
Tagliabue F, Burati M, Chiarelli M, Marando A, Simone MD, Cioffi U
- 2049** ALK-positive anaplastic large cell lymphoma presenting multiple lymphomatous polyposis: A case report and literature review
Saito M, Izumiyama K, Ogasawara R, Mori A, Kondo T, Tanaka M, Morioka M, Miyashita K, Tanino M
- 2058** Modified Tong Xie Yao Fang relieves solitary rectal ulcer syndrome: A case report
Zhang LL, Hao WS, Xu M, Li C, Shi YY
- 2065** Hydrogen gas therapy induced shrinkage of metastatic gallbladder cancer: A case report
Chen JB, Pan ZB, Du DM, Qian W, Ma YY, Mu F, Xu KC
- 2075** Giant nonfunctional ectopic adrenocortical carcinoma on the anterior abdominal wall: A case report
Zhou DK, Liu ZH, Gao BQ, Wang WL
- 2081** Oncogenic osteomalacia caused by a phosphaturic mesenchymal tumor of the femur: A case report
Tang D, Wang XM, Zhang YS, Mi XX
- 2087** Gastric duplication cyst mimicking large cystic lymphangioma in an adult: A rare case report and review of the literature
Xv FY, Sun A, Gan Y, Hu HJ
- 2094** Endometriosis of the duplex appendix: A case report and review of the literature
Zhu MY, Fei FM, Chen J, Zhou ZC, Wu B, Shen YY
- 2103** Fever and neck pain after pacemaker lead extraction: A case report
Wang SX, Bai J, Ma R, Lan RF, Zheng J, Xu W

- 2110** c.753_754delAG, a novel *CFTR* mutation found in a Chinese patient with cystic fibrosis: A case report and review of the literature
Wang YQ, Hao CL, Jiang WJ, Lu YH, Sun HQ, Gao CY, Wu M
- 2120** Common iliac artery occlusion with small intestinal transection caused by blunt abdominal trauma: A case report and review of the literature
Zhou YX, Ji Y, Chen J, Yang X, Zhou Q, Lv J
- 2128** Percutaneous coronary intervention for ostial lesions of the left main stem in a patient with congenital single left coronary artery: A case report
Wu Q, Li ZZ, Yue F, Wei F, Zhang CY

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Oncogenic osteomalacia caused by a phosphaturic mesenchymal tumor of the femur: A case report

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Abstract

BACKGROUND

Oncogenic osteomalacia caused by phosphaturic mesenchymal tumors is very difficult to detect. We report a case of tumor-induced osteomalacia caused by a phosphaturic mesenchymal tumor of the left femur in a middle-aged woman after medical imaging and biopsy.

CASE SUMMARY

A 57-year-old woman presented with progressive bone pain for five years. She was diagnosed with hypophosphatemic osteomalacia, as her laboratory data showed low serum phosphorus and low serum calcium. Her knee joint radiography revealed an osteolytic lesion of the left femur. A computed tomography scan showed mixed density shadows in the left femur. Magnetic resonance imaging of the left femur showed the presence of an oval area with a hypointense signal in T1-weighted magnetic resonance imaging (MRI) and high-low mixed signal in T2-weighted MRI. Biopsy samples revealed the presence of short spindle cells, vascularization, and characteristics of phosphaturic mesenchymal tumors. Tumor resection was performed, and the clinical presentations and laboratory abnormalities were reversed.

CONCLUSION

Diagnosis of oncogenic osteomalacia is difficult due to the varieties and

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localization of source tumors and absence of pathognomonic biomedical signs. Our case highlights the importance of a combination of medical imaging and biopsy in the diagnosis of oncogenic osteomalacia caused by a phosphaturic mesenchymal tumor.

Key words: Oncogenic osteomalacia; Phosphaturic mesenchymal tumor; Hypophosphatemia; Hypocalcemia; Case report

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Core tip: Oncogenic osteomalacia caused by phosphaturic mesenchymal tumors is not easily identifiable or detectable due to its rarity and nonspecific presentations. Herein, we provide a successful example of diagnosis of phosphaturic mesenchymal tumor-induced oncogenic osteomalacia in a female patient who presented progressive bone pain. Our case emphasizes that histologically benign phosphaturic mesenchymal tumors that are responsible for oncogenic osteomalacia can also cause bone destruction.

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INTRODUCTION

Oncogenic osteomalacia, also known as tumor-induced osteomalacia, is an uncommon cause of osteomalacia. At present, approximately 140 different tumors have been reported in association with oncogenic osteomalacia, and most osteomalacia-associated tumors are phosphaturic mesenchymal tumors^[1,2]. Phosphaturic mesenchymal tumors are found to be commonly associated with phosphaturia and a decreased level of serum 1,2-dihydroxyvitamin D3 that is resistant to vitamin D supplementation. However, oncogenic osteomalacia caused by phosphaturic mesenchymal tumors is not easily identifiable or detectable due to its rarity and nonspecific presentations. The clinical presentations of the patients include nonspecific symptoms of fatigue, bone pain, and musculoskeletal weakness^[3]. Although rare, the diagnosis of phosphaturic mesenchymal tumor should be considered in any patient who presents with hypophosphaturic osteomalacia and no other physiologic cause.

In our case, oncogenic osteomalacia was caused by a phosphaturic mesenchymal tumor localized in the patient's left femur. The patient presented with progressive bone pain with no etiology for five years. After X-ray, computed tomography (CT), magnetic resonance imaging (MRI), and biopsy, a diagnosis of oncogenic osteomalacia caused by a phosphaturic mesenchymal tumor was made. Resection of the tumor was performed, and the clinical presentations and laboratory abnormalities were reversed. Here, our case emphasizes that histologically benign phosphaturic mesenchymal tumors that are responsible for oncogenic osteomalacia can also cause bone destruction. Its diagnosis is, thus, reliably achieved by histopathological examination combined with medical imaging.

CASE PRESENTATION

Chief complaints

A 57-year-old woman presented with progressive bone pain of the whole body for three years.

History of present illness

Five years ago, there was no obvious cause for the appearance of pain in her right third toe; pain then developed into the right instep with an associated jerk and then progressively appeared in the right thigh with an associated jerk, thus affecting her ability to walk. Three years ago, systemic pain appeared, especially bone pain. There

was also pain in her muscles and skin. Reduction or even no pain was felt while lying flat. At this time, she also had the ability to do laundry or cook. Two years ago, pain prevented her from daily exercise, and she had to stay in bed. There was no accompanying fever, coma, cough, dizziness, headache, chest tightness, palpitation, nausea, vomiting, or abdominal pain. Five years ago, she was first examined at a hospital, and her laboratory workup showed slightly low levels of serum phosphorus (0.63 mmol/L, reference range: 0.80-1.48 mmol/L) and low serum calcium (1.98 mmol/L, reference range: 2.10-2.60 mmol/L). Bone density examination showed osteoporosis in her left acetabulum and osteopenia in her lumbar spine. Chest and abdomen computed tomographic scans did not reveal any abnormalities. However, the photographs were not available now. She was treated with calcium and vitamin D supplementation. However, her pain persisted. The woman was introduced to our hospital approximately 5 years after the onset of her symptoms.

FINAL DIAGNOSIS

Physical examination showed that palpation on the right upper abdomen was normal; signs such as purple striae, moon face, and central obesity were not observed.

Her laboratory data also revealed slight hypophosphatemia (0.76 mmol/L, reference range: 0.80-1.48 mmol/L) and hypocalcemia (1.86 mmol/L, reference range: 2.10-2.60 mmol/L). Her knee radiographs showed that her bony trabeculae were sparse and her bone density was widely reduced (Figure 1). The X-ray radiograph showed an oval osteolytic lesion in the inferior medullary cavity of the left femur (Figure 1B, arrow). A subsequent CT scan revealed that mixed density shadows were shown in the intramedullary cavity of the left femur (Figure 2, arrow). Non-uniform enhancement in this lesion area was observed. However, no obvious abnormalities were seen in the surrounding soft tissues. MRI of the left knee showed the presence of an intramedullary tumor in the left femur, which showed a hypointense signal on the T1-weighted image (Figure 3A, arrow) and a high-low mixed signal intensity on the T2-weighted image (Figure 3B and C, arrow). Thus, a tumor-induced osteomalacia was confirmed.

TREATMENT AND OUTCOME

The tumor was resected at a local hospital, and the histology revealed a phosphaturic mesenchymal tumor with the presence of spindle cells and prominent blood vessels (Figure 4). Her serum phosphorus and calcium returned to the normal range (phosphorus: 0.89 mmol/L, reference range: 0.80-1.48 mmol/L; calcium: 2.29 mmol/L, reference range: 2.10-2.60 mmol/L), and now the woman can exercise daily and has not had any recent complaints.

DISCUSSION

The existence of tumor-induced osteomalacia is not widely recognized, and its diagnosis can often be delayed^[4]. Tumors that are involved in oncogenic osteomalacia include phosphaturic mesenchymal tumors, fibrous dysplasia, osteosarcoma, and others^[5-7]. Folpe *et al*^[2] revealed that 90% of tumor-induced osteomalacia cases are associated with phosphaturic mesenchymal tumors. Phosphaturic mesenchymal tumors are most often seen in the head and lower extremities, and approximately 53% of them occur in bone, 45% in soft tissue, and 3% in skin^[8]. Most phosphaturic mesenchymal tumors are seen in middle-aged adults, with no gender difference^[9]. The histology of phosphaturic mesenchymal tumors features proliferation of spindle cells and oval cells, vascularization, a cartilage-like matrix, and giant cells^[10]. Although rare, malignant tumors with metastasis and infiltration can also be present^[11-13]. The present case of phosphaturic mesenchymal tumor occurred in the left femur and led to hypophosphatemia osteomalacia in a middle-aged woman.

Hypophosphatemia in tumor-induced osteomalacia is caused by the mRNA overexpression of FGF-23, a protein that is produced at low levels by osteocytes^[10,14]. FGF-23 plays important roles in phosphate homeostasis and vitamin D metabolism. After binding with the FGFR1 receptor and the transmembrane protein Klotho, FGF-23 exerts bioactivity at the proximal tubules, where it inhibits phosphate resorption. FGF-23 also impairs the activity of hydroxylation of 25-hydroxyvitamin (OH) D₃. These mechanisms mainly lead to hypophosphatemia and osteomalacia^[15,16]. However, in China, the serum FGF-23 test is not routinely provided in most hospitals.



Figure 1 X-rays of knee joints. A: Anteroposterior view; B: Lateral view. Bone trabeculae of both knees are sparse, bone density is widely reduced, and an oval osteolytic area is shown in the inferior medullary cavity of the left femur (arrow).

This highlights the need for our clinicians to be aware of its entity and to give an appropriate investigation of phosphaturic mesenchymal tumor-induced osteomalacia.

Phosphaturic mesenchymal tumors are often very small in size and grow slowly, which makes them difficult to locate^[10]. Malignant tumors and metastasis can often be detected. Infiltration of the surrounding tissue can also happen. Widespread bone metastases may lead to the occurrence of pathological fractures and spinal cord compression, thus significantly affecting patient outcomes. There are no established guidelines for the treatment of metastatic phosphaturic mesenchymal tumors. Complete tumor resection corrects the biochemical abnormalities and remineralization of bone. In our case, we did not observe metastases of the tumors, and resection of the tumor relieved pain and reversed the biochemical abnormalities in the patient. Our case demonstrated that histologically benign phosphaturic mesenchymal tumors can also cause bone pain.

In conclusion, we report a case of oncogenic osteomalacia caused by a phosphaturic mesenchymal tumor of the left femur in a middle-aged woman. Our case emphasizes that histologically benign phosphaturic mesenchymal tumors that are responsible for oncogenic osteomalacia can also cause bone destruction. Its diagnosis is, thus, reliably achieved by histopathological examination combined with medical imaging. We expect that the detailed description of this case presentation of oncogenic osteomalacia will provide a valuable resource to facilitate the diagnosis of such diseases in the future.

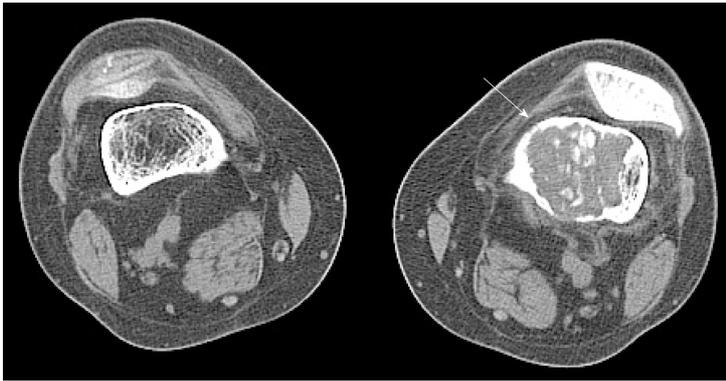


Figure 2 Computed tomography scans of knee joints. Mixed density shadows are shown in the intramedullary cavity of the left femur (arrow). Computed tomography values are 45-70 HU.

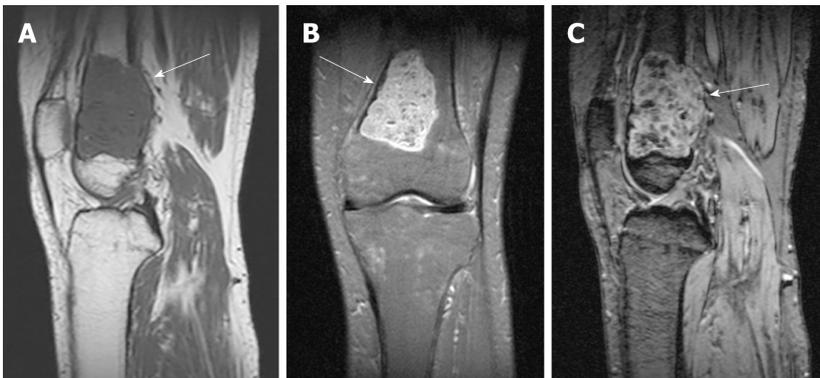


Figure 3 Magnetic resonance imaging of the left knee. A: T1WI sagittal view; B: PDWI coronal view; C: PDWI sagittal view. T1 hypointense (arrow, A) and T2 high-low mixed signal (arrows, B and C) are shown.

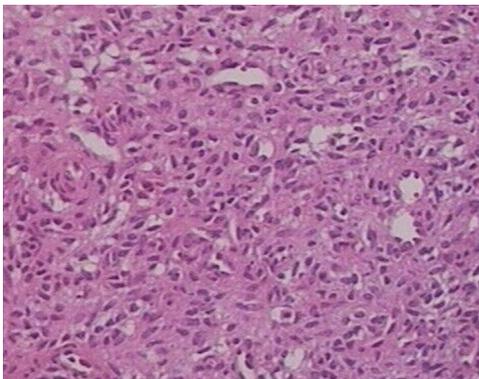


Figure 4 Histology of the resected tumor. Note the presence of short spindle cells and a large number of blood vessels. Some spindle cells grew around blood vessels. HE staining, 100 \times .

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