ORIGINAL ARTICLE

JBMR

Tumor-Induced Osteomalacia: An Important Cause of Adult-Onset Hypophosphatemic Osteomalacia in China: Report of 39 Cases and Review of the Literature

Yan Jiang,[1] Wei-bo Xia,[1] Xiao-ping Xing,[1] Barbara C Silva,[8] Mei Li,[1] Ou Wang,[1] Hua-bing Zhang,[1] Fang Li,[2] Hong-li Jing,[2] Ding-rong Zhong,[3] Jin Jin,[4] Peng Gao,[4] Lian Zhou,[5] Fang Qi,[6] Wei Yu,[7] John P Bilezikian,[8] and Xun-wu Meng[1]

[1]Department of Endocrinology, Key Laboratory of Chinese Health Ministry, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[2]Department of Nuclear Medicine, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[3]Department of Pathology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[4]Department of Orthopaedics, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[5]Department of Stomatology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[6]Ear, Nose, and Throat (ENT) Department, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[7]Department of Radiology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing, China
[8]Department of Medicine, Division of Endocrinology, College of Physicians & Surgeons, Columbia University, New York, NY, USA

ABSTRACT

Tumor-induced osteomalacia (TIO) is an acquired form of hypophosphatemia. Tumor resection leads to cure. We investigated the clinical characteristics of TIO, diagnostic methods, and course after tumor resection in Beijing, China, and compared them with 269 previous published reports of TIO. A total of 94 patients with adult-onset hypophosphatemic osteomalacia were seen over a 6-year period (January, 2004 to May, 2010) in Peking Union Medical College Hospital. After physical examination (PE), all patients underwent technetium-99m octreotide scintigraphy ($^{99}Tc^{m}$-OCT). Tumors were removed after localization. The results demonstrated that 46 of 94 hypophosphatemic osteomalacia patients had high uptake in $^{99}Tc^{m}$-OCT imaging. Forty of them underwent tumor resection with the TIO diagnosis established in 37 patients. In 2 patients, the tumor was discovered on PE but not by $^{99}Tc^{m}$-OCT. The gender distribution was equal (M/F = 19/20). Average age was 42 ± 14 years. In 35 patients (90%), the serum phosphorus concentration returned to normal in 5.5 ± 3.0 days after tumor resection. Most of the tumors (85%) were classified as phosphaturic mesenchymal tumor (PMT) or mixed connective tissue variant (PMTMCT). Recurrence of disease was suggested in 3 patients (9%). When combined with the 269 cases reported in the literature, the mean age and sex distribution were similar. The tumors were of bone (40%) and soft tissue (55%) origins, with 42% of the tumors being found in the lower extremities. In summary, TIO is an important cause of adult-onset hypophosphatemia in China. $^{99}Tc^{m}$-OCT imaging successfully localized the tumor in the overwhelming majority of patients. Successful removal of tumors leads to cure in most cases, but recurrence should be sought by long-term follow-up. © 2012 American Society for Bone and Mineral Research.

KEY WORDS: TUMOR-INDUCED OSTEOMALACIA; TECHNETIUM-99M OCTREOTIDE SCINTIGRAPHY; HYPOPHOSPHATEMIA; FIBROBLAST GROWTH FACTOR-23

Received in original form September 6, 2011; revised form April 9, 2012; accepted April 11, 2012. Published online April 24, 2012.
Address correspondence to: Xun-wu Meng, MD, Department of Endocrinology, Key Laboratory of Chinese Health Ministry, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science. Shuaifuyuan 1, Dong Cheng District, Beijing, 100730 China. E-mail: mengxunwu@sina.com
Additional Supporting Information may be found in the online version of this article.

Journal of Bone and Mineral Research, Vol. 27, No. 9, September 2012, pp 1967–1975
DOI: 10.1002/jbmr.1642

Introduction

Tumor-induced osteomalacia (TIO), also known as oncogenic osteomalacia, is an acquired form of hypophosphatemia commonly associated with benign mesenchymal tumors.[1] Resection of the tumor leads to cure of osteomalacia. TIO is characterized clinically by bone pain and fracture, renal phosphate wasting, hypophosphatemia, low or normal serum $1,25(OH)_2D$ concentrations, and elevated serum alkaline phosphatase levels.[2] Fibroblast growth factor-23 (FGF-23), a phosphatonin, has been identified as a major pathophysiological factor responsible for phosphate wasting in TIO.[3,4] Until this time, there were only 269 cases described in the world's literature over 61 years.[5–98]

The diagnosis of TIO can be challenging because the tumors are often small and hard to find. Bone scanning, computerized tomography (CT),[3] magnetic resonance imaging (MRI), Indium-111 pentetreotide or octreotide scintigraphy, and positron emission tomography (PET) have all been employed in an effort to localize the tumor.[99] Using technetium-99m octreotide scintigraphy ($^{99}Tc^m$-OCT), we diagnosed 39 TIO patients after tumor surgery out of 94 patients who presented with hypophosphatemic osteomalacia. This is one of the largest cohorts reported to date.[17,100]

Patients and Methods

Patients

From January, 2004 through May, 2010, 94 patients with adult-onset hypophosphatemic osteomalacia, without family history, were seen in the Department of Endocrinology, Peking Union Medical College Hospital, Beijing, China. These patients sought care or were referred to our institution with symptoms of fatigue, bone pain, and/or pathological fractures. Among these 94 patients, one case has previously been reported.[101]

Methods

After obtaining a detailed medical and family history, physical examination (PE) and $^{99}Tc^m$-OCT were performed on all 94 patients. If a tumor mass was found on PE or high uptake was detected by $^{99}Tc^m$-OCT, and depending upon where the lesion was found, ultrasonography(US), CT, or MRI was recommended for further localization of the tumor. After successful localization, the tumor was removed by surgery and examined by histopathology. Serum calcium, phosphorus, alkaline phosphatase (ALP), parathyroid hormone (PTH), and $1,25(OH)_2D$ levels were measured before surgery. Tubular maximum of phosphate/glomerular filtration rate (TMP/GFR) was calculated from the nomogram of Walton and Bijvoet.[102] Serum FGF-23 levels were monitored before and after tumor resection in 6 cases using an ELISA kit from Kainos Laboratories (Tokyo, Japan). The normal range in healthy controls is 10 to 50 pg/mL in our laboratory.[101,103]

Patients were followed for an average of 27 months (3–81 months) after tumor resection.

$^{99}Tc^m$-OCT

Regional, whole-body, and single-photon emission computed tomography (SPECT)/CT (in positive cases) images were obtained at 1 and 4 hours after an intravenous injection of 350 to 400 MBq $^{99}Tc^m$-OCT. Immediately thereafter, SPECT/CT or SPECT images of the positive location were obtained (Millennium VG, Hawkeye; GE Healthcare). SPECT data were acquired in a 128×128 matrix through 360-degree rotation with 64 projections. The acquisition time for each projection was 40 seconds.

Review of the literature

In addition to the cases described here, we reviewed 269 cases of TIO previously reported in the English literature.[5–98] We searched for all original and review articles in PubMed without restriction to dates. The search terms we used were "Tumor induced osteomalacia" and "oncogenic osteomalacia." Patient's age and sex, tumor location and histological type, and serum FGF-23 levels before and after surgery were tabulated. Tumor histological type was based upon the original description or as revised. Case reports describing the finding of phosphaturic mesenchymal tumors (PMT), but without biochemical evidence of TIO, or cases in which the tumor was not localized, precluding a definitive diagnosis of TIO, were excluded. Cases reported more than once were counted only once. Cases of TIO associated with hematologic malignancies, polyostotic fibrous dysplasia of bone, neurofibromatosis, and prostate cancer have been described as TIO-like syndromes,[104] but strictly speaking do not meet the definition of TIO and thus were excluded in our review.

Results

A total of 94 patients (M:F = 47:47, 40 ± 13 years of age) with adult-onset hypophosphatemic osteomalacia were seen in our hospital. Forty-six of them (49%) demonstrated high uptake by $^{99}Tc^m$-OCT scanning. Four patients (patients 1, 6, 8, and 23) had negative $^{99}Tc^m$-OCT results 1 to 5 years before, whereas 6 patients (patients 15, 17, 22, 36, 38, and 39) had previous tumor resection at the same sites. There were no clinical differences between patients with positive or negative octreotide scans. Following successful localization by $^{99}Tc^m$-OCT, and further localization by US, CT, or MRI, 40 subjects agreed to tumor resection. Thirty-seven patients were shown to have TIO by histological examination of the tumor. One patient showed only necrotic soft tissue and blood clots without clear delineation of a tumor. Two patients were defined as having TIO-like syndrome[104]; 1 had neurofibromatosis type 1, and 1 had kidney clear cell carcinoma. These patients were excluded from the analysis. Six patients who had positive $^{99}Tc^m$-OCT results but the visualized mass was not confirmed by US, CT, or MRI did not have surgery. For 48 patients with the negative octreotide scans, the tumor was found in 2 patients only by PE. These patients had their tumors removed (patient 9 in lower thigh, and patient 32 in lower gingiva) with alleviation of symptoms. Totally, out of the 94 patients who presented with adult-onset hypophosphatemic osteomalacia, 41% (39/94) were shown to have TIO. The general characteristics and biochemical parameters of these 39 patients are showed in Supplementary Table 1.

The 54 patients without confirmed evidence of tumor were followed and treated with oral phosphate, calcium, and calcitriol.

The general characteristics of TIO patients

The gender distribution was even (M:F = 19:20) with an average age of 42 ± 14 years (20–69 years). Their course of disease was 6.7 ± 5.3 years (1.5–28 years). Their symptoms included muscle weakness/fatigue (100%), bone pain (100%), trouble walking (100%), reduced height (25/39, 64.1%), and pathological fractures (33/39, 84.6%), primarily in the ribs, vertebral bodies, and femoral neck. By radiograph, vertebral compression fractures were verified in 29 of 39 (74.4%), pelvis deformities in 15 of 39 (38.5%), pseudofractures in 12 of 39 (30.8%) and blurred pubic symphyses in 4 of 39 (10.3%). Laboratory tests revealed the following results (mean ± SD): serum calcium 9.3 ± 0.5 mg/dL, phosphorus 1.4 ± 0.4 mg/dL, ALP 270 ± 133 U/L, creatinine 0.8 ± 0.2 mg/dL, intact PTH 75 ± 58 pg/mL, $1,25(OH)_2D$ 14.8 ± 10.4 pg/mL ($n = 29$), 24-hour urine calcium 104 ± 64 mg, 24-hour urine phosphate 720 ± 416 mg, and TMP/GFR 0.9 ± 0.4 mg/dL ($n = 26$) (Supplementary Table 1).

Fifteen patients (patients 1, 2, 8, 10, 11, 15, 16, 18, 21, 22, 26, 30, 31, 38, and 39) received oral phosphate, calcium, and vitamin D_2 or calcitriol for 1 to 22 years (median 4 years). Two patients (patients 10 and 26) had markedly elevated PTH levels (336–560 pg/mL). In patient 10, whose serum calcium was 11.3 mg/dL and serum PTH level 560 pg/mL, a parathyroid adenoma was removed, following which serum calcium and PTH levels became normal, 8.5 mg/dL and 35.3 pg/mL, respectively, whereas serum phosphate remained low. Patient 26, whose serum calcium concentration remained in the normal range, did not undergo parathyroidectomy until resection of the phosphaturic tumor.

Localization of tumors

The tumors were detected by $^{99}Tc^m$-OCT in all patients except 2 (37/39; 95%) whose tumors were discovered only by PE. In general, PE was helpful in 44% (17/39) of patients. In all cases, the localization of the tumor by PE and octreotide scan agreed with each other. Further localization by US (21/22, 95.5%), CT (24/24, 100%), or MRI (16/16, 100%) is shown in Supplementary Table 2. Localization of tumor by $^{99}Tc^m$-OCT, CT, and MRI images in patients 21, 29, and 36 are shown in Fig. 1*A–F*.

On the whole, 56% (22/39) of the tumors were in the lower extremities, 5% (2/39) were in the upper extremities, 3% (1/39) was in the hip, 31% (12/39) were in the head (eight in mandible and maxilla, four in nasal sinus), and 5% (2/39) were in the thorax region (Supplementary Table 2).

Histological characteristics of tumors

The tumors were found in a variety of soft tissues (67%, 26/39) and skeletal sites (33%, 13/39), and ranged from 1.0 to 7.0 cm. The majority (69%, 27/39) were characterized as PMT, with 15% (6/39) described as PMT mixed connective tissue variant (PMTMCT). In addition, there were three odontogenic fibromas, two hemangiopericytomas, and one giant cell tumor of a tendon sheath (Supplementary Table 2). Three malignant tumors (8%, 3/39) were detected, including one PMTMCT (patient 4), and two PMTs (patients 12 and 17).

Tumor resection and follow-up

After resection of the tumors, serum phosphorus levels became normal in 90% (35/39) of patients after 5.5 ± 3.0 days (2–16 days), including 2 patients (patients 12 and 17) with a malignant PMT. After lower extremity amputation, their serum phosphorus levels normalized. Serum phosphorus levels did not improve after surgery in 4 patients (patients 15, 22, 23, and 26) because their tumors were incompletely removed. Of these patients, the tumors were in the lower extremity (patient 15), foot (patient 22), elbow (patient 23), and scapula (patient 26), and were classified histopathologically as PMT.

During an average follow-up period of 27 months (3–81 months), complete symptomatic relief was achieved within 2 to 6 months. The majority (91%, 32/35) maintained a normal serum phosphorus level. In 3 patients (patients 36, 3, and 10), recurrent disease was suggested by recurrent hypophosphatemia 8, 12, and 28 months after tumor resection, respectively. Without worsening symptomatology, they were still on observation.

Serum FGF23 and phosphorus before and after tumor resection

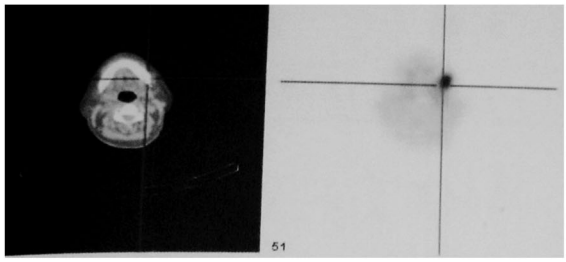
In 6 TIO patients (patients 3, 4, 10, 23, 25, and 29) who had measurements of serum FGF-23, levels were above normal (median 496 pg/mL, range 62–2979 pg/mL). In 5 patients, FGF-23 levels normalized rapidly (in 2–24 hours) after tumor resection. Serum phosphorus increased more slowly (in 2–10 days). In 1 patient (patient 23), whose tumor could not be completely removed, serum FGF-23 and phosphorus levels did not normalize (Fig. 2).

Review of the literature

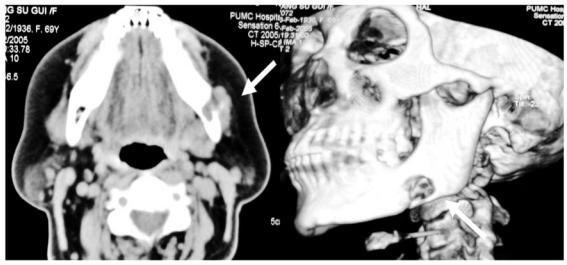
The 39 patients described here were combined with the 269 cases reviewed in the literature.[5–98] The majority of the cases were adults, with a mean age of 45 ± 16 years (range, 2–86 years). Women (47%) and men (53%) appear to be equally affected. The tumors were of bone (40%) and soft tissue (55%) origins (Fig. 1*G*; Supplementary Table 3). In 3% of the reports, the tumor location was not provided. A few patients (2%) were reported as having tumors in more than one site,[46,63,68,74,83] sometimes representing metastases.[46,74,83]

Of the tumors, 66% were histologically classified simply as PMT or as one of the 4 morphological types of PMT suggested by Weidner and Santa Cruz[105]: PMTMCT; PMT, nonossifying fibroma-like; PMT, ossifying fibroma-like; and PMT, osteoblastoma-like. Forty-two percent (42%) were categorized as PMTMCT, whereas 13 patients (4%) were reported as having malignant PMT/PMTMCT. In the remaining 34% of tumors, a variety of histological types was reported such as hemangiopericytoma, hemangioma, osteosarcoma, and giant cell tumor (Supplementary Table 4).

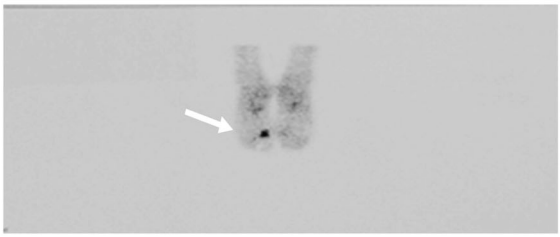
Measurements of circulating FGF-23 levels before and after surgical removal of the tumor were reported in 47 cases in the literature and measured in 6 patients in this series (Supplementary Table 5). Assays that exclusively detect the full-length FGF-23 or both the full-length FGF-23 and



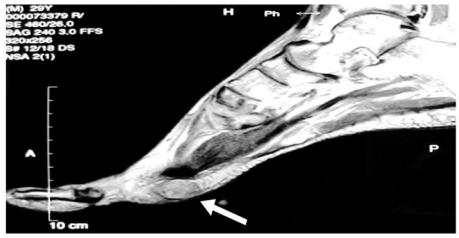
Patient #29 A. $^{99}Tc^{m}$-OCT



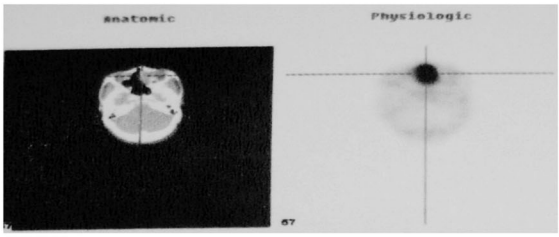
B. CT



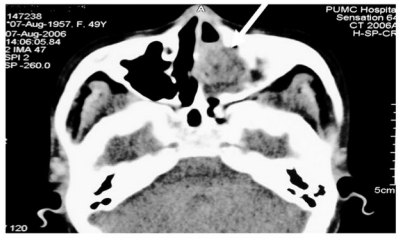
Patient #21 C. $^{99}Tc^{m}$-OCT



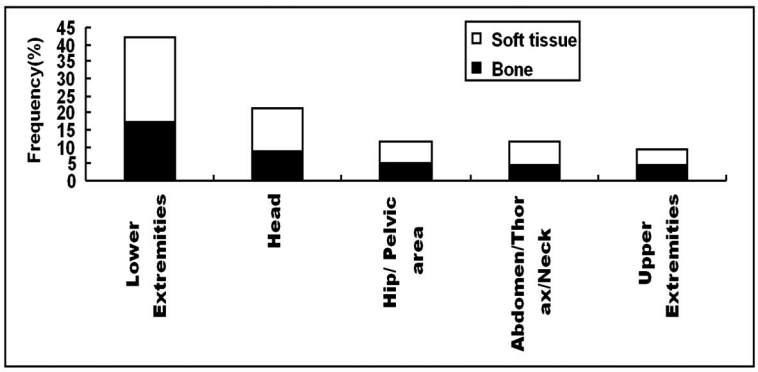
D. MRI



Patient #36 E. $^{99}Tc^{m}$-OCT



F. CT



G. Frequency of tumors per region

Fig. 1. (*A–G*) Localization of TIO tumors.

the carboxyl-terminal fragment of FGF-23 have been used. All 53 cases with FGF-23 measurements, except 1, had elevated serum or plasma levels before tumor resection. In the majority of individuals (87%), FGF-23 concentrations fell to within, or only slightly above, the normal range after surgical removal of the tumor. Five individuals reported in the literature as having persistent disease,[31,88,90,91] and one case in this study (patient 23) did not have reductions in FGF-23 after surgery. In one case, FGF-23 serum concentration measured 5 years after surgical resection remained above the reference range, despite normalization of the hypophosphatemia and complete resolution of the symptoms.[55]

Discussion

Our experience in diagnosing and treating 39 cases of TIO at one medical center in China over a relatively short period of time adds to a literature that has emphasized the rarity of this condition, with most reports describing only a few cases at a time.[17,100]

Although the biochemical manifestations of TIO are similar to those of patients with autosomal-dominant hypophosphatemic rickets (ADHR), X-linked hypophosphatemic rickets (XLH), and autosomal-recessive hypophosphatemic rickets (ARHR), TIO appears mostly in adulthood, and frequently manifests with

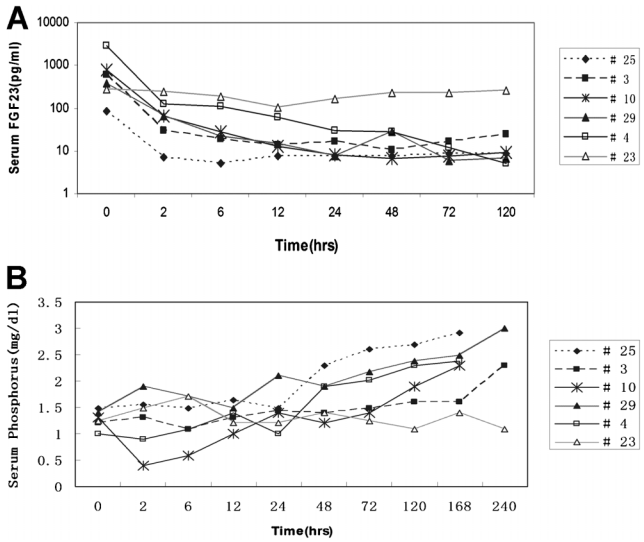


Fig. 2. Changes in serum FGF-23 and phosphorus concentrations before and after surgery in 6 TIO Chinese patients. Note: the normal range for serum FGF-23 10–50 pg/mL,[101,103] for serum phosphorus 2.2–4.2 mg/dL.

muscle weakness/fatigue, which is virtually absent in patients with XLH.[100,106]

Current approaches of TIO, in addition to surgical removal of the tumor, include phosphate, calcium, vitamin D, and/or calcitriol, just like the treatment in hereditary hypophosphatemic rickets. Obviously, these medical approaches do not cure the disorder and may be associated with hyperparathyroidism,[100,107] as shown in 2 of our patients (patients 10 and 26).

Notably, one of the most challenging aspects of TIO is to find the tumor. In 1999, Nguyen and Wang[57] reported the first case using Indium-111 pentetreotide scintigraphy to detect a mesenchymal tumor associated with TIO. Several reports followed thereafter.[33,108,109] In our study, we successfully used $^{99}Tc^{m}$-OCT scintigraphy to locate tumors in 95% (37/39) of patients with TIO. Despite this success, it is important to note several limitations with this imaging technology. Inflammatory reactions or a fracture will be associated with a false-positive scan. This might account for 1 of our patients who had a positive $^{99}Tc^{m}$-OCT scan but in whom no tumor was found at surgery. In this patient, the false-positive result might have been caused by a nonspecific uptake by the inflammatory tissue, because lymphocytes can express octreotide receptors. The possibility of a false-positive scan emphasizes the need, in many cases, to further identify the tumor by US, CT, or MRI. In recent years, there have been a few reports illustrating the application of PET in detection of tumors associated with TIO.[27,69,98] A second limitation is that a negative octreotide scan does not rule out a diagnosis of TIO. For example, 2 patients in this series (patients 9 and 32) did not have a positive $^{99}Tc^{m}$-OCT scan and 4 patients (patients 1, 6, 8, and 23) showed negative $^{99}Tc^{m}$-OCT scans initially, only to be followed by positive localization when the test was repeated later. Because the tumors are usually small, and grow slowly, repeating the scan after 1 to 2 years would seem to be indicated in those whose initial scan is negative. This could explain some of our patients in whom a tumor has not yet been identified. In those with persistently negative scans but in whom there is a high index of suspicion of TIO (ie, high levels of FGF-23, associated with adult-onset hypophosphatemic osteomalacia), the octreotide receptor subtype in the tumor might help to explain the findings. If the tumor expresses highly responsive receptor subtype 2 or 5, the scan is likely to be positive, whereas receptor subtypes 1, 3, or 4 are not usually associated with a positive scan.[109]

Although successful scanning results are a key component to the definitive, surgical management of TIO, it is important to emphasize the value of the general PE (eg, patients 9 and 32). Careful questioning of the patient asking whether any "lumps and bumps" have been felt and then on PE carefully and completely feeling for tumors in areas such as the soles of the feet and the popliteal area can be very revealing.

The mean age of our patients, 42 years, is similar to a previous report.[100] The tumor was more frequently located in the lower extremities than in other places. The distribution map of these tumors in our patients is similar to previous reports (Fig. 1*G*; Supplementary Table 3). The histological types are varied and include the following pathologies: hemangioma, hemangiopericytoma, giant cell tumor, and osteosarcoma, from previous reports.[5–99] Recently, PMT, furthermore, PMTMCT, has been recognized as the majority pathological category of TIO. PMTMCT is characterized by a distinctive admixture of spindled cells, osteoclast-like giant cells, microcysts, prominent blood vessels, cartilage-like matrix, and metaplastic bone. Eighty-five percent (85%, 33/39) of our TIO cases were best described as either PMTMCT or simply PMT.

Serum phosphorus levels in 10% (4/39) of our TIO patients did not increase to normal after tumor removal. As reported previously, hypophosphatemia is not likely to resolve if the tumor is not completely removed or multiple/metastatic foci are present. All these 4 patients had tumor burden either by size or inaccessible locations that could not be completely removed (patients 15, 22, 23, and 26). In 2 patients (patients 12 and 17) in whom lower-extremity amputation was necessary because of a malignant PMT, serum phosphorus levels became normal.

Despite the fact that the majority of these tumors are benign, they can recur. In 8 of our patients (patients 3, 10, 15, 17, 22, 36, 38, and 39) recurrence was seen, representing 20% of the entire population. Thus, it is important to follow these patients for years after apparent cure.

All the 6 cases reported here in whom FGF-23 levels were measured, and the majority of cases reviewed, had elevated FGF-23 levels at the time of presentation (Fig. 2; Supplementary Table 5). In 5 of our patients, rapid return of elevated FGF-23 levels to normal levels was shown (Fig. 2). The increase of serum phosphorus level follows more slowly after the FGF-23 levels normalize. A clue to successful removal of the entire tumor burden can be inferred by the return of FGF-23 levels to normal. When FGF-23 levels do not return to normal, as was the case in our patient 23 or in several cases reported in the literature,[31,88,90,91] residual tumor is suggested.

Recent studies have implicated iron in a pathophysiological mechanism of TIO associated with FGF-23.[110–115] Clinical and biochemical manifestations of TIO have been observed both in

the setting of parenteral iron administration[110–113] and in association with low concentrations of serum iron.[114] In wild-type mice and normal human subjects, serum iron levels are negatively correlated with circulating C-terminal FGF-23 levels, but not with intact FGF-23.[114,115] These findings raise the possibility that in TIO and other hypophosphatemic states, iron-associated molecular mechanism of FGF-23 metabolism may be involved.

In summary, we report here success in diagnosing and managing 39 cases of TIO, suggesting that the syndrome is an important cause of adult-onset hypophosphatemic osteomalacia in China. Our experience in a single hospital adds 13% to the published repository reported since the original cases. $^{99}Tc^{m}$-OCT scintigraphy is an effective method to detect the tumors that cause TIO. In cases of a negative scan, other imaging modalities can be helpful, along with repeat scintigraphy 1 to 2 years later. Successful removal of tumor leads to cure of the disease. Recurrence should be sought by long-term follow-up.

Disclosures

JPB is a consultant for Merck, Eli Lilly, NPS, Novartis, Amgen, and Radius. All of the other authors state that they have no conflicts of interest.

Acknowledgments

We are indebted to Ying-ying Hu (Department of Endocrinology, Peking Union Medical College Hospital) for the measurement of serum FGF-23.

References

1. Whyte MP, Liberman UA. Rickets and osteomalacia (acquired and heritable forms) and skeletal dysplasias. In: Wass J, Stewart PM, editors. Oxford textbook of endocrinology and diabetes. 2nd ed. Vol. 1. New York: Oxford University Press; 2011. p. 743–4.
2. Econs MJ, Drezner MK. Tumor-induced osteomalacia—unveiling a new hormone. N Engl J Med. 1994;330(23):1679–81.
3. White KE, Jonsson KB, Carn G, Hampson G, Spector TD, Mannstadt M, Lorenz-Depiereux B, Miyauchi A, Yang IM, Ljunggren O, Meitinger T, Strom TM, Juppner H, Econs MJ. The autosomal dominant hypophosphatemic rickets (ADHR) gene is a secreted polypeptide overexpressed by tumors that cause phosphate wasting. J Clin Endocrinol Metab. 2001;86(2):497–500.
4. Jan DeBeur SM, Finnegan RB, Vassiliadis J, Cook B, Barberio D, Estes S, Manavalan P, Petroziello J, Madden SL, Cho JY, Kumar R, Levine MA, Schiavi SC. Tumors associated with oncogenic osteomalacia express genes important in bone and mineral metabolism. J Bone Miner Res. 2002;17(6):1102–10.
5. Ahn JM, Kim HJ, Cha CM, Kim J, Yim SG. Oncogenic osteomalacia: induced by tumor, cured by surgery. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103(5):636–41.
6. Andreopoulou P, Dumitrescu CE, Kelly MH, Brillante BA, Peck CM, Wodajo FM, Chang R, Collins MT. Selective venous catheterization for the localization of phosphaturic mesenchymal tumors. J Bone Miner Res. 2011;26(6):1295–302.
7. Bahrami A, Weiss SW, Montgomery E, Horvai AE, Jin L, Inwards CY, Folpe AL. RT-PCR analysis for FGF23 using paraffin sections in the diagnosis of phosphaturic mesenchymal tumors with and without known tumor induced osteomalacia. Am J Surg Pathol. 2009; 33(9):1348–54.
8. Beech TJ, Rokade A, Gittoes N, Johnson AP. A haemangiopericytoma of the ethmoid sinus causing oncogenic osteomalacia: a case report and review of the literature. Int J Oral Maxillofac Surg. 2007; 36(10):956–8.
9. Casari S, Rossi V, Varenna M, Gasparini M, Parafioriti A, Failoni S, Sinigaglia L. A case of oncogenic osteomalacia detected by 111In-pentetreotide total body scan. Clin Exp Rheumatol. 2003;21(4): 493–6.
10. Cheung FM, Ma L, Wu WC, Siu TH, Choi PT, Tai YP. Oncogenic osteomalacia associated with an occult phosphaturic mesenchymal tumour: clinico-radiologico-pathological correlation and ultrastructural studies. Hong Kong Med J. 2006;12(4):319–21.
11. Chouhan V, Agrawal K, Vinothkumar TK, Mathesul A. Bilateral insufficiency fracture of the femoral head and neck in a case of oncogenic osteomalacia. J Bone Joint Surg Br. 2010;92(7): 1028–31.
12. Colt E, Gopan T, Chong HS. Oncogenic osteomalacia cured by removal of an organized hematoma. Endocr Pract. 2005;11(3): 190–3.
13. Dissanayake AM, Wilson JL, Holdaway IM, Reid IR. Oncogenic osteomalacia: culprit tumour detection whole body magnetic resonance imaging. Intern Med J. 2003;33(12):615–6.
14. Duet M, Kerkeni S, Sfar R, Bazille C, Liote F, Orcel P. Clinical impact of somatostatin receptor scintigraphy in the management of tumor-induced osteomalacia. Clin Nucl Med. 2008;33(11):752–6.
15. Dupond JL, Mahammedi H, Magy N, Blagosklonov O, Meaux-Ruault N, Kantelip B. Detection of a mesenchymal tumor responsible for hypophosphatemic osteomalacia using FDG-PET. Eur J Intern Med. 2005;16(6):445–6.
16. Elston MS, Stewart IJ, Clifton-Bligh R, Conaglen JV. A case of oncogenic osteomalacia with preoperative secondary hyperparathyroidism: description of the biochemical response of FGF23 to octreotide therapy and surgery. Bone. 2007;40(1):236–41.
17. Folpe AL, Fanburg-Smith JC, Billings SD, Bisceglia M, Bertoni F, Cho JY, Econs MJ, Inwards CY, Jan de Beur SM, Mentzel T, Montgomery E, Michal M, Miettinen M, Mills SE, Reith JD, O'Connell JX, Rosenberg AE, Rubin BP, Sweet DE, Vinh TN, Wold LE, Wehrli BM, White KE, Zaino RJ, Weiss SW. Most osteomalacia-associated mesenchymal tumors are a single histopathologic entity: an analysis of 32 cases and a comprehensive review of the literature. Am J Surg Pathol. 2004;28(1):1–30.
18. Fuentealba C, Pinto D, Ballesteros F, Pacheco D, Boettiger O, Soto N, Fernandez W, Gabler F, Gonzales G, Reginato AJ. Oncogenic hypophosphatemic osteomalacia associated with a nasal hemangiopericytoma. J Clin Rheumatol. 2003;9(6):373–9.
19. Furco A, Roger M, Mouchet B, Richard O, Martinache X, Fur A. Osteomalacia cured by surgery. Eur J Intern Med. 2002;13(1): 67–9.
20. Gascon A, Cobeta-Garcia JC, Iglesias E, Lazaro JM, Muniesa JA. Oncogenic osteomalacia in a patient with a fibrocystic nodule of the breast. Nephrol Dial Transplant. 1999;14(6):1561–3.
21. Gore MO, Welch BJ, Geng W, Kabbani W, Maalouf NM, Zerwekh JE, Moe OW, Sakhaee K. Renal phosphate wasting due to tumor-induced osteomalacia: a frequently delayed diagnosis. Kidney Int. 2009;76(3):342–7.
22. Haeusler G, Freilinger M, Dominkus M, Egerbacher M, Amann G, Kolb A, Schlegel W, Raimann A, Staudenherz A. Tumor-induced hypophosphatemic rickets in an adolescent boy—clinical presentation, diagnosis, and histological findings in growth plate and muscle tissue. J Clin Endocrinol Metab. 2010;95(10):4511–7.
23. Halperin F, Anderson RJ, Mulder JE. Tumor-induced osteomalacia: the importance of measuring serum phosphorus levels. Nat Clin Pract Endocrinol Metab. 2007;3(10):721–5.

24. Hannan FM, Athanasou NA, Teh J, Gibbons CL, Shine B, Thakker RV. Oncogenic hypophosphataemic osteomalacia: biomarker roles of fibroblast growth factor 23, 1,25-dihydroxyvitamin D3 and lymphatic vessel endothelial hyaluronan receptor 1. Eur J Endocrinol. 2008;158(2):265–71.
25. Harbeck B, Schocklmann H, Seekamp A, Czech N, Monig H. Tumor-induced osteomalacia: successful treatment by radio-guided tumor surgery. J Clin Rheumatol. 2009;15(1):31–4.
26. Harish S, Jurriaans E, Jan E, Sur M, Colterjohn N. Giant cell tumour of soft tissue causing oncogenic osteomalacia: report demonstrating the use of octreotide scintigraphy in tumour localization. Clin Radiol. 2008;63(1):101–7.
27. Hesse E, Moessinger E, Rosenthal H, Laenger F, Brabant G, Petrich T, Gratz KF, Bastian L. Oncogenic osteomalacia: exact tumor localization by co-registration of positron emission and computed tomography. J Bone Miner Res. 2007;22(1):158–62.
28. Hoogendoorn EH, White KE, Econs MJ, Hermus AR. Hypophosphatemia, osteomalacia and proximal muscle weakness treated by surgery. Clin Endocrinol (Oxf). 2003;58(6):796–7.
29. Inokuchi G, Tanimoto H, Ishida H, Sugimoto T, Yamauchi M, Miyauchi A, Nibu K. A paranasal tumor associated with tumor-induced osteomalacia. Laryngoscope. 2006;116(10):1930–3.
30. Ishii A, Imanishi Y, Kobayashi K, Hashimoto J, Ueda T, Miyauchi A, Koyano HM, Kaji H, Saito T, Oba K, Komatsu Y, Kurajoh M, Nagata Y, Goto H, Wakasa K, Sugimoto T, Miki T, Inaba M, Nishizawa Y. The levels of somatostatin receptors in causative tumors of oncogenic osteomalacia are insufficient for their agonist to normalize serum phosphate levels. Calcif Tissue Int. 2010;86(6):455–62.
31. Ito N, Shimizu Y, Suzuki H, Saito T, Okamoto T, Hori M, Akahane M, Fukumoto S, Fujita T. Clinical utility of systemic venous sampling of FGF23 for identifying tumours responsible for tumour-induced osteomalacia. J Intern Med. 2010;268(4):390–4.
32. Jacob JJ, Finny P, Thomas M, Thomas N, John M. Oncogenic osteomalacia. J Assoc Physicians India. 2007;55:231–3.
33. Jan de Beur SM, Streeten EA, Civelek AC, McCarthy EF, Uribe L, Marx SJ, Onobrakpeya O, Raisz LG, Watts NB, Sharon M, Levine MA. Localisation of mesenchymal tumours by somatostatin receptor imaging. Lancet. 2002;359(9308):761–3.
34. Jung GH, Kim JD, Cho Y, Chung SH, Lee JH, Sohn KR. A 9-month-old phosphaturic mesenchymal tumor mimicking the intractable rickets. J Pediatr Orthop B. 2010;19(1):127–32.
35. Jonsson KB, Zahradnik R, Larsson T, White KE, Sugimoto T, Imanishi Y, Yamamoto T, Hampson G, Koshiyama H, Ljunggren O, Oba K, Yang IM, Miyauchi A, Econs MJ, Lavigne J, Juppner H. Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia. N Engl J Med. 2003;348(17):1656–63.
36. Kaul M, Silverberg M, Dicarlo EF, Schneider R, Bass AR, Erkan D. Tumor-induced osteomalacia. Clin Rheumatol. 2007;26(9):1575–9.
37. Kaylie DM, Jackson CG, Gardner EK. Oncogenic osteomalacia caused by phosphaturic mesenchymal tumor of the temporal bone. Otolaryngol Head Neck Surg. 2006;135(4):653–4.
38. Kenealy H, Holdaway I, Grey A. Occult nasal sinus tumours causing oncogenic osteomalacia. Eur J Intern Med. 2008;19(7):516–9.
39. Khosravi A, Cutler CM, Kelly MH, Chang R, Royal RE, Sherry RM, Wodajo FM, Fedarko NS, Collins MT. Determination of the elimination half-life of fibroblast growth factor-23. J Clin Endocrinol Metab. 2007;92(6):2374–7.
40. Kim YG, Choi YS, Lee SC, Ryu DM. Tumor-induced osteomalacia associated with lesions in the oral and maxillofacial region: report of two cases. J Oral Maxillofac Surg. 1996;54(11):1352–7.
41. Kimizuka T, Ozaki Y, Sumi Y. Usefulness of 201Tl and 99mTc MIBI scintigraphy in a case of oncogenic osteomalacia. Ann Nucl Med. 2004;18(1):63–7.
42. Kobayashi K, Nakao K, Kawai K, Ito K, Hukumoto S, Asakage T, Oota S, Motoi R. Tumor-induced osteomalacia originating from the temporal bone: a case report. Head Neck. 2011;33(7):1072–5.
43. Koriyama N, Nishimoto K, Kodama T, Nakazaki M, Kurono Y, Yoshida H, Tei C. Oncogenic osteomalacia in a case with a maxillary sinus mesenchymal tumor. Am J Med Sci. 2006;332(3):142–7.
44. Kurien R, Manipadam MT, Rupa V. Oncogenic osteomalacia in a patient with an ethmoid sinus tumour. J Laryngol Otol. 2010; 124(7):799–803.
45. Ladha SS, Whitaker MD, Bosch EP. Oncogenic osteomalacia: muscular weakness and multiple fractures. Neurology. 2006;67(2):364–5.
46. Lamont EB, Cavaghan MK, Brockstein BE. Oncogenic osteomalacia as a harbinger of recurrent osteosarcoma. Sarcoma. 1999;3(2):95–9.
47. Lee DY, Choi IH, Lee CK, Chung CY, Cho KH. Acquired vitamin D-resistant rickets caused by aggressive osteoblastoma in the pelvis: a case report with ten years' follow-up and review of the literature. J Pediatr Orthop. 1994;14(6):793–8.
48. Lewiecki EM, Urig EJ Jr, Williams RC Jr. Tumor-induced osteomalacia: lessons learned. Arthritis Rheum. 2008;58(3):773–7.
49. Lui CY, Khoo R, Law TC, Chong SF. Case report. Tumour-induced osteomalacia in a patient with osseous haemangioma. Clin Radiol. 2002;57(12):1125–7.
50. Mannstadt M, Lorente C, Juppner H. Rapid detection of intact FGF-23 in tumor tissue from patients with oncogenic osteomalacia. Clin Chem. 2008;54(7):1252–4.
51. Mekinian A, Ladsous M, Balavoine AS, Carnaille B, Aubert S, Soudan B, Wemeau JL. Curative surgical treatment after inefficient long-acting somatostatin analogues therapy of a tumor-induced osteomalacia. Presse Med. 2011;40(3):309–13.
52. Mori Y, Ogasawara T, Motoi T, Shimizu Y, Chikazu D, Tamura K, Fukumoto S, Takato T. Tumor-induced osteomalacia associated with a maxillofacial tumor producing fibroblast growth factor 23: report of a case and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109(3):e57–63.
53. Mussig K, Oksuz MO, Pfannenberg C, Adam P, Zustin J, Beckert S, Petersenn S. Somatostatin receptor expression in an epitheloid hemangioma causing oncogenic osteomalacia. J Clin Endocrinol Metab. 2009;94(11):4123–4.
54. Nasu T, Kurisu S, Matsuno S, Tatsumi K, Kakimoto T, Kobayashi M, Nakano Y, Wakasaki H, Furuta H, Nishi M, Sasaki H, Suzuki H, Ito N, Fukumoto S, Nanjo K. Tumor-induced hypophosphatemic osteomalacia diagnosed by the combinatory procedures of magnetic resonance imaging and venous sampling for FGF23. Intern Med. 2008;47(10):957–61.
55. Nawrot-Wawrzyniak K, Varga F, Nader A, Roschger P, Sieghart S, Zwettler E, Roetzer KM, Lang S, Weinkamer R, Klaushofer K, Fratzl-Zelman N. Effects of tumor-induced osteomalacia on the bone mineralization process. Calcif Tissue Int. 2009;84(4):313–23.
56. Nelson AE, Bligh RC, Mirams M, Gill A, Au A, Clarkson A, Juppner H, Ruff S, Stalley P, Scolyer RA, Robinson BG, Mason RS, Bligh PC. Clinical case seminar: fibroblast growth factor 23: a new clinical marker for oncogenic osteomalacia. J Clin Endocrinol Metab. 2003;88(9):4088–94.
57. Nguyen BD, Wang EA. Indium-111 pentetreotide scintigraphy of mesenchymal tumor with oncogenic osteomalacia. Clin Nucl Med. 1999;24(2):130–1.
58. Ogura E, Kageyama K, Fukumoto S, Yagihashi N, Fukuda Y, Kikuchi T, Masuda M, Suda T. Development of tumor-induced osteomalacia in a subcutaneous tumor, defined by venous blood sampling of fibroblast growth factor-23. Intern Med. 2008;47(7):637–41.
59. Oka M, Kamo T, Sasaki E, Kaji H, Nishizawa H, Imanishi Y, Nishigori C. A case of phosphaturic mesenchymal tumour (mixed connective tissue variant) that developed in the subcutaneous tissue of a

patient with oncogenic osteomalacia and produced fibroblast growth factor 23. Br J Dermatol. 2007;157(1):198–200.

60. Park YK, Unni KK, Beabout JW, Hodgson SF. Oncogenic osteomalacia: a clinicopathologic study of 17 bone lesions. J Korean Med Sci. 1994;9(4):289–98.
61. Pedrazzoli M, Colletti G, Ferrari M, Rossetti G, Moneghini L, Autelitano L. Mesenchymal phosphaturic neoplasm in the maxillary sinus: a case report. Int J Oral Maxillofac Surg. 2010;39(10):1027–32.
62. Peters KB, McLendon R, Morse MA, Vredenburgh JJ. Treatment of recurrent intracranial hemangiopericytoma with SRC-related tyrosine kinase targeted therapy: a case report. Case Rep Oncol. 2010;3(1):93–7.
63. Peterson NR, Summerlin DJ, Cordes SR. Multiple phosphaturic mesenchymal tumors associated with oncogenic osteomalacia: case report and review of the literature. Ear Nose Throat J. 2010; 89(6):E11–5.
64. Pirola E, Vergani F, Casiraghi P, Leone EB, Guerra P, Sganzerla EP. Oncogenic osteomalacia caused by a phosphaturic mesenchymal tumor of the thoracic spine. J Neurosurg Spine. 2009;10(4):329–33.
65. Policarpio-Nicolas ML, Abbott TE, Dalkin AC, Bennett-Wick J, Frierson HF Jr. Phosphaturic mesenchymal tumor diagnosed by fine-needle aspiration and core biopsy: a case report and review of literature. Diagn Cytopathol. 2008;36(2):115–9.
66. Radaideh AR, Jaradat D, Abu-Kalaf MM, Nusier MK. Resolution of severe oncogenic hypophosphatemic osteomalacia after resection of a deeply located soft-tissue tumour. Curr Oncol. 2009;16(5): 87–90.
67. Ratanasuwan T, Chetsurakarn S, Ongphiphadhanakul B, Damrongkitchaiporn S. A case report of tumor-induced osteomalacia: eight year followed-up. J Med Assoc Thai. 2008;91(12):1900–2.
68. Rendina D, De Filippo G, Tauchmanova L, Insabato L, Muscariello R, Gianfrancesco F, Esposito T, Cioffi M, Colao A, Strazzullo P, Mossetti G. Bone turnover and the osteoprotegerin-RANKL pathway in tumor-induced osteomalacia: a longitudinal study of five cases. Calcif Tissue Int. 2009;85(4):293–300.
69. Roarke MC, Nguyen BD. PET/CT localization of phosphaturic mesenchymal neoplasm causing tumor-induced osteomalacia. Clin Nucl Med. 2007;32(4):300–1.
70. Romualdo-Silva DD, Silva BC, Caetano CV, Tiburcio AM, Nunes MB, Chagas SA, Polito ET, Ferreira AR, Purisch S. Tumor-induced osteomalacia: a case report. Arq Bras Endocrinol Metabol. 2009;53(3): 378–82.
71. Sahnoune I, Tazi-Mezalek Z, Essaadouni L, Harmouche H, Ismael F, Adnaoui M, Aouni M, Kettani F, Maaouni A. Oncogenic osteomalacia in a patient with hemangioma: a clinical diagnosis. Joint Bone Spine. 2006;73(1):115–8.
72. Sato K, Obara T, Yamazaki K, Kanbe M, Nakajima K, Yamada A, Yanagisawa T, Kato Y, Nishikawa T, Takano K. Somatic mutations of the MEN1 gene and microsatellite instability in a case of tertiary hyperparathyroidism occurring during high phosphate therapy for acquired, hypophosphatemic osteomalacia. J Clin Endocrinol Metab. 2001;86(11):5564–71.
73. Savage CR, Zimmer LA. Oncogenic osteomalacia from pterygopalatine fossa mass. J Laryngol Otol. 2009;123(9):1052–4.
74. Seijas R, Ares O, Sierra J, Perez-Dominguez M. Oncogenic osteomalacia: two case reports with surprisingly different outcomes. Arch Orthop Trauma Surg. 2009;129(4):533–9.
75. Shane E, Parisien M, Henderson JE, Dempster DW, Feldman F, Hardy MA, Tohme JF, Karaplis AC, Clemens TL. Tumor-induced osteomalacia: clinical and basic studies. J Bone Miner Res. 1997;12(9): 1502–11.
76. Shulman DI, Hahn G, Benator R, Washington K, White KE, Farber J, Econs MJ. Tumor-induced rickets: usefulness of MR gradient echo recall imaging for tumor localization. J Pediatr. 2004;144(3):381–5.
77. Siris ES, Clemens TL, Dempster DW, Shane E, Segre GV, Lindsay R, Bilezikian JP. Tumor-induced osteomalacia. Kinetics of calcium, phosphorus, and vitamin D metabolism and characteristics of bone histomorphometry. Am J Med. 1987;82(2):307–12.
78. Takeuchi Y, Suzuki H, Ogura S, Imai R, Yamazaki Y, Yamashita T, Miyamoto Y, Okazaki H, Nakamura K, Nakahara K, Fukumoto S, Fujita T. Venous sampling for fibroblast growth factor-23 confirms preoperative diagnosis of tumor-induced osteomalacia. J Clin Endocrinol Metab. 2004;89(8):3979–82.
79. Tartaglia F, Minisola S, Sgueglia M, Blasi S, Brunelli D, Degli Effetti E, Maturo A, Cola A, Custureri F, Campana FP. Tumor-induced hypophosphatemic osteomalacia associated with tertiary hyperparathyroidism: a case report. G Chir. 2006;27(1–2):9–13.
80. Teasell RW, Shapiro AP. Misdiagnosis of conversion disorders. Am J Phys Med Rehabil. 2002;81(3):236–40.
81. Toyosawa S, Tomita Y, Kishino M, Hashimoto J, Ueda T, Tsujimura T, Aozasa K, Ijuhin N, Komori T. Expression of dentin matrix protein 1 in tumors causing oncogenic osteomalacia. Mod Pathol. 2004;17(5): 573–8.
82. Ungari C, Rocchi G, Rinna C, Agrillo A, Lattanzi A, Pagnoni M. Hypophosphaturic mesenchymal tumor of the ethmoid associated with oncogenic osteomalacia. J Craniofac Surg. 2004;15(3):523–7.
83. Uramoto N, Furukawa M, Yoshizaki T. Malignant phosphaturic mesenchymal tumor, mixed connective tissue variant of the tongue. Auris Nasus Larynx. 2009;36(1):104–5.
84. van Boekel G, Ruinemans-Koerts J, Joosten F, Dijkhuizen P, van Sorge A, de Boer H. Tumor producing fibroblast growth factor 23 localized by two-staged venous sampling. Eur J Endocrinol. 2008;158(3):431–7.
85. Vandergheynst F, Van Dorpe J, Goldman S, Decaux G. Increased 18F fluorodeoxyglucose uptake of a vertebral hemangioma responsible for oncogenic osteomalacia. Eur J Intern Med. 2006;17(3):223.
86. Vollbrecht JE, Rao DS. Images in clinical medicine. Tumor-induced osteomalacia. N Engl J Med. 2008;358(12):1282.
87. Ward LM, Rauch F, White KE, Filler G, Matzinger MA, Letts M, Travers R, Econs MJ, Glorieux FH. Resolution of severe, adolescent-onset hypophosphatemic rickets following resection of an FGF-23-producing tumour of the distal ulna. Bone. 2004;34(5):905–11.
88. Woo VL, Landesberg R, Imel EA, Singer SR, Folpe AL, Econs MJ, Kim T, Harik LR, Jacobs TP. Phosphaturic mesenchymal tumor, mixed connective tissue variant, of the mandible: report of a case and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(6):925–32.
89. Yamazaki Y, Okazaki R, Shibata M, Hasegawa Y, Satoh K, Tajima T, Takeuchi Y, Fujita T, Nakahara K, Yamashita T, Fukumoto S. Increased circulatory level of biologically active full-length FGF-23 in patients with hypophosphatemic rickets/osteomalacia. J Clin Endocrinol Metab. 2002;87(11):4957–60.
90. Yoshioka K, Nagata R, Ueda M, Yamaguchi T, Konishi Y, Hosoi M, Inoue T, Yamanaka K, Iwai Y, Sato T. Phosphaturic mesenchymal tumor with symptoms related to osteomalacia that appeared one year after tumorectomy. Intern Med. 2006;45(20):1157–60.
91. Zimering MB, Caldarella FA, White KE, Econs MJ. Persistent tumor-induced osteomalacia confirmed by elevated postoperative levels of serum fibroblast growth factor-23 and 5-year follow-up of bone density changes. Endocr Pract. 2005;11(2):108–14.
92. Hesse E, Rosenthal H, Bastian L. Radiofrequency ablation of a tumor causing oncogenic osteomalacia. N Engl J Med. 2007;357(4):422–4.
93. Khadgawat R, Singh Y, Kansara S, Tandon N, Bal C, Seith A, Kotwal P. PET/CT localisation of a scapular haemangiopericytoma with tumour-induced osteomalacia. Singapore Med J. 2009;50(2): e55–7.
94. Lee HK, Sung WW, Solodnik P, Shimshi M. Bone scan in tumor-induced osteomalacia. J Nucl Med. 1995;36(2):247–9.

95. Auethavekiat P, Roberts JR, Biega TJ, Toney MO, Christensen RS, Belnap CM, Berenberg JL. Case 3. Oncogenic osteomalacia associated with hemangiopericytoma localized by octreotide scan. J Clin Oncol. 2005;23(15):3626–8.

96. Gershinsky M, Croitoru S, Dickstein G, Bardicef O, Gelman R, Barmeir E. Imaging of oncogenic osteomalacia. Isr Med Assoc J. 2007;9(7): 566–7.

97. Marshall AE, Martin SE, Agaram NP, Chen JH, Horn EM, Douglas-Akinwande AC, Hattab EM. A 61-year-old woman with osteomalacia and a thoracic spine lesion. Brain Pathol. 2010;20(2):499–502.

98. Dupond JL, Mahammedi H, Prie D, Collin F, Gil H, Blagosklonov O, Ricbourg B, Meaux-Ruault N, Kantelip B. Oncogenic osteomalacia: diagnostic importance of fibroblast growth factor 23 and F-18 fluorodeoxyglucose PET/CT scan for the diagnosis and follow-up in one case. Bone. 2005;36(3):375–8.

99. Farrow EG, White KE. Tumor-induced osteomalacia. Expert Rev Endocrinol Metab. 2009;4(5):435–42.

100. Ryan EA, Reiss E. Oncogenous osteomalacia. Review of the world literature of 42 cases and report of two new cases. Am J Med. 1984;77(3):501–12.

101. Xia WB, Jiang Y, Li M, Xing XP, Wang O, Hu YY, Zhang HB, Liu HC, Meng XW, Zhou XY. Levels and dynamic changes of serum fibroblast growth factor 23 in hypophosphatemic rickets/osteomalacia. Chin Med J (Engl). 2010;123(9):1158–62.

102. Walton RJ, Bijvoet OL. Nomogram for derivation of renal threshold phosphate concentration. Lancet. 1975;2(7929):309–10.

103. Xia W, Meng X, Jiang Y, Li M, Xing X, Pang L, Wang O, Pei Y, Yu LY, Sun Y, Hu Y, Zhou X. Three novel mutations of the PHEX gene in three Chinese families with X-linked dominant hypophosphatemic rickets. Calcif Tissue Int. 2007;81(6):415–20.

104. Chong WH, Molinolo AA, Chen CC, Collins MT. Tumor-induced osteomalacia. Endocr Relat Cancer. 2011;18(3):R53–77.

105. Weidner N, Santa Cruz D. Phosphaturic mesenchymal tumors. A polymorphous group causing osteomalacia or rickets. Cancer. 1987;59(8):1442–54.

106. Brame LA, White KE, Econs MJ. Renal phosphate wasting disorders: clinical features and pathogenesis. Semin Nephrol. 2004;24(1): 39–47.

107. Firth RG, Grant CS, Riggs BL. Development of hypercalcemic hyperparathyroidism after long-term phosphate supplementation in hypophosphatemic osteomalacia. Report of two cases. Am J Med. 1985;78(4):669–73.

108. Rhee Y, Lee JD, Shin KH, Lee HC, Huh KB, Lim SK. Oncogenic osteomalacia associated with mesenchymal tumour detected by indium-111 octreotide scintigraphy. Clin Endocrinol (Oxf). 2001; 54(4):551–4.

109. Seufert J, Ebert K, Muller J, Eulert J, Hendrich C, Werner E, Schuuze N, Schulz G, Kenn W, Richtmann H, Palitzsch KD, Jakob F. Octreotide therapy for tumor-induced osteomalacia. N Engl J Med. 2001; 345(26):1883–8.

110. Sato K, Nohtomi K, Demura H, Takeuchi A, Kobayashi T, Kazama J, Ozawa H. Saccharated ferric oxide (SFO)-induced osteomalacia: in vitro inhibition by SFO of bone formation and 1,25-dihydroxyvitamin D production in renal tubules. Bone. 1997;21(1):57–64.

111. Schouten BJ, Doogue MP, Soule SG, Hunt PJ. Iron polymaltose-induced FGF23 elevation complicated by hypophosphataemic osteomalacia. Ann Clin Biochem. 2009;46(Pt 2):167–9.

112. Shimizu Y, Tada Y, Yamauchi M, Okamoto T, Suzuki H, Ito N, Fukumoto S, Sugimoto T, Fujita T. Hypophosphatemia induced by intravenous administration of saccharated ferric oxide: another form of FGF23-related hypophosphatemia. Bone. 2009;45(4): 814–6.

113. Schouten BJ, Hunt PJ, Livesey JH, Frampton CM, Soule SG. FGF23 elevation and hypophosphatemia after intravenous iron polymaltose: a prospective study. J Clin Endocrinol Metab. 2009; 94(7):2332–7.

114. Imel EA, Peacock M, Gray AK, Padgett LR, Hui SL, Econs MJ. Iron Modifies Plasma FGF23 Differently in Autosomal Dominant Hypophosphatemic Rickets and Healthy Humans. J Clin Endocrinol Metab. 2011;96(11):3541–9.

115. Farrow EG, Yu X, Summers LJ, Davis SI, Fleet JC, Allen MR, Robling AG, Stayrook KR, Jideonwo V, Magers MJ, Garringer HJ, Vidal R, Chan RJ, Goodwin CB, Hui SL, Peacock M, White KE. Iron deficiency drives an autosomal dominant hypophosphatemic rickets (ADHR) phenotype in fibroblast growth factor-23 (Fgf23) knock-in mice. Proc Natl Acad Sci U S A. 2011 Nov 15; 108(46): E1146–55.