

Case Report

Tumor induced osteomalacia: a rare case report

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Received: 17 August 2026

Accepted: 21 September 2026

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ABSTRACT

Tumor-induced osteomalacia is a rare paraneoplastic syndrome caused by excessive fibroblast growth factor 23 (FGF23) secretion from phosphaturic mesenchymal tumors, leading to hypophosphatemia and osteomalacia. We present a 36-year-old female with progressive bilateral hip pain and pathological femoral neck fractures without trauma history. Despite being treated for hyperparathyroidism, she developed progressive mobility decline, becoming bedridden. Laboratory investigations revealed persistent hypophosphatemia (1.1-1.8 mg/dl) and elevated FGF23 levels (131.50; normal: 23.20-95.40). Parathyroid scanning was negative, but Ga-68 DOTA scan identified a somatostatin receptor-expressing lesion in the left superior gingivobuccal sulcus. Following complete surgical excision and endocrine treatment, serum phosphorus normalized (3.8 mg/dl), fractures healed progressively, and the patient regained independent mobility within seven months. This case emphasizes the importance of considering tumor-induced osteomalacia in adults with unexplained bone pain, pathological fractures, and hypophosphatemia, highlighting the diagnostic value of FGF23 measurement and functional imaging for successful management.

Keywords: Tumor-induced osteomalacia, Fibroblast growth factor 23, Hypophosphatemia, Phosphaturic mesenchymal tumor, 68Ga-DOTATE PET/CT, Pathological fractures

INTRODUCTION

Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome characterized by bone pain, fractures, and muscle weakness.¹ The condition is caused by excessive production of fibroblast growth factor 23 (FGF23), a phosphate and vitamin D regulating hormone.² FGF23 inhibits renal phosphate reabsorption and reduces 1,25-dihydroxyvitamin D production, resulting in hypophosphatemia, inappropriate phosphaturia, and defective bone mineralization.³ Most commonly, TIO is associated with phosphaturic mesenchymal tumors (PMTs), which are typically small, slow-growing, and can be located in virtually any soft tissue or bone, making their detection challenging.⁴ Diagnosis often requires a combination of clinical evaluation, biochemical testing showing hypophosphatemia with elevated or inappropriately normal FGF23 levels, and advanced imaging techniques. Complete surgical resection of the causative tumor is the definitive treatment, typically

resulting in normalization of phosphate metabolism and resolution of symptoms. We present a rare case of TIO in a 36-year-old female with bilateral femoral neck fractures, highlighting the diagnostic workup and successful management of this challenging condition.

CASE REPORT

A 36-year-old female presented with complaints of bilateral hip pain for 5 months, which had worsened over the previous 3 months. She had no history of recent trauma or falls. The patient was a known case of hyperparathyroidism and hypophosphatemia on treatment. Her mobility had progressively declined, requiring walker support for 2 months before becoming bedridden for the 3 months prior to presentation.

On physical examination, tenderness was present over the base of the scarpa's triangle bilaterally. Both lower limbs were externally rotated. Range of motion at the hips could

not be assessed due to pain. Active ankle and toe movements were present with intact sensations and palpable distal pulses, with no distal neurovascular compromise.

Initial laboratory investigations revealed significant abnormalities as shown in Table 1.

To investigate the cause of hyperparathyroidism, a parathyroid scan was performed on 03 June 2024, as thyroid function tests were normal and ultrasound of the neck was within normal limits. The parathyroid scan showed no evidence of parathyroid adenoma in the neck or mediastinum.

Given the persistent hypophosphatemia despite normal parathyroid imaging, the patient was advised to undergo fibroblast growth factor 23 (FGF-23) testing to rule out tumor-induced osteomalacia. On 26/06/2024, the FGF-23 level was reported as 131.50 (normal range: 23.20-95.40), which was significantly elevated.

Following the positive FGF-23 result, a gallium-68 DOTA scan was performed to localize the potential tumor. The scan revealed a soft tissue lesion with somatostatin receptor expression in the left superior gingivobuccal sulcus, consistent with tumor-induced osteomalacia.

The patient underwent surgical excision of the tumor on 08 July 2024 and was started on endocrine treatment. Histopathological examination confirmed the diagnosis of phosphaturic mesenchymal tumor.



Figure 1 (A-C): X-ray images showing bilateral neck of femur fracture (08 June 2024).

Serial radiographs documented the healing process of bilateral femoral neck fractures following tumor excision and endocrine treatment - 11 July 2024: initial post-excision X-ray, 28 August 2024: X-ray showing uniting bilateral neck of femur fractures; patient ambulating with full weight-bearing using walker support, 13 November 2024: follow-up X-ray showing progressive healing, and 12 February 2025: X-ray showing united left neck of femur fracture and right neck of femur fracture in coxa vara; patient ambulating with full weight-bearing without support.

The patient demonstrated significant clinical improvement with resolution of pain and restoration of mobility over the 7-month follow-up period, progressing from being bedridden to ambulating without support.

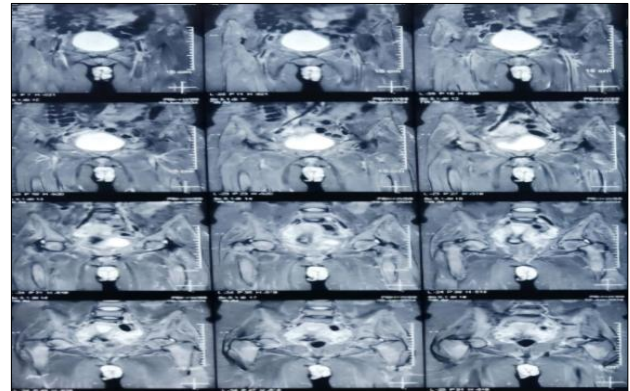


Figure 2: MRI images showing bilateral neck of femur fracture (08 June 2024).

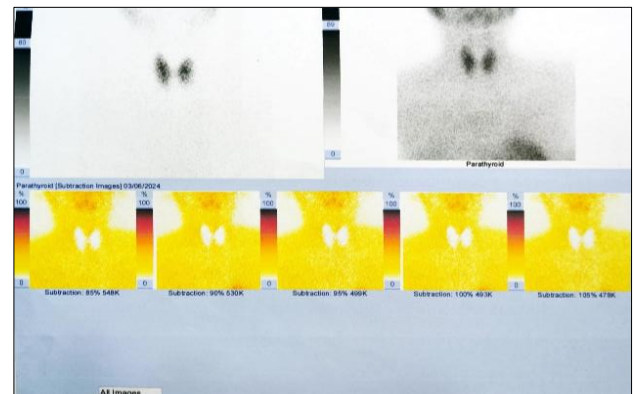


Figure 3: Parathyroid scan (03 June 2024) showing no evidence of parathyroid adenoma.

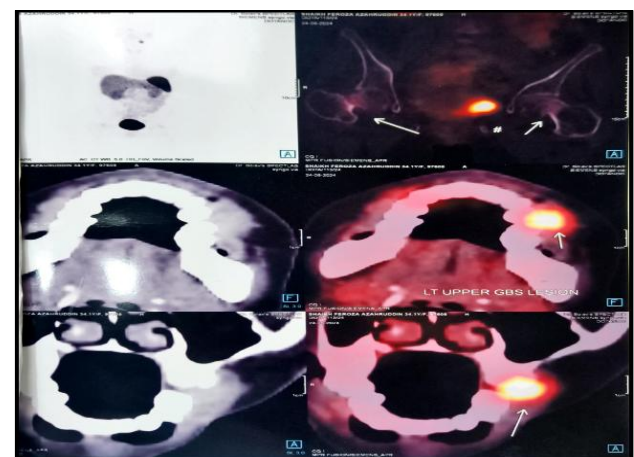


Figure 4: Ga-68 DOTA scan showing soft tissue lesion with somatostatin receptor expression in left superior gingivobuccal sulcus.

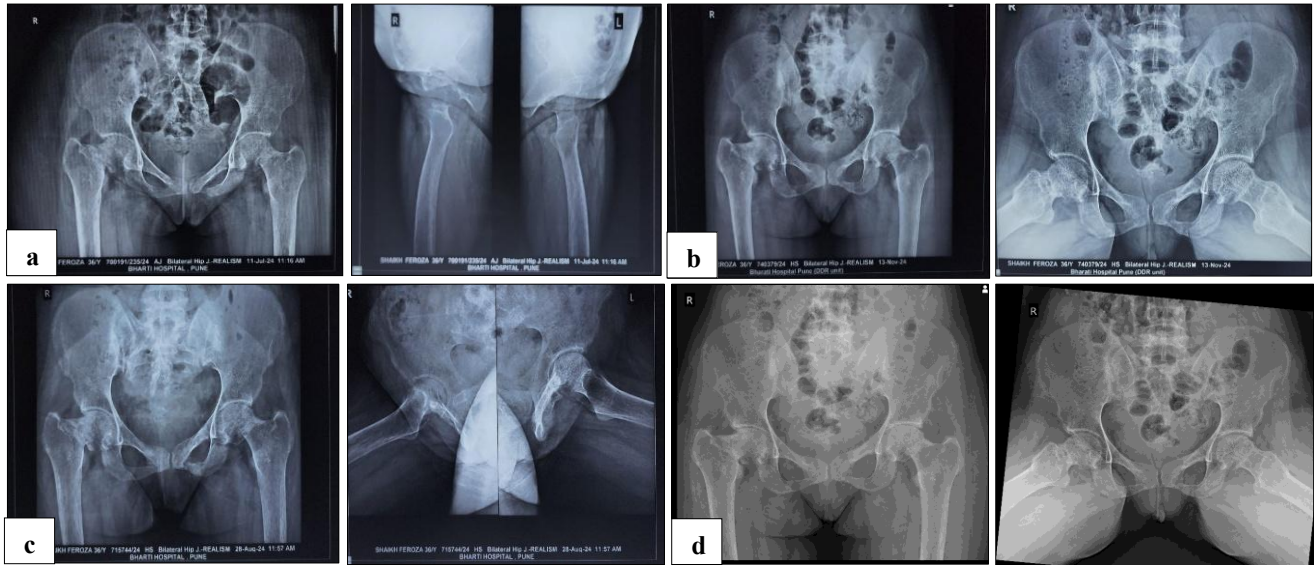


Figure 5: Serial X-rays showing fracture healing after tumor excision (a) 11 July 2024, (b) 13 November 2024, (c) 28 August 2024: uniting bilateral neck of femur fracture patient ambulating full weight bear with walker support, and (d) 12 February 2025: left united neck of femur fracture, right side united neck of femur fracture in coxa vara, patient ambulating full weight bear without support.

Table 1: Laboratory findings at presentation and follow-up.

Parameters	08 May 2024	31 May 2024	10 June 2024	12 June 2024	13 June 2024
PTH (pg/ml)	112.7 (150-300)	85.8	-	-	-
Serum alkaline phosphatase (U/l)	217 (40-150)	-	-	-	-
Serum calcium (mg/dl)	8.54 (8.5-24)	9.52	7.92	-	-
Creatinine (mg/dl)	-	-	0.46	-	-
Chloride (mmol/l)	-	-	113	-	-
Potassium (mmol/l)	-	-	3.8	-	-
Sodium (mmol/l)	-	-	139	-	-
Serum phosphorous (mg/dl)	1.5 (2-4.5)	1.8	1.1	-	-
Urea (mg/dl)	-	-	14	-	-
Serum T3 (ng/ml)	-	0.51	-	-	-
Serum T4 (µg/dl)	-	7.28	-	-	-
Serum TSH (µIU/ml)	-	1.24 (0.5-5)	-	-	-
Serum 25-OH-Vitamin D (ng/ml)	-	23.4 (20-50)	-	-	-
Urine phosphorus (24 hour) (gm/day)	-	-	-	0.55 (0.4-1.3)	-
Urine calcium (24 hour) (mg/day)	-	-	-	28 (50-150)	-
Urine calcium spot (mg/dl)	-	-	-	-	2.4 (calcium free 5-40)
Urine phosphorus spot (mg/dl)	-	-	-	-	23.9 (0.4-1.3)
Urine creatinine (mg/dl)	-	-	-	-	40.43 (45-106)

Table 2: Laboratory values before and after tumor excision and endocrine treatment.

Parameter	08 May 2024	31 May 2024	10 June 2024	10 June 2024	24 July 2024	11 February 2025
Serum calcium (mg/dl)	8.54	9.52	7.92	-	-	9.16
Serum phosphorous (mg/dl)	1.5	1.8	-	1.1	3.8	2.9
Serum 25-OH-vitamin D (ng/ml)	-	23.4	-	-	-	-

DISCUSSION

TIO is a fascinating paraneoplastic syndrome caused by unregulated over-secretion of FGF23, a phosphate and vitamin D regulating hormone.¹ The clinical presentation of TIO is often non-specific, with patients typically exhibiting bone pain, muscle weakness, and fractures, causing difficulties in early diagnosis of the disease.² Our case exemplifies this diagnostic challenge, as the patient presented with bilateral hip pain and pathological femoral neck fractures without a history of significant trauma.

The diagnosis of TIO depends on clinical evaluation, biochemical testing, and tumor identification.² Biochemically, patients with TIO demonstrate hypophosphatemia, elevated alkaline phosphatase, normal or low 1,25-dihydroxyvitamin D levels, and elevated or inappropriately normal FGF23 levels. In our patient, the persistent hypophosphatemia (1.1-1.8 mg/dl) despite treatment for hyperparathyroidism raised suspicion for an alternative diagnosis. The elevated FGF23 level of 131.50 (normal range: 23.20-95.40) confirmed the diagnosis of FGF23-mediated hypophosphatemia. This aligns with Endo et al.'s finding that the sensitive threshold for diagnosing FGF23-induced hypophosphatemia is more than 30 pg/ml of the FGF23 level in patients with hypophosphatemia.³

Tumor localization represents a significant challenge in TIO management, as these tumors are often small, slow-growing, and can be located virtually anywhere in the body. Conventional imaging modalities frequently fail to identify these lesions. Functional imaging with 68Ga-DOTATE PET/CT has emerged as the modality with highest sensitivity and specificity for detecting phosphaturic mesenchymal tumors due to their high expression of somatostatin receptor SSTR-2. In our case, 68Ga-DOTATE scanning successfully localized the tumor to the left superior gingivobuccal sulcus, an unusual location that might have been missed with conventional imaging alone.

Complete surgical resection of the causative tumor is currently the standard treatment for TIO.² Following successful tumor removal, abnormal biochemical indicators typically return to normal, and clinical symptoms will ease within a few weeks of surgery. In our patient, serum phosphorus levels improved dramatically from pre-operative values of 1.1-1.8 mg/dl to 3.8 mg/dl by 24/07/2024, approximately two weeks post-surgery. This biochemical improvement was accompanied by clinical improvement, with fracture healing and progressive restoration of mobility, consistent with the resolution of osteomalacia.

The pathophysiology of TIO involves FGF23-mediated inhibition of sodium-phosphate co-transporters in the proximal renal tubule, resulting in phosphaturia and hypophosphatemia. Additionally, FGF23 suppresses 1-alpha-hydroxylase activity, leading to decreased 1,25-

dihydroxyvitamin D production.² The resulting defective bone mineralization manifests as osteomalacia, characterized by inadequate mineralization of osteoid and predisposition to fractures, as observed in our patient.

Jiang et al reviewed 39 cases of TIO in China and emphasized the importance of considering this diagnosis in adults with unexplained osteomalacia and hypophosphatemia.⁴ Their findings highlighted the diversity of tumor locations and the diagnostic challenges associated with TIO. Our case adds to this literature by documenting an unusual presentation with bilateral femoral neck fractures and tumor location in the gingivobuccal sulcus.

The excellent outcome in our patient, with fracture healing and restoration of mobility within seven months of tumor excision, underscores the importance of prompt diagnosis and definitive treatment in TIO. Careful attention in assessing patients with osteoporosis who also have a low serum phosphate should alert the clinician to either a hereditary form of hypophosphatemia or an oncogenic condition, such as tumor-induced osteomalacia.² In cases where complete tumor resection is not feasible or in patients awaiting surgery, medical management with phosphate supplements, active vitamin D analogs, and newer targeted therapies such as burosumab (an anti-FGF23 monoclonal antibody) may be considered. However, definitive treatment ultimately requires removal of the FGF23-producing tumor.

CONCLUSION

Tumor-induced osteomalacia remains a diagnostic challenge due to its rarity and non-specific presentation. This case highlights the importance of considering TIO in the differential diagnosis of adult patients presenting with unexplained bone pain, fractures, muscle weakness, and hypophosphatemia. The diagnostic approach should include serum FGF23 measurement and functional imaging with 68Ga-DOTATE PET/CT scans when conventional imaging fails to identify the tumor. Complete surgical excision of the causative tumor is curative, leading to normalization of phosphate metabolism and resolution of symptoms. Our case demonstrates the dramatic improvement in both biochemical parameters and clinical outcomes following successful tumor removal, with the patient progressing from being bedridden to independently ambulatory within months of surgery. Early recognition and appropriate management of this rare condition can prevent progressive bone disease and significantly improve patient quality of life. This case emphasizes the need for a multidisciplinary approach involving endocrinologists, orthopedic surgeons, radiologists, and pathologists in the successful management of patients with TIO.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Varute S, Patil S, Pundkare G. Tumor induced osteomalacia: a rare case report. *Int J Res Orthop* 2026;12:2093-7.