

The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELS), 2026

Volume 22, Pages 34-37

ICMeHeLS 2026: International Conference on Medical, Health and Life Sciences

Tumor-Induced Osteomalacia in a Patient with Metastatic Prostate Cancer Presenting with Refractory Hypophosphatemia

Aparajita Roy

Barking, Havering and Redbridge University Hospitals NHS Trust

Kieran Mullins

Barking, Havering and Redbridge University Hospitals NHS Trust

Argyris Kyriakou

Barking, Havering and Redbridge University Hospitals NHS Trust

Emily Williams

Barking, Havering and Redbridge University Hospitals NHS Trust

Abstract: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome caused by fibroblast growth factor 23 (FGF23) overproduction, which leads to renal phosphate wasting and hypophosphatemia. Herein, we present the case of an 81-year-old man with metastatic prostate adenocarcinoma who presented with fatigue, diffuse bone pain, paresthesia, carpopedal spasms, and muscle cramps. Laboratory tests revealed severe hypophosphatemia, 0.28 mmol/L (0.87 mg/dL; reference, 0.80–1.50 mmol/L [2.5–4.5 mg/dL]) and markedly elevated serum levels of alkaline phosphatase (786 U/L) and FGF23 (>1,525 RU/mL; reference, <100 RU/mL). Despite intensive oral and intravenous phosphate supplementation and cholecalciferol therapy, serum phosphate levels remained persistently low. Phosphate wasting was confirmed with a 24-hour urine phosphate excretion test. The patient had mildly elevated parathyroid hormone level with normal 25-hydroxyvitamin D level and preserved renal function, excluding common secondary causes. Therefore, TIO secondary to metastatic prostate cancer was established as the final diagnosis. This case underscores that TIO should be considered in patients with refractory hypophosphatemia and musculoskeletal symptoms. Urine phosphate excretion and serum FGF23 level measurement is essential for timely diagnosis. Burosumab, an anti-FGF23 monoclonal antibody, can be considered for treatment, although its use in malignancy-associated cases is often limited to off-label use.

Keywords: TIO, Hypophosphatemia, FGF23, Oncogenic osteomalacia, Tumor-induced osteomalacia

Introduction

In hospitalized patients, hypophosphatemia is a common biochemical abnormality often overlooked in the absence of symptoms. Persistent and severe hypophosphatemia can indicate underlying phosphate wasting syndromes, including tumor-induced osteomalacia (TIO), a rare but critical paraneoplastic syndrome resulting from excessive fibroblast growth factor 23 (FGF23) secretion that promotes renal phosphate loss and impairs vitamin D metabolism (Chong et al., 2011). Timely recognition of TIO is essential because targeted therapy can reverse symptoms (Insogna KL, Briot K, Imel EA, et al., 2020). Herein, we describe a patient with metastatic prostate adenocarcinoma and refractory hypophosphatemia who was eventually diagnosed with TIO.

Case Presentation

- This is an Open Access article distributed under the terms of the Creative Commons Attribution-Noncommercial 4.0 Unported License, permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

- Selection and peer-review under responsibility of the Organizing Committee of the Conference

©2026 Published by ISRES Publishing: www.isres.org

An 81-year-old man with metastatic prostate adenocarcinoma presented with progressive fatigue, diffuse musculoskeletal pain, paresthesia, and carpopedal spasms. He reported worsening lower limb weakness and frequent muscle cramps. His medical history included prostate adenocarcinoma with osseous metastases initially diagnosed 4 years ago. He had previously received cytotoxic chemotherapy and was currently treated with zoledronic acid, 4 mg every 3 months, dexamethasone 2 mg, omeprazole 20 mg, leuporelin and bicalutamide as hormonal therapy.

Diagnostic Assessment

On examination, he appeared well, with an Eastern Cooperative Oncology Group performance status score of 1. Vital signs were within normal limits. No focal neurologic or musculoskeletal findings were noted. See Table 1 for initial laboratory investigations.

Table 1. Laboratory findings at admission

Parameter	Result (SI units)	Result (Conventional units)	Reference range (SI units)	Reference range (Conventional units)
Serum phosphate	0.28 mmol/L	0.87 mg/dL	0.80–1.50 mmol/L	2.5–4.5 mg/dL
Adjusted serum calcium	2.11 mmol/L	8.44 mg/dL	2.20–2.60 mmol/L	8.8–10.4 mg/dL
Parathyroid hormone	8.4 pmol/L	79 pg/mL	1.6–6.9 pmol/L	15–65 pg/mL
Alkaline phosphatase	786 U/L	786 U/L	30–130 U/L	30–130 U/L
Serum creatinine	88 µmol/L	1.0 mg/dL	60–110 µmol/L	0.68–1.24 mg/dL
Estimated glomerular filtration rate	71 mL/min/1.73 m ²	71 mL/min/1.73 m ²	>60 mL/min/1.73 m ²	>60 mL/min/1.73 m ²
Serum magnesium	0.89 mmol/L	2.16 mg/dL	0.70–1.00 mmol/L	1.7–2.4 mg/dL
25-Hydroxyvitamin D	71 nmol/L	28.4 ng/mL	>50 nmol/L	>20 ng/mL

Based on these findings, the initial diagnosis was drug-induced hypocalcemia with secondary reactive hyperparathyroidism and hypophosphatemia. The patient was initiated on intravenous (50 mmol) and oral phosphate supplementation (32 mmol twice daily) in addition to cholecalciferol (800 IU once daily). However, despite aggressive replacement, phosphate levels remained persistently low. Etiology of hypophosphatemia can be classified into three principal mechanisms: decreased gastrointestinal absorption, intracellular redistribution, and increased urinary phosphate excretion. In the present case, gastrointestinal malabsorption was unlikely as the patient did not have a history of chronic diarrhea or steatorrhea and did not use phosphate-binding agents such as aluminum- or magnesium-containing antacids. Intracellular redistribution was ruled out based on the absence of a history of recent insulin, glucagon or β -adrenergic agonist use and the lack of evidence of respiratory alkalosis. Increased urinary phosphate excretion was suspected and confirmed based on a 24-hour urine phosphate excretion of 62 mmol/day (1.92 g/day; reference range, 15–20 mmol/day [0.46–0.62 g/day]). Common causes of renal phosphate wasting were investigated. Vitamin D deficiency was ruled out based on a normal 25-hydroxyvitamin D level. Regarding primary and secondary hyperparathyroidism, parathyroid hormone level was mildly elevated but not consistent with a primary cause. Fanconi syndrome was ruled out based on urinalysis, which was negative for glycosuria and aminoaciduria. X-linked hypophosphatemic rickets was not applicable in our adult patient. The final diagnosis was TIO based on an elevated serum FGF23 level of >1,525 RU/mL (reference <100 RU/mL).

Treatment

The patient continued to receive aggressive oral (32 mmol twice daily) and intravenous (50 mmol) phosphate supplementation and cholecalciferol (800 IU once daily). However, serum phosphate persisted at critically low levels, limited by the gastrointestinal side effects of treatment, such as diarrhea, and the risk of nephrocalcinosis. Surgical localization of an FGF23-secreting lesion was not feasible, given widespread metastases. Off-label use

of burosumab, an anti-FGF23 monoclonal antibody approved for TIO, was considered a promising targeted therapy.

Outcome and Follow-Up

Serum phosphate levels remained refractory despite supplementation. Discussion regarding burosumab therapy included the consideration of access limitations in malignancy-associated TIO and the need for compassionate- or trial-based access. At the last follow-up evaluation, the treatment plan included monitoring of symptoms, serum phosphate levels, and bone markers while exploring access to burosumab. See Figure 1 showing the clinical timeline of our patient with TIO.

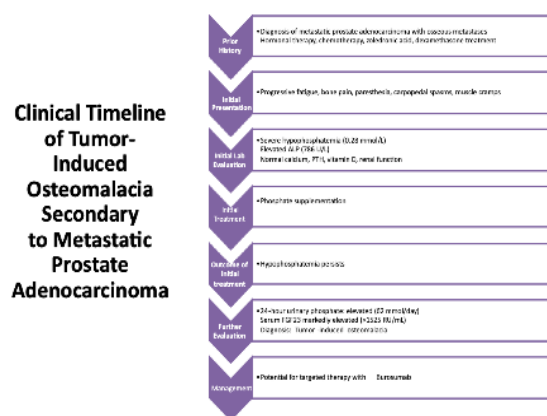


Figure 1. Clinical timeline of tumor-induced osteomalacia secondary to metastatic prostate adenocarcinoma. Abbreviations: ALP, alkaline phosphatase, FGF23, fibroblast growth factor 23; TIO, tumor-induced osteomalacia.

Discussion

TIO, also known as oncogenic osteomalacia, is caused by ectopic FGF23 secretion, commonly from mesenchymal tumors, but may occasionally originate from other malignancies, such as prostate cancer (Chong WH, Molinolo AA, Chen CC, Collins MT.,2011). Excess FGF23 can lead to the downregulation of renal NaPi-IIa/IIc cotransporters, causing phosphate wasting and the suppression of renal 1- α -hydroxylase, which reduces 1,25-dihydroxyvitamin D synthesis (Jonsson KB, Zahradnik R, Larsson T, et al.,2003). TIO diagnosis relies on the presence of renal phosphate wasting and elevated FGF23 levels (Jan de Beur SM.,2005). In patients with TIO, treatment options include surgical resection of the tumor, which is often curative, and conventional supplementation of phosphate and active vitamin D, which is limited by adverse effects. Burosumab has emerged as a targeted, effective therapeutic option for TIO in refractory cases, although its use in malignancy-associated disease remains off-label and may require special access (Insogna KL, Briot K, Imel EA, et al.,2020). The present case underscores the need for awareness of TIO in patients with refractory hypophosphatemia, especially in the setting of cancer and the potential of novel therapies to improve outcomes.

Learning Points

- Tumor-induced osteomalacia (TIO) should be included in the differential diagnosis of persistent hypophosphatemia, especially when accompanied by musculoskeletal symptoms and poor response to replacement therapy.
- Key diagnostic tests include the measurement of urine phosphate excretion and serum fibroblast growth factor 23 levels.
- TIO may occur in association with metastatic malignancies, including prostate adenocarcinoma.
- Burosumab, an anti-FGF23 monoclonal antibody, offers a targeted therapeutic approach for TIO, although its use may be off-label in patients with cancer.

Scientific Ethics Declaration

* The authors declare that the scientific ethical and legal responsibility of this article published in EPHELS journal belongs to the authors.

Conflict of Interest

* The authors declare that they have no conflicts of interest.

Funding

* No public or commercial funding has been received.

Acknowledgements or Notes

* This article was presented as an oral presentation at the International Conference on Medical, Health and Life Sciences (www.icmehels.net) held in Batumi/Georgia on July 09-12, 2026.

References

- Chong, W. H., Molinolo, A. A., Chen, C. C., & Collins, M. T. (2011). Tumor-induced osteomalacia. *Endocrine Related Cancer*, 18(3), R53–R77. <https://doi.org/10.1530/ERC-11-0006>
- Jonsson, K. B., Zahradnik, R., Larsson, T., White, K. E., Sugimoto, T., Imanishi, Y., ... & Jüppner, H. (2003). Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia. *The New England Journal of Medicine*, 348(17), 1656–1663. <https://doi.org/10.1056/NEJMoa020881>
- Jan de Beur, S. M. (2005). Tumor-induced osteomalacia. *JAMA*, 294(10), 1260–1267. <https://doi.org/10.1001/jama.294.10.1260>
- Insogna, K. L., Briot, K., Imel, E. A., Kamenický, P., Ruppe, M. D., Portale, A. A., Weber, T. J., Pitukcheewanont, P., Cheong, H. I., Jan de Beur, S. M., & Peacock, M. (2020). A randomized, double-blind, placebo-controlled, phase 3 trial of burosumab in tumor-induced osteomalacia. *The Journal of Clinical Endocrinology & Metabolism*, 105(10), e3987–e3999. <https://doi.org/10.1210/clinem/dgaa482>

Author(s) Information

Aparajita Roy

Barking, Havering and Redbridge University,
Hospitals NHS Trust, King George Hospital, Barley
Lane, Ilford, Essex, United Kingdom, IG3 8YB
ORCID iD: <https://orcid.org/0009-0001-7401-5913>
Contact e-mail: aparajita.roy1@nhs.net

Kieran Mullins

Barking, Havering and Redbridge University
Hospitals NHS Trust, King George Hospital, Barley
Lane, Ilford, Essex, United Kingdom, IG3 8YB
ORCID iD: <https://orcid.org/0000-0001-8793-9093>

Argyris Kyriakou

Barking, Havering and Redbridge University,
Hospitals NHS Trust, King George Hospital, Barley
Lane, Ilford, Essex, United Kingdom, IG3 8YB
ORCID iD: <https://orcid.org/0009-0001-7531-9580>

Emily Williams

Barking, Havering and Redbridge University
Hospitals NHS Trust, King George Hospital, Barley
Lane, Ilford, Essex, United Kingdom, IG3 8YB
<https://orcid.org/0009-0007-7500-7089>

Corresponding author(s) contact email

To cite this article:

Roy, A., Mullins, K., Kyriakou, A. & Williams, E. (2026). Tumor-induced osteomalacia in a patient with metastatic prostate cancer presenting with refractory hypophosphatemia. *The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELS)*, 22, 34-37.