Case Report

An uncommon cause of polyarthralgia

Sudarsanababu Lalitha Soumya[1], Kripa Elizabeth Cherian[1], Riddhi Das Gupta[1], Pradeep M. Poonnoose[2], Julie Hephzibah[3], Anne Jennifer Prabhu[4], Thomas Vizhalil Paul[1], Nitin Kapoor[1]

Departments of [1]Endocrinology, [2]Orthopedics, [3]Nuclear Medicine and [4]Pathology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India

Abstract

Tumour induced osteomalacia (TIO) is a paraneoplastic syndrome characterized by renal phosphate wasting and hypophosphatemic osteomalacia, caused by FGF-23 (Fibroblast growth factor-23) producing mesenchymal tumours. Here, we report the case of a 40 year old lady referred by her family physician for multiple joint pains of 2 years duration. There was no evidence of inflammatory arthritis. Biochemical investigations revealed low phosphorus, with raised alkaline phosphatase and high levels of FGF-23. As a TIO was considered likely, functional imaging with a DOTATATE PET scan was done, which revealed a DOTA avid lesion in the right foot. Following surgical excision of the tumour, there was significant relief in symptoms and gradual recovery of phosphate to normal levels. It is relevant and important for family physicians as in subjects with symptom like polyarthralgia, a simple measurement of analytes like phosphate, calcium and alkaline phosphatase in primary care setting will help to arrive at a cause and referral for further evaluation as this condition is potentially treatable.

Keywords: Mesenchymal tumour, oncogenic osteomalacia, polyarthralgia

Introduction

Tumor induced osteomalacia (TIO) is a rare paraneoplastic syndrome, characterized by severe hypophosphatemia and osteomalacia, with renal phosphate wasting that commonly occurs in association with FGF-23 producing mesenchymal tumors. Clinical presentation is often non- specific and include polyarthalgia, myalgia, bone pains, fragility fractures, and muscle weakness. A high index of suspicion and awareness is the key to diagnosis and management of this potentially treatable condition as patients may present to primary care physicians with non-specific symptom such as joint pains. Here, we report a case of a female patient presented with polyarthralgia and was diagnosed to have TIO.

Address for correspondence: Dr. Nitin Kapoor, Department of Endocrinology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
E-mail: nitin.endocrine@gmail.com

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_299_19

Case Report

A 40-year-old female referred by her family physician with a history of polyarthralgia of two years duration. This was associated with difficulty in climbing stairs, getting up from squatting position, and combing hair. There was no history of fever, photosensitivity, oral ulcers, fractures, or renal stones. There was no history of antecedent trauma. There was a progressive worsening of her symptoms, and over the last 6 months, her mobility was severely restricted. Her medical history was remarkable for type 2 diabetes mellitus and systemic hypertension diagnosed 8 years back. She was on regular medications, and her glycemic status and blood pressure were under control at the time of admission. She was conservatively managed with analgesics, calcium, and vitamin D supplements. There was no relief in her symptoms, and she was referred to us for further management.

On examination, her vitals were stable. Musculoskeletal examination revealed the presence of bony tenderness

How to cite this article: Soumya SL, Cherian KE, Gupta RD, Poonnoose PM, Hephzibah J, Prabhu AJ, *et al*. An uncommon cause of polyarthralgia. J Family Med Prim Care 2019;8:1801-3.

and severe proximal muscle weakness. There was no joint swelling or erythema. Her biochemical evaluation showed persistent hypophosphatemia with the lowest value being 1.1 [N: 2.5–4.5] mg/dL and albumin-corrected calcium level of 9.6 [N: 8.3–10.4] mg/dL, creatinine of 0.9 (0.6–1.4) mg/dL, alkaline phosphatase of 242 [N: 40–125] U/L, 25-OH vitamin D level of 34 [N: 30–75] ng/mL, PTH of 46.6 [N: 8–50] pg/mL. The tubular maximum for phosphate, corrected for glomerular filtration rate (TmP/GFR) was 1.3 mg/dL (indicative of phosphaturia). Serum electrolytes were within normal limits, and there was no evidence of renal tubular dysfunction. Thus, a diagnosis of hypophosphate micosteomalacia was made, and in this clinical setting, a possibility of oncogenic osteomalacia was considered. Her FGF-23 level was greater than 1500 (N: 10–44) RU/mL, which further favored a diagnosis of tumor induced osteomalacia. Functional imaging was planned to localize the tumor. Meanwhile, she was initiated on calcitriol and phosphate supplements.

Her Ga^{68} DOTATATE PET scan showed a well-defined lobulated homogenously enhancing soft tissue density lesion in the plantar aspect of right foot [Figure 1]. The tumor was resected [Figure 2] and the histopathology showed [Figure 3] sheets of bland spindle to stellate shaped cells with minimally pleomorphic nuclei, inconspicuous nucleoli, and indistinct cell borders set in a smudgy basophilic matrix showing large areas of grungy calcification diagnostic of phosphaturic mesenchymal tumor. Following surgery, her phosphate supplements and calcitriol were stopped. Her condition improved gradually, and phosphate levels normalized without supplements.

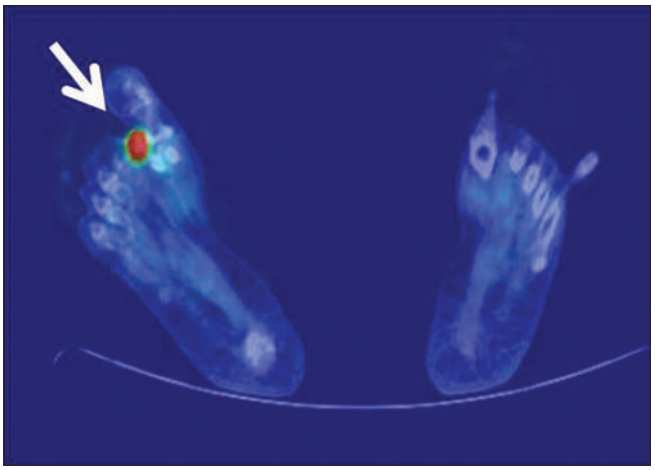

Figure 1: Ga^{68} DOTATATE PET scan showing a well-defined soft tissue density lesion in plantar aspect of the right foot

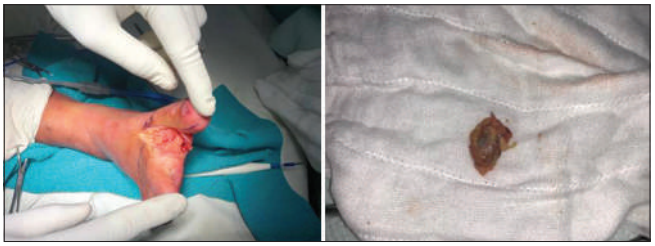

Figure 2: Resected Tumor specimen

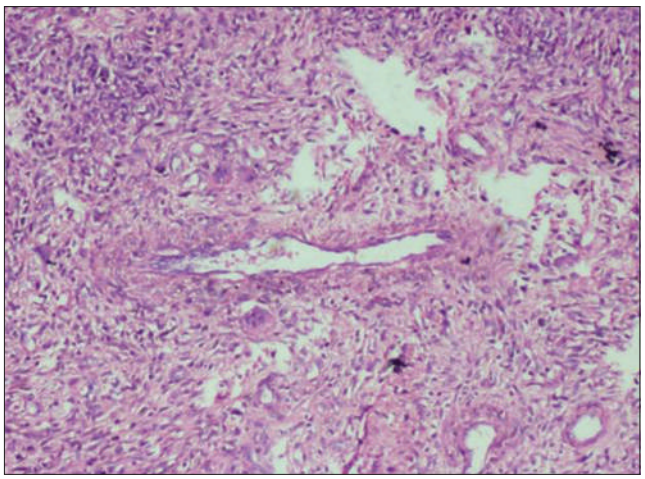

Figure 3: Histopathology showing mesenchymal phosphaturic tumor showing ectatic vessels and spindle cells in collagen stroma with grungy calcification

Discussion

A good analysis of patient history followed by performing basic biochemical investigations including serum phosphorus, calcium, and alkaline phosphatase will help in making a diagnosis of hypophosphate micosteomalacia in a primary care setting. Many laboratories in the Indian rural setting are equipped to perform these investigations. In addition, physicians at primary care setting need to be aware of these conditions and their mode of presentation like polyarthralgia.

Tumor induced osteomalacia (TIO) is a rare paraneoplastic syndrome characterized by renal phosphate wasting, severe hypophosphatemia, and osteomalacia, which occurs in association with FGF-23 producing mesenchymal tumors. This condition was first described by Robert McCance in 1947 wherein he reported a patient with pain, gait abnormalities, weakness, and low phosphorus levels whose symptoms completely resolved after excision of a tumor in the femur.[1] Clinical features of TIO are often nonspecific, progressive, and include bone pains, muscle weakness, pseudofractures, and sometimes loss of height. High circulating FGF-23 levels reduce the expression of type II sodium-phosphate co-transporters (NaPi-IIa and NaPi-IIc) in the proximal tubule, which are the transport proteins responsible for phosphate reabsorption in the kidney, leading to renal phosphate wasting. Although FGF-23 is most commonly implicated, other phosphatonins responsible for this syndrome include secreted frizzled related protein , FGF-7, and matrix extracellular phosphor glycoprotein.[2,3]

The tumors associated with TIO are usually small and mesenchymal in origin. Most tumors are located in the thigh and femur (22.7%), craniofacial region (20.7%), ankle and foot (8.8%), pelvis (8.2%), tibia and fibula (6.5%), and arms (6.5%).[4,5] The histology of these mesenchymal tumors shows neoplastic cells that are spindle to stellate shaped with small nuclei and indistinct nucleoli, low nuclear grade, and absent mitotic activity. To localize

these tumors, functional imaging such as somatostatin receptor scintigraphy or positron emission tomography followed by anatomic imaging (CT and MRI) should be performed. Treatment of TIO is resection of the tumor with a wide margin. Tumor removal is usually always curative, with gradual recovery of symptoms. In case of incompletely resected tumors, subsequent radiotherapy may be used to avoid recurrence or metastases.

Conclusion

It is essential for family physicians to be knowledgeable about this condition as in subjects presenting with non-specific symptom like polyarthralgia, simple measurement of blood parameters such as phosphate, calcium, and alkaline phosphatase in primary care setting will help to arrive at a cause, and referral for further evaluation as this condition is potentially treatable. The patients are often misdiagnosed with a variety of musculoskeletal, rheumatological, and rarely even psychiatric disorders. Therefore, primary care physicians need to be aware of this rare but potentially treatable condition to avoid delay in diagnosis and management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. McCance RA. Osteomalacia with looser'snodes (Milkman's syndrome) due to a raised resistance to vitamin D acquired about the age of 15 years.Q J Med 1947;16:33-46.
2. White KE, Larsson TE, Econs MJ. The roles of specific genes implicated as circulating factors involved in normal and disordered phosphate homeostasis: Frizzled related protein-4, matrix extracellular phosphoglycoprotein, and fibroblast growth factor 23. Endocr Rev 2006;27:221-41.
3. Carpenter TO. The expanding family of hypophosphatemic syndromes. J Bone Miner Metab 2012;30:1-9.
4. Jiang Y, Xia W, Xing X, Silva BC, Li M, Wang O, *et al.* Tumor-induced osteomalacia: An important cause of adult-onset hypophosphatemicosteomalacia in China: Report of 39 cases and review of the literature. J Bone Miner Res 2012;27:1967-75.
5. Gardner KH, Shon W, Folpe AL, Wieland CN, Tebben PJ, Baum CL. Tumor-induced osteomalacia resulting from primary cutaneous phosphaturicmesenchymal tumor: A case and review of the medical literature. J CutanPathol 2013;40:780-4. quiz 779.