Phosphaturic mesenchymal tumor: A case report and review of surgical outcomes in elderly patients

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INTRODUCTION

Phosphaturic mesenchymal tumors (PMTs) are very rare, usually benign, solitary neoplasms of bone or soft tissue most commonly found in middle-aged individuals and associated with tumor-induced osteomalacia, a paraneoplastic syndrome that manifests as renal phosphate wasting and decreased mineralization of mature bone.[1-9] Early diagnosis and localization of the tumor are critical first steps in management, as timely surgical resection can be curative. Due to the varied presentations of PMT, surgical resection techniques may vary depending on location and surgeon preference. Before surgery, or when surgery is not indicated, oral phosphate can temporarily help alleviate metabolic imbalance and symptoms. For inoperable lesions, new techniques are currently being investigated, including image-guided tumor ablation and use of the anti-fibroblast growth factor 23 (FGF23) monoclonal antibody KRN23.[1-5] We describe a case of PMT in an elderly female accompanied by a literature review and evaluation of surgical outcomes in elderly patients with PMT.

Abbreviations used:

FGF23: fibroblast growth factor 23
PMT: phosphaturic mesenchymal tumor

CASE REPORT

A 66-year-old Caucasian woman presented to an outpatient dermatology clinic on referral from an outside primary care provider with a mass of the posterior aspect of the left thigh. On examination a non-erythematous, soft, moveable subcutaneous tumor distributed on the posteromedial aspect of the left thigh measuring 4.5 × 2.8 × 2.2 cm was identified. The patient denied pathological fractures, bone pain, muscle weakness, or other constitutional symptoms. There was no pain or discharge at the tumor site. While initially concerning for lipoma, pilomatrixoma, or epidermal inclusion cyst, microscopic examination following incisional biopsy revealed aggregates of basophilic granular material with surrounding fibrosis, admixed with mononuclear cells of varying morphology. Focal multinucleated giant cells were also observed. Upon examination of histologic evidence, a PMT was suspected. FGF23 levels, serologic lab work, and imaging studies were recommended. The patient indicated that she preferred to follow up at her referring clinic, which was unable to be reached to retrieve the laboratory data.

Following incisional biopsy, the patient requested the whole tumor be removed, and a 7 × 3.5 cm-wide local excision was performed. Histopathologic examination of the excisional biopsy confirmed the diagnosis of PMT with more classic hyper- and hypocellular areas, irregular calcifications (Fig 1), and increased blood vessel proliferation (Figs 2 and 3). On review, the margins were clear of residual tumor, and

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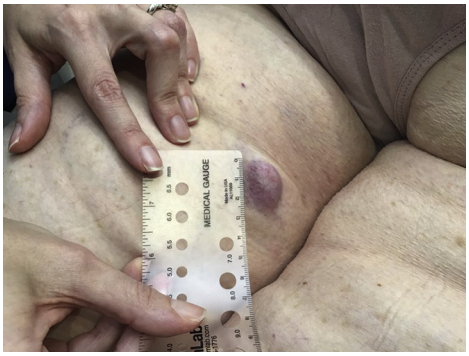

Fig 1. Gross image of the lesion on posterior aspect of the left thigh.

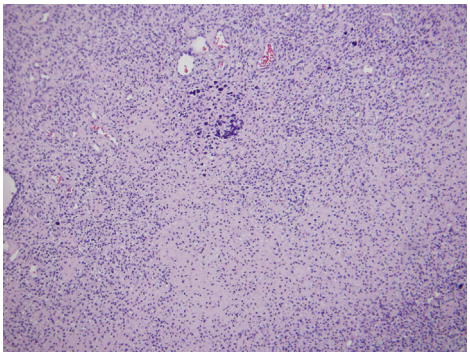

Fig 2. Collections of blood vessels admixed with the cellular stroma of epithelioid cells with areas of calcifications and focal hyalinized stroma.

the patient was discharged without complication. Serial monitoring of FGF-23 levels was recommended to assess for recurrence but was not performed since the patient was lost to follow-up.

DISCUSSION

Osteomalacia is a disorder characterized by decreased mineralization of mature bone.[2] While osteomalacia is often found to occur secondary to vitamin D deficiency or chronic kidney disease, PMT remains a rare cause of this disorder.[1,2,4,6,8] The osteomalacia that occurs secondary to PMTs is best understood by investigating the proteins produced by these functional tumors.

PMT tumor cells secrete several proteins, including the peptide hormone-like substance FGF23.[1,8] A physiologic regulator of phosphate levels, FGF23 inhibits renal sodium phosphate co-transporters and suppresses the activity of 1α-hydroxylase, an enzyme necessary in the synthesis of 1,25 dihydroxy-vitamin D.[1,2,5,8] Together, these actions lead to increased urinary phosphate excretion, decreased renal absorption of serum phosphate, and reduced levels of physiologically active vitamin

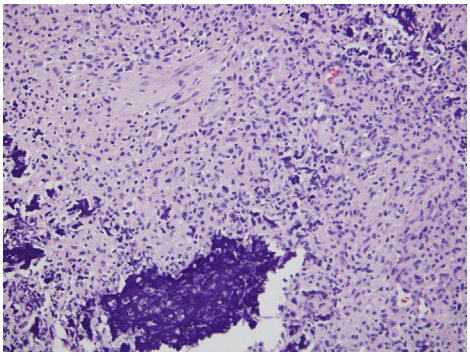

Fig 3. Areas of calcifications with admixture of the epithelial and spindle cells. Rare multinucleated cells are noted at the periphery.

D.[1,2,5,8] Clinical features of osteomalacia include bone pain and skeletal deformity.[2] osteomalacia can be caused by a deficiency in vitamin D secondary to resistance, impaired metabolism, or decreased absorption. Less commonly, osteomalacia may be caused by hypophosphatemia.[2,4] While clinical symptoms of PMT are often difficult to discern, patients who develop tumor-induced osteomalacia secondary to the neoplasm may present with pathological fractures, bone pain, and muscle weakness.[8] In these patients, laboratory tests reveal increased levels of FGF23, hypophosphatemia, and hyperphostaturia.[5] Confirmatory imaging, including radionucleotide scans, can localize the tumor.[4] The most common treatment is tumor resection, which nearly always leads to reversal of osteomalacia and the associated symptoms of chronic hypophosphatemia.[1-4]

On review of the literature, approximately 450 cases of PMT have been reported, the majority of which were diagnosed in middle-aged adults.[1,7-10] While not a tumor commonly seen in elderly individuals, post-menopausal elderly women are more likely to present with oncogenic osteomalacia, as diminished estrogen reserves increase susceptibility to the symptoms of hypophosphatemia induced by these PMTs.[4] Treatment options for elderly individuals are largely based on surgical resection with follow-up surveillance of FGF23 levels to monitor for recurrence.

To evaluate the efficacy of surgical resection as a treatment option in elderly patients (defined as patients aged >65 years) with PMT, a retrospective review of the literature from 1979 to 2020 was conducted in PubMed using the key words "phosphaturic mesenchymal tumor," "tumor-induced osteomalacia," and "oncogenic osteomalacia."

Efficacy of surgical resection as a treatment for PMT was evaluated by determining postoperative

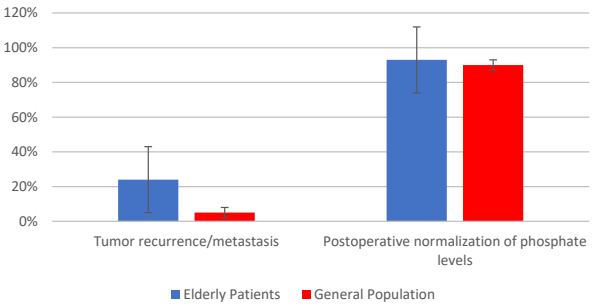

Fig 4. Surgical outcomes in phosphaturic mesenchymal tumor (PMT).

normalization of phosphate levels, tumor recurrence, or presence of metastasis. Forty cases of PMT in elderly patients were identified and analyzed. Postoperative normalization of phosphate levels was observed in 25 of the 27 (93%) cases for which phosphate levels had been reported. Tumor recurrence/metastasis was observed in 5 (24%) of the 21 cases for which a follow-up data were available. Additionally, the most common sites of tumor localization were the head and neck (16/40, 40%) and extremities (14/40, 35%); less common sites of localization were the spine (5/40, 12.5%), pelvis (3/40, 7.5%), and trunk (2/40, 5%).

The rate of postoperative normalization of phosphate levels in elderly patients (93%) was similar to the rate found in the general population of patients with PMT (approximately 90%).[6] However, the rate of tumor recurrence/metastasis in the elderly (24%) was significantly higher than the recurrence and metastasis rate in the general population (<5%) (Fig 4). Additionally, elderly patients had a much higher rate of localization in the head and neck (40%) compared with the general population (5%). The rate of localization in the extremities in the elderly population (35%) was lower than that reported for the general population (95%).[7]

In conclusion, elderly patients with PMT may be particularly susceptible to tumor recurrence/metastasis and should be closely monitored following tumor resection. Despite postoperative normalization of phosphate levels being similar to that of the general population, elderly patients should be more intensively screened for tumor recurrence and metastasis.

Conflicts of interest

None disclosed.

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