**ABSTRACT**

Phosphaturic mesenchymal tumors are rare neoplasms with the potential to incite osteomalacia from paraneoplastic processes. Malignant variants are exceedingly rare and often share several histologic characteristics with giant cell tumors. Despite these similarities, malignant phosphaturic mesenchymal tumors have several unique characteristics; failure to recognize this neoplasm as distinct entity may have significant treatment implications. We present the first reported case involving the larynx, and emphasize the importance of vigilance in both histopathological and clinical actions so that appropriate treatment can be provided in a timely manner.

**INTRODUCTION**

Phosphaturic mesenchymal tumors (PMT) are rare neoplasms that are associated with decreased serum 1,25-dihydroxyvitamin D$_3$ levels, vitamin D resistance, and renal phosphate wasting. This entity was initially described as part of a group of soft tissue neoplasms with the potential to incite osteomalacia by virtue of a paraneoplastic process. Included in this initial characterization of tumors causing "oncogenous osteomalacia" were hemangiopericytomas, giant cell tumors, osteoblastomas and hemangiomas. Despite similarities between these neoplasms, PMT are now thought by many to share specific histological characteristics, which together make them a morphologic entity distinct from these other soft tissue tumors.

Clinically, patients often present with evidence of renal phosphaturia and osseous changes, including pathologic fractures, bone pain and generalized fatigue. This owes in large-part to the location of the primary lesion being frequently limited to the extremities and trunk, which allow the tumor to remain physically elusive yet pathologically active.

Histologically, PMT demonstrate spindle cells with granular chromatin and elongated nuclei in a mixture of giant cells, cartilaginous or myxomatous areas, prominent blood vessels, and metaplastic bone. The vast majority of specimens lack nuclear atypia, necrosis, or mitotic figures. Interestingly, despite the low nuclear grade, many lesions have been shown to invade surrounding tissue. Rarely, these lesions demonstrate evidence of malignancy, including increased cellularity, a high nuclear grade and excessive mitotic activity. This histological description shares similarities with giant cell neoplasms, and these tumors can therefore be mistaken as such. In addition, the immunohistochemical profile of PMTs is highly similar to that of malignant hemangiopericytomas, staining positive for vimentin, CD34 and factor XIIIa.

Within one month, there was aggressive regrowth of the lesion. (Fig. 1) Further CO$_2$ laser debulking was performed. The lesion consisted of a cellular proliferation of stellate to spindled-shaped cells with scattered osteoclast-type multinucleated giant cells embedded within a myxoid to hyalinized, collagenous stroma. (Fig. 2 and 3) There were several areas exhibiting hypercellularity, high nuclear grade, and mitotic activity of >5 mitoses per 10 high power fields. In addition, characteristic foci of "grunny" calcification and osteoid were present (Fig. 4) These features were determined to be most consistent with a malignant phosphaturic mesenchymal tumor, mixed connective tissue (PMTMCT) type. Collectively, these features argued against a giant cell tumor of larynx. The young age of the patient as well as negative stains for numerous cytokeratins did not support a diagnosis of spindle cell carcinoma with heterologous elements. A high-grade osteosarcoma was excluded based on the characteristic features of PMTMT. The patient underwent several courses of neoadjuvant chemotherapy. There was only limited response to chemotherapy and the patient subsequently underwent a total laryngectomy and postoperative radiation therapy. She is free of disease at four months follow-up.

**DISCUSSION**

Although other phosphaturic tumors have been described in the head and neck, the vast majority of reports discuss benign, noninvasive neoplasms. One other malignant lesion of the head and neck was reported in a patient at the Kanazawa University in Japan. This lesion involved the tongue and was treated with both radiation and surgery. The authors describe a successful reduction in tumor size with radiation, however gross tumor remained after radiotherapy. While external beam radiation was not utilized preoperatively in our patient, she received postoperative radiotherapy and remains free of disease at early follow-up.

Finally, despite our limited success in reducing gross tumor burden with the use of neoadjuvant chemotherapy, significant tumor destruction was noted on histological evaluation. While this may merely reflect rapid growth of the neoplasm, it may also be attributable to a more pronounced chemotherapeutic effect than was first appreciated.

**CONCLUSIONS**