CASE REPORT

Primary osteosarcoma of the parotid gland: A case report and literature review

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ABSTRACT

Extraskeletal osteosarcoma is a rare soft tissue, high grade malignant mesenchymal neoplasm. It accounts for 1%-2% of all soft tissue sarcomas and 2%-4% of all osteosarcomas. While conventional osteosarcoma of the bone usually occurs in children and adolescents, extraskeletal osteosarcoma is more often seen in mid to late adulthood. The most common sites of this tumor are thigh and buttock. The tumor has a very poor prognosis with a 5-year survival rate of less than 25%. Only 5 cases of primary osteosarcoma have been reported in the parotid gland. We report a case of primary osteosarcoma of the parotid gland in a 68-year-old man. The clinical, radiographic and pathologic features of the tumor are discussed. Despite the very low survival rate of the tumor, our patient was disease free 41 months post surgery.

Key Words: Extraskeletal osteosarcoma, Soft tissue osteosarcoma, Parotid osteosarcoma and parotid gland

1. INTRODUCTION

Extraskeletal osteosarcoma is a rare malignant neoplasm consists of osteoblast like mesenchymal cells that form osteoid or bone matrix[1] in the soft tissue without involvement of the underlying skeleton. This tumor is responsible for 1%-2% of all soft tissue sarcomas[2–4] and 2%-4% of all osteosarcomas.[2,3] While conventional osteosarcoma usually affects children in the first decade of life, extraskeletal osteosarcoma occurs often in mid to late adulthood.[1–4] The common sites of involvement are thighs and buttocks.[1,3,5] Trunk, retroperitoneum and shoulder girdles are less common sites of involvement.[1] Visceral involvement also have been reported.[2,6–11] Since 1980s (see Table 1),[12,13] only five cases of primary osteosarcomas in the parotid gland were reported in the literature.

This tumor is usually high grade with frequent local recurrence and distant metastasis.[5] Although extraskeletal osteosarcoma can have the usual histomorphologic subtypes of conventional skeletal osteosarcoma, osteoblastic form is usually the most common subtype.[1,2] The presence of malignant osteoid or bone matrix is crucial for the diagnosis, while its absence can make it difficult to differentiate from other soft tissue sarcomas,[2,3] because hyalinized stroma closely mimics the malignant osteoid. A nuclear protein, called Special A-T Rich Binding protein 2 (SATB2), plays a critical role in osteoblastic lineage maturation. Although this protein is not specific for osteosarcoma, it can be useful in differentiation between hyalinized collagen and osteoid.[14] The five-year survival rate for patients afflicted with this neoplasm is less than 25%.[1,3,5] Therefore, aggressive treatments with radical surgery, radiotherapy and chemotherapy are warranted to improve the survival rate.[3,5]

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Table 1. Characteristics of previously reported cases of osteogenic sarcoma of parotid gland

Reported by	Age/Gender	Presentation	Treatment	Survival
Manning et al.,1986	73/M	Painless swelling in the right parotid region	Excision of superficial and adjacent parts of deep parotid lobes (no enough data about further management after diagnosis)	No enough data
Stimson et al., 1989	64/F	No enough data	Parotidectomy	DOD 6 months
Stimson et al., 1989	52/M	No enough data	Parotidectomy, Radiation therapy, Chemotherapy	DOD 2 years
Stimson et al., 1989	67/M	No enough data	Parotidectomy, Chemotherapy	LWD 2 years
Stimson et al., 1989	73/M	No enough data	Parotidectomy	Lost to follow up
Vaziri Fard et al., 2015 (present case)	68/M	Mildly painful growing mass	Parotidectomy with adjuvant chemotherapy	No evidence of disease after 41 months of follow up post surgery

Note. DOD: dead of disease; LWD: living with disease.

2. Case presentation

A 68-year-old man presented with a two-month history of a mildly painful, enlarged mass in the right parotid gland. On physical examination, a 1.5 cm mobile mass in the right parotid gland was palpated at the level of tragus. Ultrasound evaluation showed a 1.9 cm $\times$ 1.3 cm $\times$ 1.6 cm right periauricular calcified nodule with peripheral vascular flow suggestive of a calcified node/mass or sialolithiasis. CT scan of the region (with and without contrast) disclosed a 1.4 cm $\times$ 1.5 cm $\times$ 1.6 cm calcified structure in the superior aspect of the parotid gland. The remaining gland had normal attenuation and enhancement. There was also no inflammatory change of the surrounding tissue or underlying bony involvement. The left parotid gland was unremarkable (see Figure 1). The lateral spaces of the neck contained no enlarged lymph nodes, and the neurovascular bundles were intact.

The patient underwent a right parotidectomy with facial nerve dissection and right sternocleidomastoid muscle flap reconstruction. Gross examination of the parotid gland disclosed a well circumscribed calcified nodule measuring 1.5 cm $\times$ 1.2 cm $\times$ 1.0 cm. Microscopic examination of the lesion revealed a high grade neoplasm with osteoid formation infiltrating into the peri-parotid fat. The neoplastic cells showed pleomorphic, hyperchromatic nuclei with frequent nucleoli and moderate amount of eosinophilic cytoplasm (see Figure 2A-B) admixed with scattered multinucleated giant cells and abnormal mitosis (see Figure 2C-D). An unremarkable intra-parotid lymph node was also identified. Immunohistochemistry showed the tumor cells were positive for SATB2 and vimentin, and were negative for pancytokeratin, EMA, CAM5.2 and CK5/6. The overall findings favored a diagnosis of a high grade osteosarcoma. Thereafter, a full body PET/CT scan showed no evidence of a primary or metastatic disease. The patient received 4 cycles of chemotherapy with AIM regimen (doxorubicin, ifosfamide, mesna) with cumulative dose of 60 mg/m^2 of doxorubicin. He tolerated the chemotherapy well. Periodic follow-up with PET/CT scan failed to disclose evidence of disease progression or distant metastasis 41 months post surgery.

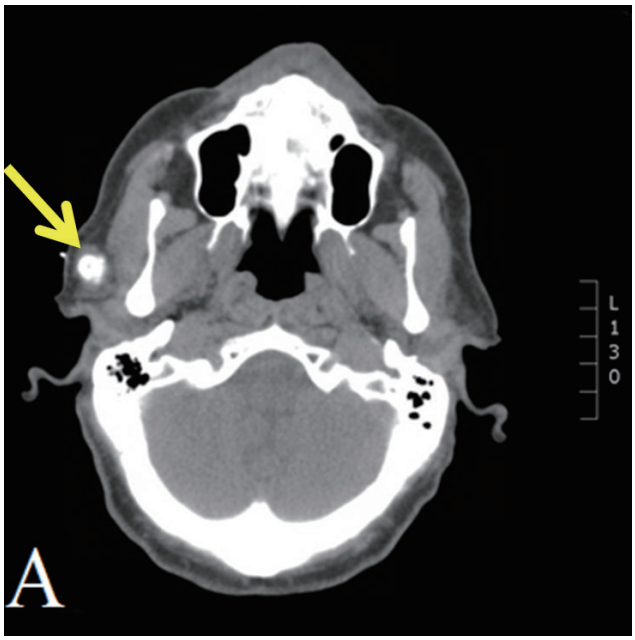

Figure 1. CT scan imaging of the head showing a calcified mass measuring 1.4 cm $\times$ 1.5 cm $\times$ 1.6 cm in the superior aspect of right parotid gland with no involvement of the adjacent bony structures (A, arrow)

3. Discussion

Extraskeletal osteosarcoma (EO) is a malignant mesenchymal tumor consists of neoplastic cells with phenotypic char-

acteristics of osteoblasts capable of producing bone. Extraskeletal osteosarcoma accounts for 1%-2% of all soft tissue sarcomas[2–4] and 2%-4.6% of all osteosarcomas.[2,3] In contrast with skeletal osteosarcoma that generally afflicts children and adolescents, extraskeletal osteosarcoma usually occurs in the mid to late adulthood, and sometimes seen in the 5^{th}-7^{th} decades of life.[1–4] There is a slight preponderance for male population.[1,2]

The most common sites for this tumor are thighs and buttocks.[1,3,5] Other less frequent sites of involvement are shoulder girdle, trunk and retroperitoneum.[1] Extraskeletal osteosarcoma of gall bladder, esophagus, colon-rectum, larynx, pleura, kidney, small intestine, liver, heart, urinary bladder and breast are also have been reported in the literature.[2,6–11] However, primary extraskeletal osteosarcoma in the parotid gland is extremely rare. Only five cases have been reported. One case was reported by Manning et al. in 1986[12] and the remaining four cases were reported by Stimson et al. in a case series published in 1989 (see Table 1).[13]

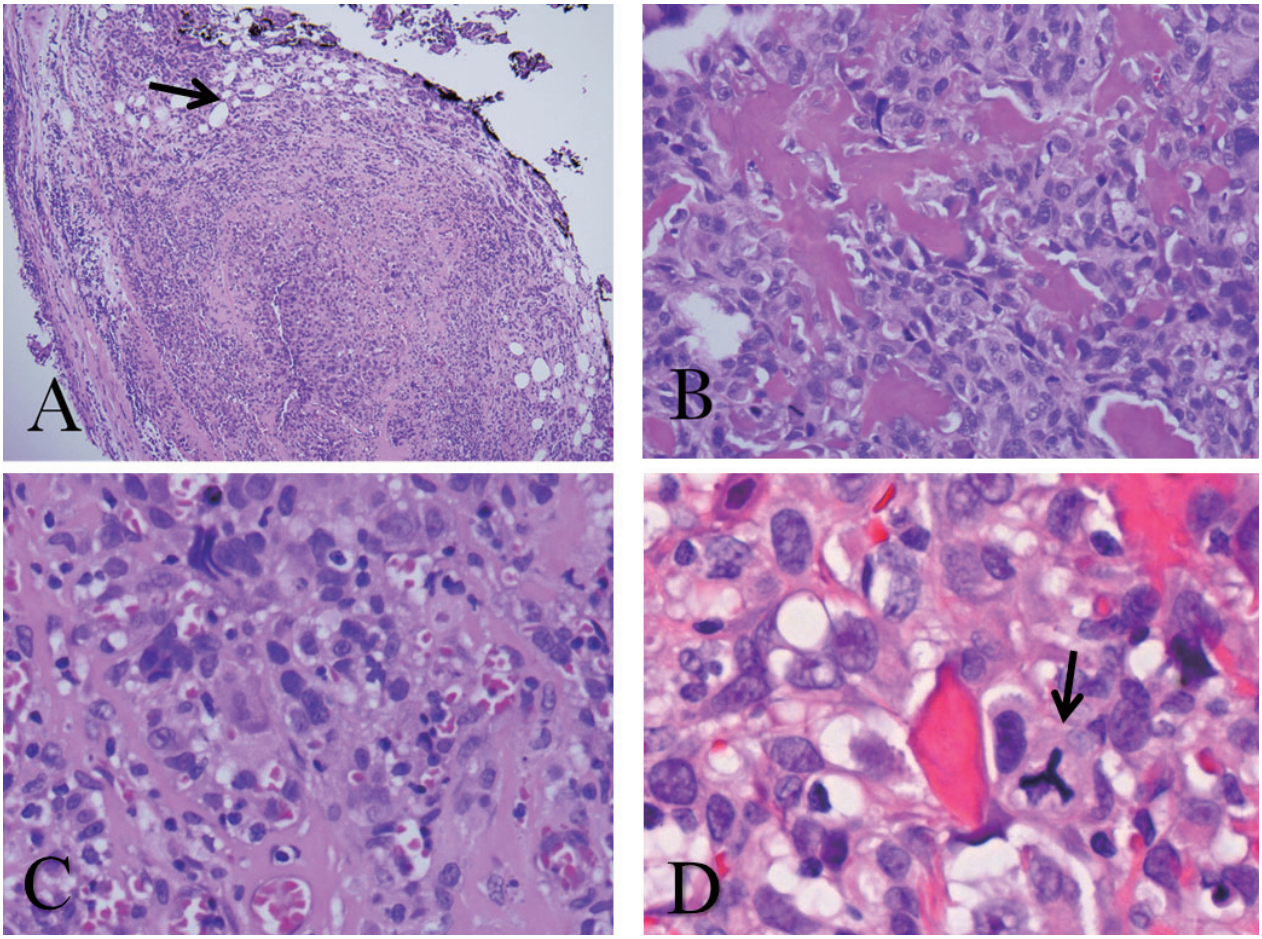

Figure 2. Low magnification view of the tumor showing the normal parotid tissue (arrow) entrapped by the malignant cells of extraskeletal osteosarcoma (A); Higher magnification showing epithelioid neoplastic cells with associated osteoid formation. Tumor cells show pleomorphic nuclei with frequent conspicuous micronucleoli (B); Another closer magnification of osteoid depositions between tumor cells (C); abnormal mitotic figure (D arrow).

History of radiation is a well-known predisposing factor for the development of skeletal and extraskeletal osteosarcoma. Trauma has also been implicated in the development of this tumor, but its etiologic significance remains unclear.[1,3,4] Approximately 10% of osteosarcomas have a history of an obvious predisposing factor, but the majority of the cases appear to be de novo with no known predisposing factor.[1,3]

For a diagnosis of EO, it is mandatory to exclude adjacent skeletal involvement or metastasis from an occult primary site.[4,12] If the adjacent bone is involved, most likely the sarcoma originates from the bone rather than the soft tissue.[5] Radiographic images usually show a soft tissue mass with spotty to massive calcification unassociated with bone erosion or destruction.[2,3]

Most EOs are high grade tumors.[2] All major histomorphologic subtypes of skeletal osteosarcoma, namely, osteoblastic, fibroblastic, chondroid, telangiectatic, small cell and well differentiated types can be seen in EO, but osteoblastic subtype is most common.[1,2] In histopathology, atypical spindle or polyhedral cells with high mitotic rate are usually noted. The neoplastic trabecular bone or sheet like deposition of malignant osteoid is common in all subtypes and is the single most important criterion for diagnosis.[5] In the absence of malignant osteoid and malignant chondrocytes, the lesion may resemble malignant giant cell tumor or undifferentiated pleomorphic sarcoma. Therefore, for a precise diagnosis, a generous amount of tissue for thorough microscopic examination is required.[2,3]

In the osteoblastic type of ES, bone matrix is abundant. In the fibroblastic subtype, spindle cells with herringbone or storiform pattern characterize the lesion. In the chondroid variant, a predominance of malignant cartilage tissue is seen, and the cells usually have large nuclei with irregular contours. In some cases, collagen is abundant in extracellular matrix and electron dense crystals of hydroxyapatite are present in areas of bone deposition.[1]

Special A-T Rich Binding protein 2 (SATB2) is a nuclear protein. It has a role in osteoblastic lineage commitment and is useful in differentiating between hyalinized collagen and osteoid.[14] In previous studies, this tumor was 100% positive for vimentin, 68% for smooth muscle actin, 25% for desmin, 20% for S100, 52% for EMA, 8% for keratin, 25% for p53 and 0% for PLAP and bcl-2.[1,5] If fresh tissue is available, alkaline phosphatase staining performed on cryostat sections or imprint smears helps to differentiate an osteosarcoma from undifferentiated pleomorphic sarcoma. A strongly positive reaction is highly suggestive of an osteosarcoma.[5]

The prognosis of EOs is very poor with a high rate of local recurrence and distant metastasis (91.1% recurrence or metastasis after one year follow up).[5] Five-year survival rate for these patients is 15%-25%.[1,3,5] Most local recurrence and distant metastasis appear in the first 3 postoperative years. Metastasis occurs more frequently than local recurrence and lung is the most common site of metastasis.[4] Studies have shown that size of the tumor of < 5 cm[1–3] and fibroblastic subtype[1,3,4] have a slightly better prognosis. Deep versus superficial tumor growth and immunohistochemical findings such as p53 positivity do not affect the outcome significantly.[5] However, Lidang Jensen et al. showed significant longer survival of patients whose tumors had MIB-1 values less than 24%.[5]

Multidisciplinary treatment plan such as radical surgery with at least 5 cm clear margins, radiotherapy and adjuvant or neoadjuvant chemotherapy should be used to improve survival rate.[3,5] Although the tumor has a very poor prognosis, cases of long survival after treatment have also been reportd.[4]

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CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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