Extraskeletal Osteosarcoma in the Parotid Gland: A Case Report and Review of Literature

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Research Article

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Abstract

Background: Extraskeletal osteosarcoma (EOS) is a rare malignant soft tissue neoplasm. Notably, there are few reports on primary EOS in parotid gland and we report the highly malignant one.

Case presentation: A 51-year-old man came to our hospital with a quickly growth mass in the left face discharge for 3 weeks. Computed tomography (CT) scan showed a 4.0 × 3.2 × 4.5cm mass in the left parotid area with significantly contrast enhancement. Unfortunately, recurrence of the lesions occurred after surgery in short time. Following magnetic resonance (MR) scan revealed a soft mass smaller than first one in the left maxillofacial and single-photon emission computed tomography/computed tomography (SPECT/CT) scan showed increased focal uptake in the lesion. Further, microscopic examination revealed a spindle cell malignant neoplasm with osteoid matrix. Immunohistochemical stains were positive for stabilin-2 and MDM2. The tumor was confirmed as a high-grade EOS in the parotid gland. The patient recovered well and no tumor recurrence was identified by MRI examination 7 months after operation. However, two subsequent chest CT examinations demonstrated a metastatic nodule in his upper lobe of the right lung and died in April, 2021 (13 months after radical surgery), due to lung metastatic complications.

Conclusions: EOS in the parotid gland can quickly grow to giant proportions with no obvious symptoms initially. Radical surgery and adjuvant chemotherapy may be curative and need to further investigation. Clinicians should also pay attention to distant metastasis for such patients and need to timely deal with the complications if necessary.

Background

Extraskeletal osteosarcoma (EOS) is a malignant tumor of soft tissue origin comprising tumor cells that produce osteoid matrix. EOS is extremely rare, accounting for about 4% of all osteosarcomas[1–6]. Unlike osteosarcoma, which frequently occurs in teenagers, the onset age of EOS is generally older, most of the victims being middle-aged and elderly patients[2, 5]. The site of EOS is widespread, and it is prevalent in the deep soft tissues of the extremities, specifically in the thigh muscles[1, 3]. Herein, we report one case of primary parotid EOS with pulmonary metastasis and discuss its clinical findings in view of the cases previously reported in the literature.

Case Presentation

A 51-year-old male, reported a mass in the anterior and inferior part of the left earlobe, about the size of a broad bean on January 15, 2020. As he did not have other symptoms, not attach importance to it initially. More than 20 days after, He felt left face swelled again and was referred to our hospital. An irregular exophytic mass was observed on the left cheek of the patient. Medical history was otherwise unremarkable. Neck examination using computed tomography (CT) revealed a 4.0 × 3.2 × 4.5cm circular mass with less calcification (Fig. 1A-C). The radiologist diagnosed melanoma. The mass grew to 6 × 7 × 7cm on February 24, 2020. An emergency operation was performed. Intraoperatively, the mass was found in the left parotid region, the pedicle was located in front of the left ear, and the base of the mass was located in the superficial lobe of the parotid gland and masseter muscle. Hematoxylin-eosin staining showed spindle cells and osteoid matrix in the tumor (Fig. 2A-B). Severe cellular atypia of neoplastic cells and mitotic figures (5/10 high power field) were noted. Immunohistochemical (IHC) examination demonstrated that the tumor cells were positive for MDM2, stabilib-2 (STAB-2), CDK4, Vimentin (Fig. 2C-E), but negative for S-100, Desmin, HMB-45, pan-cytokeratin (AE1/3), Melan-A, cytokeratin. The Ki-67 proliferative index of the tumor cells was approximately 30% (Fig. 2F). Two weeks post-surgery further loco-regional recurrence was diagnosed on MR and radionuclide static bone scan (Fig. 1D-G). The multi-disciplinary-team (MDT) confirmed that the tumor was high-grade parotid EOS with recurrence, moreover, we were told that no bone was found and that parotid gland should be ruled out as a metastatic site. Re-operation was performed on March 17, 2020. During the operation, the size of the tumor was about 4 × 3cm, which base involved the left parotid gland and masseter area. Two subsequent chest CT examinations revealed a nodule in the upper lobe of the right lung, which was highly suspected to be a metastasis of EOS. Due to refusal to treatment, the lesion was not pathologically confirmed as metastasis of EOS (Fig. 1H, I). The patient received a 3 cycles of chemotherapy regimen (cisplatin 70mg/m^2 and doxorubicin 50mg/m^2). No local tumor recurrence was identified by MRI examination 7 months after operation. However, a chest CT scan demonstrated significantly enlarged the metastatic disease (Fig. 1J). Unfortunately, patient died of lung metastasis 13 months (in April, 2021) after radical surgery.

Discussion

Review of the English-language literature showed that parotid gland as a primary site is a rare event[1–4, 6] (Table 1). Consistent with previous reports that EOS predominantly occurs in patients older than 40 and a slight predilection for males, all 5 patients were males and median age was 44.8 years old [17–73]. The present case whose age and sex are also in line with the trend reported in the literature. As mentioned above, these 5 cases, together with the cases we reported, show that primary EOS of the parotid gland is an extremely rare. Moreover, there was one case of EOS with giant cell-rich, among them, which was an exceedingly rare variant[6].

Table 1
Review of reported cases of primary EOS in parotid gland

Case	Author (Year) Reference number	Age (Years)/sex	Site	Clinical presentation	Tumor size (cm)	Immunohistochemistry	Therapy	Follow-up	Notes
1	Manning JT et al. (1986)[4]	73/M	Parotid gland	A non-tender and firm mass	3 × 3 × 2	Unknown	S	Unknown	-
2	Hatano H et al. (2005)[3]	25/M	Jaw	An enlarging subcutaneous mass	1.5 × 1.3	Vimentin(+)/AE1/3, EMA(-)	S and CT	NR or NMD/16 months/NRD	-
3	Saito Y et al. (2008)[2]	17/M	Submandibular	Swelling	4 × 3.5 × 5	Vimentin and S-100(+)	S, RT and CT	LR and MD/19 months/DOD	-
4	Huang EC et al. (2016)[6]	62/M	Parotid Gland	Swelling	6.2 × 4.6 × 3.9	Pan-K, AE1/AE3, and CAM5.2(-)	S, RT and CT	NR and MD/6 months/DOD	Numerous multinucleated giant cells
5	Hamamoto T et al. (2018)[1]	47/M	Parotid gland	A painful lump	6 × 4 × 3	Vimentin, EMA(+)/AE1/3, S-100(-)/Ki-67(98%)	S and RT	NR and MD/17 months/DOD	-
6	Our case (2021)	51/M	Parotid Gland	A growing lump	4 × 3	Vimentin, MDM2, STAB-2(+)/AE1/3, S-100(-)/Ki-67(30%)	S and CT	LR and MD/13 months/DOD	Recurrence twice in a short time

M, male; F, female; EOS, extraskeletal osteosarcoma; EMA, epithelial membrane antigen; S, surgery; RT, radiotherapy; CT, chemotherapy; DOD, dead of disease; NRD, nonrelated dead; NR, no local recurrence; LR, local recurrence; NMD, no metastatic disease; MD, metastatic disease.

The presenting signs and symptoms of parotid EOS are progressive swelling of soft tissue masses with pain, occasionally with swelling or tenderness, but it depends on tumor size and location. When the lesion is small and does not have extensive mineralization, it may look quite harmless and may look like a small lymph node. It has been reported that the inducement of EOS might be related to the history of trauma or radiotherapy[1, 3, 4]. In the Table 1, neither radiation nor trauma could have been a documented predisposing factor in the case we report here nor in the other 5 cases. It seems that radiation is not the main factor of parotid EOS.

The most important criterion for the diagnose of this tumor is based on the presence of sarcomatous pleomorphic cells producing an osteoid or bone matrix. Macroscopically, the majority of the tumors are solitary masses with a diameter of 5cm to 10cm[3]. The tumor size will not become smaller because the parotid region is small, therefore, most of the cases in Table 1 (from 1.3cm to 6.2cm) are within that range. The pathological features and IHC phenotype corroborated with those of osteosarcoma. The tumor cells usually presented positivity for Vimentin, Bcl-2, CDK4, and STAB-2. The case we present met 3 of the above diagnostic criteria, however, it is important to note that the IHC results of the 5 cases mentioned above (Table 1) were not specific. To our knowledge, this is the most complete IHC record of EOS in parotid gland so far. Melanocytes and epithelial markers (S-100, pan-cytokeratin, HMB-45, Melan-A) were all negative, thus, melanoma was excluded. Previous studies showed that high-and low-grade EOS expressed MDM2, and STAB-2 positivity in tumor cells was confirmed around the osteoid matrix in some cases with only immature osteoids[7]. Based on the World Health Organization (WHO) system, the tumor was classified as high-grade (grade 3). Calcification or osteoid matrix is present in approximately 50% of primary lesions[3]. The lack of calcification in our case was may attributed to acute onset (Fig. 1A). Also, reports indicate EOS different from traditional osteosarcoma with rare calcification, hence, calcification is not specific for EOS[1, 3, 5].

Metastatic osteosarcoma should be ruled out during the diagnosis of primary EOS. Radionuclide static bone scan of our patient revealed no tumors in bone and other organs of his body (Fig. 1D). Clinically, the differential diagnosis of EOS has vital significance, specifically from MO[3]. For parotid EOS, biopsy is the main means to make diagnosis and radiographic examination is essential for early detection of the disease and to plan surgery[1–3, 6].

We need more cases to clearly identification of the exact biobehavioral criteria for this disease, to determine the best treatment. Therefore, so far, its treatment is still controversial, referring to the treatment of osteosarcoma or soft tissue sarcoma to a large extent. Conventionally, radical resection is the primary surgical treatment but has no effect on distant metastasis[1, 2, 6]. One report does suggest surgery and combined a chemotherapy (doxorubicin, cisplatin, and ifosfamide etc.) regimen was used to treat EOS, giving a high survival rate[8]. For parotid EOS, nevertheless, postoperative chemoradiotherapy have not shown benefits in survival rates to date[1–3, 6]. Further exploration of the utility of chemoradiotherapy is certainly warranted. The recurrence rate and metastasis rate after EOS was about 70%, with a poor prognosis, and a 5-year survival rate of 25%-77%[1, 3, 4]. The data in Table 1 note that except for one patient's follow-up information was unavailable, only 1 case were observed to be alive as well as no local recurrence and metastatic disease, the rest all died of disease in the end. In the 4 death cases (including our case), all patients exhibited distant metastases after surgery and 2 developed tumor recurrences. In fact, however, no long-term survivor of primary parotid EOS has ever been reported[1, 2, 6]. Thus, we suppose that the poor prognosis of parotid EOS may be caused by tumor recurrence and metastasis. Another series showed that tumor size was a vital factor influencing prognosis, on the other hand, histological types and other clinicopathological features demonstrated no significant effect on the prognosis[9]. There were several limitations in the management of this case. The tumor was not diagnosed at an early stage, the range of the previous operation was small and was an emergency operation, neither of which was the standard

treatment plan of EOS. Multiple surgical stress destroyed the homeostasis in the body affecting tumor growth microenvironment. The resulting immunosuppressive effect accelerated the metastasis of the residual tumor and increased the risk of disease progression among patients. As such, the tumor relapses and metastases in a short time. After a definite diagnosis, the tumor was removed by radical resection, followed by doxorubicin or cisplatin-based chemotherapy regimen. During the follow-up for more than one year, we observed no sign of local recurrent tumor.

Conclusions

We provide a review of the similar cases and the latest status of current diagnosis and treatment recommendations. If a patient shows the suspicious parotid gland signs of EOS, a correct and definitive diagnosis should be promptly performed. Although appropriate surgery in terms of excision as well as adjuvant chemotherapy is a prerequisite, controlling distant metastasis was relatively limited. Thus, further work is required to develop appropriate therapeutic strategy for parotid EOS.

Abbreviations

EOS: Extraskeletal osteosarcoma

CT: Computed tomography

MR: Magnetic resonance

MRI: Magnetic resonance imaging

SPECT/CT: Single-photon emission computed tomography/computed tomography

IHC: Immunohistochemical

MDT: multi-disciplinary-team

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

The family members of patients provided written informed consent for publication of this case report and accompanying images.

Availability of data and materials

The authors declare that data supporting the findings of this study are available within the article.

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Authors' contributions

GX: data acquisition, literature search, manuscript preparation, radiological interpretation. WML: data acquisition, literature search. MJ: data acquisition. ZXF: data acquisition, pathological interpretation. LWX: literature search. WMX: literature search. WXD: data acquisition, radiological interpretation and editing. All authors read and approved the manuscript.

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Figures

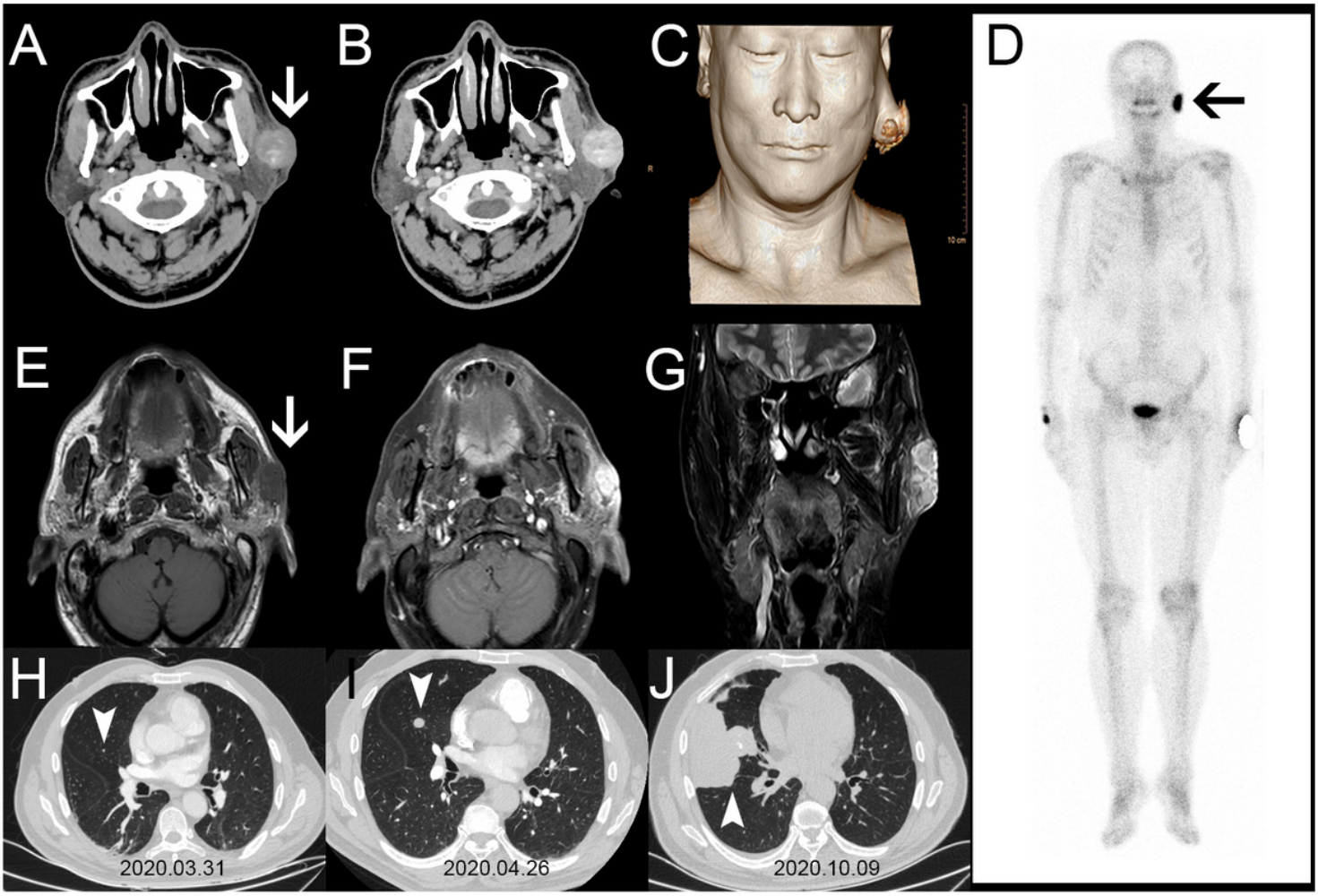

Figure 1

Imaging findings. The CT (**A**, **B**) and volume rendering (**C**) imaging before the surgery showed a tumor in the left parotid region. Axial sections showed slightly high density (calcification and bleeding) tumor invaded the fat layer and oppressed the left parotid gland and masseter muscle (**A**, arrow). The tumor was significantly enhanced after injection of iodine contrast agents (**B**). Imaging before the third operation (**D-G**). The tumor invaded the parotid gland, but it is clearly demarcated from the adjacent bone. Radionuclide static bone imaging showed a quasi-circular enhancement focus of radioactivity on the left cheek (**D**, arrow). MRI displayed a well-circumscribed mass (2.5×1.5×5.2cm) with non-uniform iso-/hypointense on T1-weighted imaging (**E**, arrow) and high signal on T2-weighted imaging (**G**), which were significantly enhanced after injection of gadolinium contrast agents (**F**). Chest CT scan showing pulmonary metastatic lesion which gradually increased during 7 months (**H-J**, arrowheads).

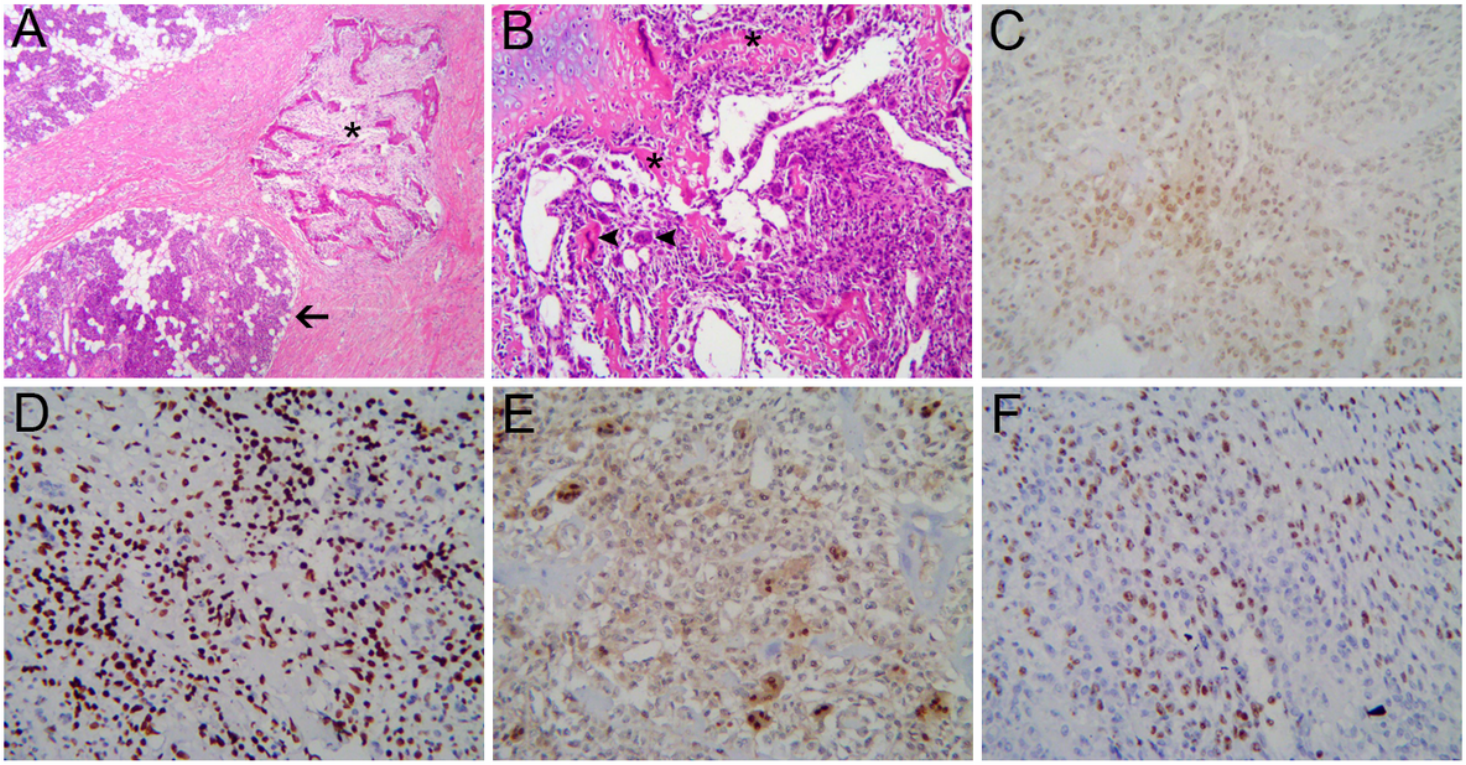

Figure 2

Microscopic histopathological features of the tumor. **(A)** Photomicrograph of the tumor stained with hematoxylin and eosin (HE) demonstrating location of the abnormal proliferation lesion (asterisk) and surrounding tissues (arrow) and **(B)** highly a malignant spindle cell tumor (arrowheads) with filigree network of osteoid matrix (asterisks). Immunohistochemistry (IHC) examination showed positivity of tumor cells to MDM2 **(C)**, STAB-2 **(D)** and CDK4 **(E)**. **(F)** Ki-67 proliferative index is approximately 30% of the tumor cell. (Original magnifications, A: ×40; B, C and E: ×200; D and F: ×100.).