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Case Report

Extraskeletal Ewing's Sarcoma of Floor of Mouth: A 1-year follow-up of the Rare Disease in a Rare Location

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Abstract

Extraskeletal Ewing's sarcoma (EES) are very rare soft tissue neoplasms, especially in the head and neck region. Only very few cases of extraskeletal ES in this site is reported in literature. A soft tissue swelling in the floor of mouth in a 15-year-old boy, which was diagnosed as extraskeletal ES of the sublingual gland after extensive investigations is reported. To the best of our knowledge, this is the first report of a case of extraskeletal ES of the sublingual gland. This case highlights the importance of considering this tumor in the differential diagnosis of soft tissue mass in the oral cavity.

Key words: Extraskeletal Ewing's sarcoma, Ewing's sarcoma, Ewing sarcoma family of tumors, Peripheral neuroectodermal tumor

INTRODUCTION

Ewing's sarcoma (ES) is a highly malignant bone tumor of long bones occurring in children and young adults and was first described by James Ewing in 1921. However, there have been reported cases of malignant soft tissue tumors which are indistinguishable from ES.[1] Extraskeletal ES (EES) is a rare round cell malignant neoplasm with rapid growth and an uncharacterized mesenchymal cell origin, and it is histologically similar to ES arising from bone.[2] The ES family of tumors (ESFT) represents a group of high-grade small round cell tumors, including ES of bone, EES, peripheral primitive neuroectodermal tumor (PNET), and Askin tumor (thoracopulmonary PNET). These tumors originate from the neuroectoderm and are composed of undifferentiated neuroepithelial cells that have the capacity to differentiate into neuronal, neuroglial, or other mesenchymal cell types.[3] Differentiation is based on cellular characteristics or anatomic location or both. ES is poorly differentiated and may arise in bones or soft tissues; PNET arises in the soft tissues and shows neuroectodermal differentiation. Fusion of the ES gene on 22p12 with one of a number of related transcription factors, the most common (90%) being FLI1 on 11q24, unites all ESFTs. The result is a protein able to interact with a number of regulators of cellular proliferation.[4] The annual incidence and mortality rates are 0.1/100,000 and 0.05/100,000, respectively.[3]

Primary ESFT can present virtually anywhere in the body.[4] Patients present with painless mass.[4] EES rarely occurs in the head and neck region, with only five cases reported in a series of 118 patients in the four largest series in English literature.[5] Another report indicated that only 5% to 11% of EES cases occur in the head and neck region, and the nose, eyelid, nasopharynx, parotid gland, scalp, and parapharyngeal space have been described.[6] We herein present a case of EES arising from sublingual gland. To the best of our knowledge, EES of sublingual gland has not been described previously.

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CASE REPORT

A 15-year-old patient came to Oral Medicine and Radiology Department with swelling under surface of tongue for 1 year and pain for 2 days (Figure 1). Swelling was gradually increasing in size and was painless. A history of difficulty in tongue protrusion and speaking started 1 month back. Pain started 2 days back due to trauma to swelling by near teeth and patient consulted for the same.

On examination, swelling of size 5×4 cm extending from left side of floor of mouth extending from 31 regions till 38 regions involving left ventral aspect of tongue noted. Mucosa overlying the swelling appeared stretched. Ulcer of size 1×1 cm noted in floor of mouth opposite to 36, 37 with irregular margins, whitish halo, necrotic slough on base. On palpation, the swelling was non-tender, firm, immobile (Figure 2). A provisional diagnosis of malignant salivary gland neoplasm was made based on clinical examination.

Figure 1: Extraoral view of the patient

Figure 2: Intraoral photograph showing swelling left floor of mouth causing tongue deviation and traumatic ulcer lingual to 46

Ultrasonographic examination of swelling was done with 8-12 MHz transducer. Sonographically, a well-defined ovoid heterogenous predominantly hypoechoic solid lesion with infiltrating margins noted in floor of mouth, extending just left of midline without significant cystic components noted (Figure 3).

Fine-needle aspiration cytology report revealed a round cell lesion with atypical features. Computed tomography (CT) features were that of a large ill-defined soft tissue mass lesion in the region of floor of mouth on left side, occupying the region of sublingual gland. The lesion was causing mass effect, displacing tongue to left side. In post contrast CT image, mild, relatively homogenous enhancement of lesion noted to a density of about 70-90 HU. The lingual artery was displaced posteromedially and stretched by the lesion. Furthermore, there was mild narrowing of oropharynx on left side. Mildly enlarged bilateral submandibular lymph nodes also noted (Figure 4). In magnetic resonance imaging (MRI), the lesion was heterogeneously hyperintense, compared to the musculature of the tongue, showed few markedly hyperintense areas, possibly cystic areas. The submandibular gland was seen separate from the lesion. A tongue-like extension was noted posterosuperiorly to

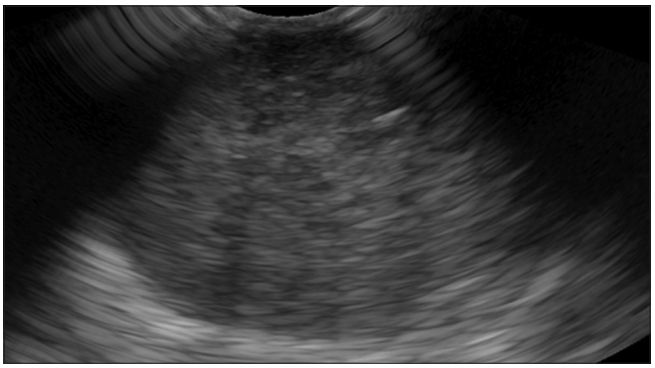

Figure 3: Ultrasonogram-Heterogenous architecture with internal hypoechoic foci

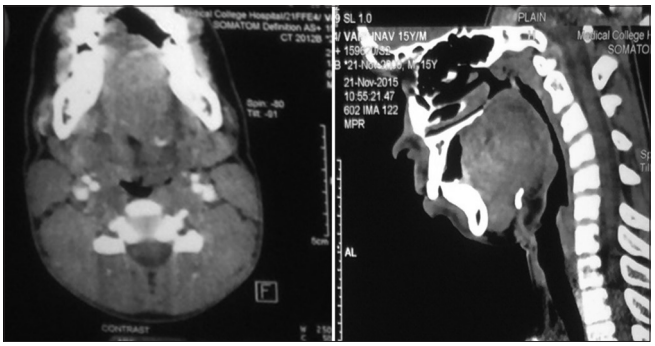

Figure 4: Postcontrast computed tomography showing large lobulated soft tissue mass lesion in floor of mouth on left side, possibly infiltrating the intrinsic and extrinsic muscles of tongue with mild enhancement

retromolar trigone and perineural extension of lesion suspected. Hence, a differential diagnosis of adenoid cystic carcinoma/schwannoma was given.

Incisional biopsy was done. Histopathology was consistent with malignant round cell neoplasm possibly PNET/ES. Immunohistochemistry showed CD99 (MIC 2) diffuse strong membrane positivity. Tumor cells were negative for LCA, desmin, and synaptophysin (Figure 5).

To assess disease status, high definition whole-body positron emission tomography (PET)/CT scan was taken. As per PET/CT, no evidence of any abnormal metabolism noted elsewhere in body. The patient responded well to chemotherapy consisting vincristine, adriamycin, and cyclophosphamide. After 12 cycles of chemotherapy, repeat PET scan was taken and no evidence of metastasis noted. After 1-year follow-up, repeat PET scan was taken and no evidence of metastasis was detected (Figures 6 and 7).

DISCUSSION

Extraosseous ES of the sublingual gland is an extremely rare soft tissue swelling. It was first described by Tefft *et al* in 1969 in four patients who had paravertebral soft tissue tumors with a histologic appearance resembling ES.[7] EES is usually seen in the second or third decades.[7] EES has equal frequency in both males and females as contrasted with ES of bone, where the male to female ratio is 2:1.[7] The sites commonly involved are soft tissues of the trunk (particularly paravertebral region) or lower extremities.[7]

Clinically, about 75% of the patients with EES present with a rapidly enlarging swelling which is usually less painful than its skeletal counterpart. It has a high propensity to spread locally, infiltrating fascial planes, and invading muscles and bone.[5] Lymphadenopathy indicating nodal metastasis is rare, reported in 0-12% of cases. In our case, there was metastatic change in level 2c lymph node.

High-resolution CT and MRI scans are useful in the diagnosis and surgical planning although the features are not specific for EES. On MRI, the tumor is usually isointense to the muscles on T1W and hyperintense on T2W images, with enhancement on postcontrast scans. In this case, the tumor was hyperintense. Although generally valuable in head and neck surgery, fine-needle aspiration cytology has limited diagnostic accuracy for the definitive diagnosis.

The classical histopathological features of ESFT consist of uniform round cells, with irregularly shaped chromatic nuclei surrounded by scanty cytoplasm. Mitotic figures may be seen. Special cellular arrangements, such as rosettes or differentiations, are not often seen. The cells often show immunohistochemical positivity for various neurofilaments, CD-99, and S-100. In our case, CD-99 was positive.

ES/PNET arising from the sublingual gland is only rarely reported, so there is a need to differentiate it from other tumors arising in this region. Schwannomas (Neurilemmoma/neurinoma) are well-encapsulated, slow-growing benign nerve sheath neoplasms are seen as central low-signal foci with an enhancing periphery on postcontrast T1W images.[7]

There are significant differences in clinical presentation, treatment strategy, and outcomes for EES compared to skeletal ES. EES may require different treatment strategies. Depending on the site of the tumor and its extension, treatment can be with surgery, chemotherapy, and

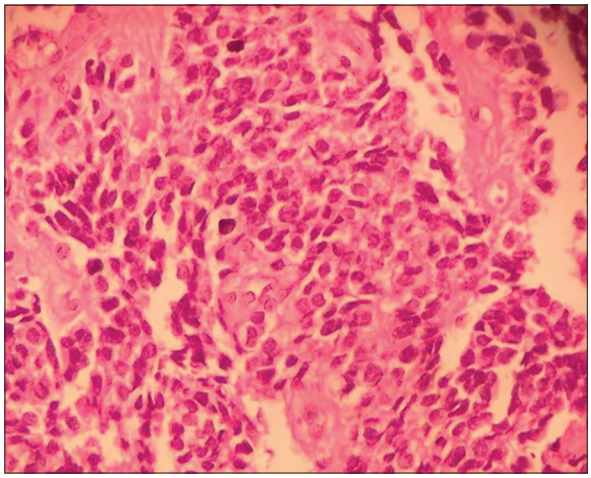

Figure 5: Histopathology-Infiltrative neoplasm composed of cells arranged in diffuse sheets and cords. Cells have moderate scanty eosinophilic clear cytoplasm. Irregular round oval hyperchromatic nuclei. Immunohistochemistry shows CD99 [MIC 2] diffuse strong membrane positivity

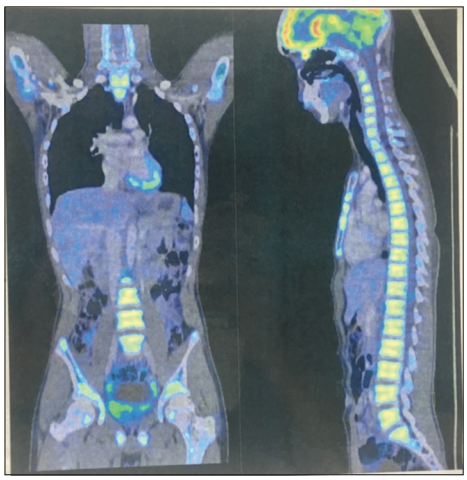

Figure 6: positron emission tomography scan showing no evidence of metastasis

Figure 7: Post treatment follow-up after 1 year showing regression of lesion

radiotherapy used separately or in various combinations. Our patient responded favorably to chemotherapy.

Treatment

Neoadjuvant chemotherapy is the standard of care before definitive radiation or surgery for localized disease. ESS is unique among sarcoma in that primary and metastatic diseases can respond dramatically to initial therapy with robust initial responses predicting a better outcome. PET/CT can play an important role in treatment response assessment because patients can show metabolically inactive tumor with reduced bulk.

CONCLUSION

In conclusion, the present case highlights a rare case of EES/PNET in the second decade of life and presented as swelling floor of mouth. The mass was seen to involve sublingual gland. Multiple imaging modalities such as US, CT, MRI, and PET-CT were used for diagnosis, and the definitive diagnosis was made by histopathological and IHC examination. MRI and PET-CT played a complimentary role in assessing local tumor resectibility and presence of metastatic disease. Diagnosis could be established only after a biopsy. The complaints resolved following chemotherapy.

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