Dental Research Journal

Case Report

Anomalous chin lesion: The many presentations of extraosseous Ewing's sarcoma

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Received: 20-Sep-2021
Revised: 13-Dec-2021
Accepted: 10-Jan-2022
Published: 01-Jun-2022

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ABSTRACT

Ewing's sarcoma (ES) is an aggressive, poorly differentiated round cell tumor in bone or soft tissues. This rare neoplasm is found primarily in the long bones of limbs and flat bone of pelvis with a predilection in the second decade in life. Primary ES of the maxillofacial region is exceptional and constitute 1% ± 4% of all cases. This case report is aimed at highlighting a very rare clinical presentation of extraosseous ES of the chin region-a first of its kind.

Key Words: Chin, Ewing's sarcoma, mandible, maxillofacial

INTRODUCTION

Primary Ewing's sarcoma (ES) is a rare neoplasm infrequently occurring in the head-and-neck region accounting for nearly 1%–4% of all neoplasms. Although tumor has both hard and soft tissue representations, in the maxillofacial area, it is commonly affects the bones of the skull, mandible and maxilla and less commonly the roof of the orbit and para-pharyngeal spaces.[1] The prevalence of ES is 0.7% more in mandible as compared to maxilla. Apart from being the primary site of ES, the mandibular involvement can also rarely be related to metastasis from another bony site.[2]

Extraosseous ES (EES) are rare soft tissue round cell neoplasm generally poorly differentiated with aggressive clinical manifestations associated with increased recurrence and metastasis.[1] Although in close proximity to the bone, osseous encroachments are rare, however, cortical/periosteal reactions may be evident. Commonly, EES is seen in paravertebral spaces, lower limbs and less likely in maxillofacial region.[3] Owing to the lesser incidence of the EES tumors, epidemiology available is unreliable because of which at present, there are no standard diagnostic or clinical guidelines outlining their management.

The extra skeletal sites include mainly kidney, ovary followed by breast, lung, and brain. According to the literature, the EES of the maxillofacial region has been seen in areas such as floor of the mouth,[4] mandibular vestibule,[5] maxillary sinus,[6] and

Access this article online

Website: www.drj.ir
www.drjjournal.net
www.ncbi.nlm.nih.gov/pmc/journals/1480

How to cite this article: Shetty TP, Jain T, Hegde P. Anomalous chin lesion: The many presentations of extraosseous Ewing's sarcoma. Dent Res J 2022;19:49.

tongue.[7] The occurrence of EES in the chin region has not been documented in our knowledge, hence, the prevalence of the same undetermined.

In this article, we present a rare case of EES of the chin, demonstrating the clinical, radiographic, histological, and immunohistochemical details for diagnosis; and review the pertinent literature with regard to clinical, radiographic, follow-up, and phenotypic information on ES and EES in the maxillofacial region, its uniqueness being presentation in the soft tissues of the lower jaw.

CASE REPORT

A 49-year-old female patient reported to our unit with the chief complaint of swelling over the right chin region for 4 months and associated with mild localized pain (ABSMIDS/2021/05108). Extraoral inspection revealed an ovoid swelling measuring approximately 5 cm × 3 cm in size over the parasymphyseal region with mild tenderness on palpation. It was soft to firm in consistency and not fixed to the surrounding bone. Intraorally the swelling was seen extending from incisor to molar region measuring 4 cm × 2 cm antero-posteriorly. An initial fine needle aspiration cytology done was suggestive of benign spindle cell neoplasm favoring peripheral nerve sheath tumors (neurofibroma/schwannoma). A computer tomography revealed a well-defined horizontally oval homogenously enhancing lesion measuring 23 × 17 × 30 mm in Craniocaudal × Anteroposterior × Transverse dimensions noted in the right gingiva-buccal sulcus with broad base toward mandible extending from central incisors to second premolar [Figure 1]. Posteriorly, the lesion was abutting the body of mandible with mild scalloping but no cortical erosions. Anterio-inferiorly, the lesion was compressing the orbicularis oris muscle. Bilateral homogeneously enhancing level IB lymph nodes were noted, largest measuring 11 mm on the right side with maintained fatty hilum.

Excisional biopsy was planned for the patient under aseptic measures and ample local anaesthesia. A vestibular incision measuring 4 cm was placed from incisor to premolar region of the right mandibular vestibule. After precise soft tissue dissection and delineation of facial and muscular planes, the mass was identified. It appeared to be well encapsulated, sessile, and freely movable. The lesion was carefully separated from the underlying the tissues, free margins identified, dissected, and removed in toto [Figure 2]. The specimen was subjected to gross and microscopic pathological review.

Histopathological examination (HE) showed nodular tissue devoid of lining epithelium, composed of a tumor arranged in sheets and perivascular pattern [Figure 3]. Tumor cells exhibited irregular vesicular nuclei, stippled chromatin, and scanty

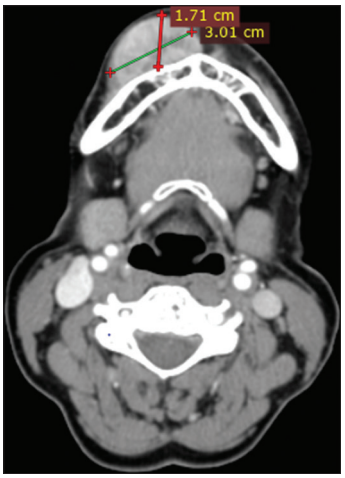

Figure 1: Computed tomography defining the extent of the lesion.

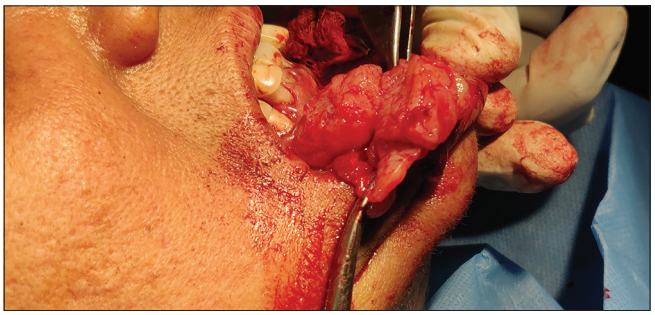

Figure 2: Resection of the lesion in toto.

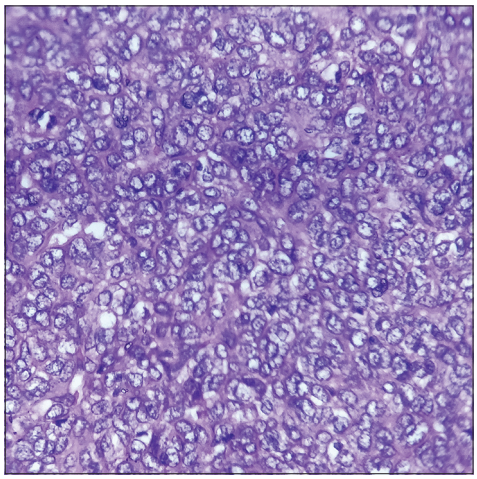

Figure 3: Histopathological examination of the excised specimen under ×40.

amount of cytoplasm indicative for malignant round cell tumor. The specimen was further subjected to immunohistochemistry (IHC) for definitive diagnosis.

IHC studies revealed the cells positive for CD99 [Figure 4], spinal muscular atrophy [Figure 5], ERG [Figure 6], and FLi (weak) while being negative for CK, CD45, CD34, CD31, HMB45, S100, DESMIN, WT1, and MyoD1. INI1 showed retained expression. Ki67 index was 20%, giving final diagnosis as malignant small round cell tumor favoring ES [Figure 7].

Positron emission tomography scan to rule out other primary or metastatic lesion showed low-grade fluorodeoxyglucose (FDG) uptake in the lesion reaching up to the midline but not crossing it. Low FDG uptake was noted in the right level IB node, suggestive of reactive/inflammatory.

Confirming the diagnosis of EES, the patient was planned for four cycles of chemotherapy of VAC regimen which included injection vincristine 1 mg + injection adriamycin 50 mg + injection endoxan 700 mg + injection neukine 300 mcg, 1 month post the excision. The patient was kept on regular monthly follow-ups to check for the healing of the operative site and monitor for any locoregional reccurence. 2 months postchemotherapy, the patient was subjected to radiographical examination which showed no significant findings. The patient has since been placed on regular follow ups.

DISCUSSION

ES being an unfamiliar disease entity comprises nearly 4%–6% of all the primary bone tumors, EES is the other spectrum this pathology which

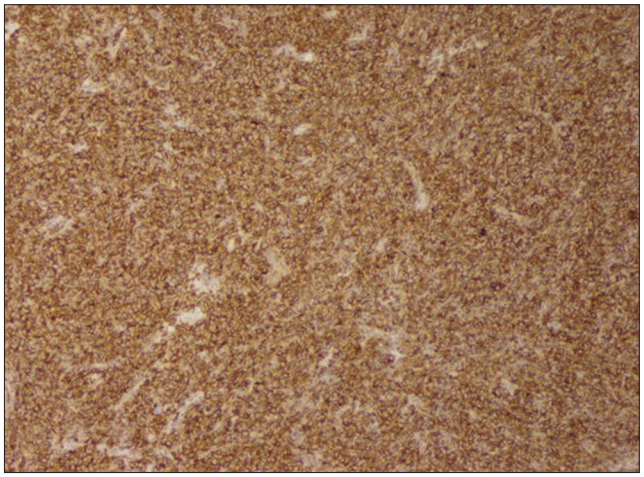

Figure 4: Immunohistochemistry slides revealed the cells positive for CD99.

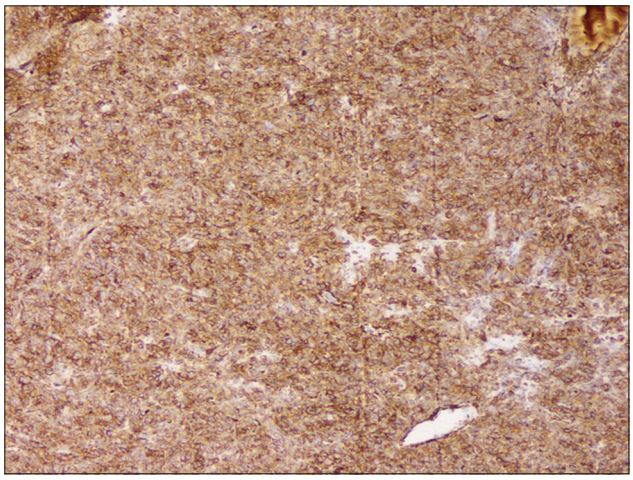

Figure 5: Immunohistochemistry slides revealed the cells positive for spinal muscular atrophy.

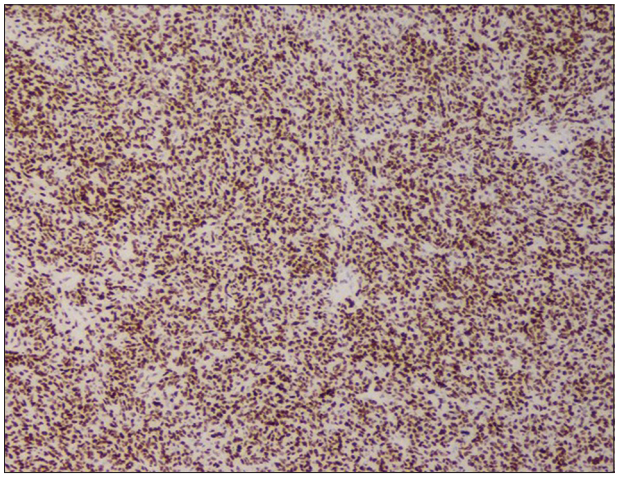

Figure 6: Immunohistochemistry slides revealed the cells positive for ERG.

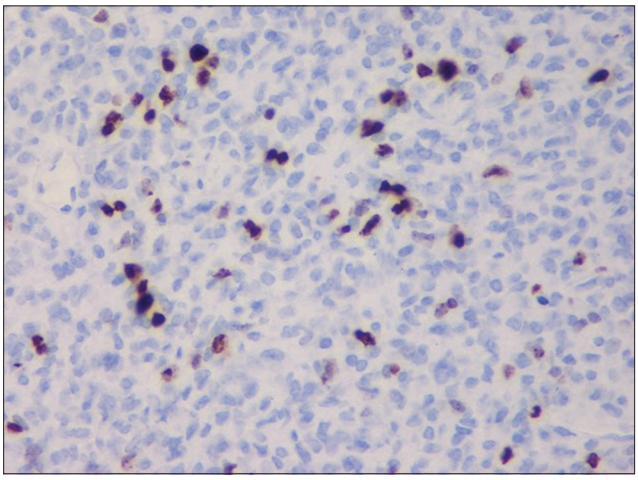

Figure 7: Immunohistochemistry slides revealed the cells positive for Ki67.

involves infrequent tumors which originates from soft tissues and the primary site of the sarcoma defines the clinical picture of the tumor occurring in higher mean age group with female predilection.[8,9]

Usually, ES presents clinically as pain, local swelling, paresthesia, hyperthermia and on laboratory investigations anemia, increased erythrocyte sedimentation rate and leukocytosis is seen. Previous history of ensuing trauma is also a common feature in the disease pathogenesis of ES. However, EES does not present any such specific definite clinical symptoms or history. Soft tissue mass with rampant growth with circumscribed pain is a frequent presentation.[10] Most of the other associated clinical features are dependent on clinical area involved and tissues of origin.

EES belongs to the small round blue cell tumors (SRBCTs) group which includes neoplasms that involve either the skeletal or corporeal soft tissue components. ES, malignant lymphoma, rhabdomyosarcoma, adrenal neuroblastoma are other predominant SRBCTS. Differentiation between these disease entities is, therefore, a challenge and is validated with diagnostic markers.[9]

Murthy *et al*. in a single-center decade long study on Extra Skeletal ES conclude that the thigh is the most common site of ES among skeletal tumors. Chest wall, retroperitoneum, and paraspinal location common among soft tissues (39.4%); and kidney, ovary, and cervix among visceral tumors (11.3%) was seen in their study.[11] In a case reported by Patel *et al*., EES was found in an unusual location that was floor of the mouth for which neoadjuvant chemotherapy was started and patient was planned for surgery on a later date.[4] Schulz *et al*. reported a case in which a male patient was primarily diagnosed with ES of the femur and later developed numbness and pain over the mandible with an ulcerated exophytic growth. After excision and histopathogical analysis, it was proved to be a confirmed case of metastasis of ES. Since the progression of the disease was aggressive, the patient died within a month of oral diagnosis.[2] Hence, it is impertinent to diagnose the disease in its early presentation, recognize rare clinical signs and symptoms along with its rare representation and provide definitive treatment at the earliest.

Characteristics of these tumors are nonspecific on radiographs and present radiographically as a well-limited mass often confused with a benign lesion. On computed tomography seen as a large, well-defined mass of relatively lesser or equivalent density in comparison to the adjoining muscle. As per literature, characteristic features seen on HE and IHC are imperative in definite diagnosis of EES.[9,12]

HE of ES usually presents as small, blue, round cell tumors with scarce intercellular stroma, rarely seen mitotic cells and most tumors mass being necrotic. Rosettes like formation may be seen by central area surrounded by tumor cells, resembling Homer-Wright rosettes, typical of neuroblastomas.[10] On Electron microscopy, specific high nucleus to cytoplasm ratio and aggregated glycogen granules in the cytoplasm is seen. Another definitive but nonpathognomonic feature common to primitive tumor cells is the intracytoplasmic glycogen.[13] Therefore, a plethora of other disease entities including osteosarcomas, rhabdomyosarcomas, neuroblastomas, mesenchymal chondrosarcoma, and malignant lymphoma encompass the differential diagnosis of ES.

IHC shows CD99 (a 32-kDa cell surface gycoprotien encoded by the MIC2 gene) though not specific is\ positive in ES. FLI-1 and O13 (HBA-71, 12E7, RFB-1) which present heightened immunoreaction and neuron-specific enolase, a neural marker, are also positive.[8] EES revealed a novel chromosomal translocation t(4;22)(q31; q12) as the sole anomaly on cytogenetic analysis whereas around 88%–95% of ES chromosomal translocations are on t(11;22) (q24; q12).[14,15]

Many varied therapeutic protocols have been suggested in treatment of EES. Complete resection with three dimensional tumor-free margins has vital impact on EES prognosis in comparison to skeletal ES in predicting a favorable survival.[9]

Treatment aims at mainly in local control and eradication of the systemic disease completely. Hence, the treatment is focused on three phases: (1) initial chemotherapy to facilitate local control of the disease, (2) using surgery, irradiation or both for local control, and (3) uninterrupted chemotherapy. Prognosis is seen to be most favorable in patients with small localized lesion that is amenable to surgical resection or local radiation therapy, as in our case.[9]

EES being radiosensitive, preoperative radiotherapy (RT) plays an important role for efficacious treatment of these lesions. Its role in unresectable EES has also shown favorable local control[16] but because of the complications associated with it, its use has been reduced.

Chemotherapy improves locoregional prognosis and sustained survival are at 85% and 60%, respectively. Vincristine, doxorubicin, actinomycin-D, cyclophosphamide are the first line of chemotherapeutic agents used.[8] The second-generation regimen includes ifosfamide followed by etoposide which improved disease-free survival in localized diseases cases.[17]

ES and EES have preponderance for metastatic spread: lung and long bones being the common areas.[8] Although RT is suggested to prevent and decrease the incidence of such spreads, chemotherapy is still the most acceptable treatment modality currently. Reports have suggested decreased toxicity and improved survival rates as its most important advantages. Another indispensable factor for prognosis is the site of the primary lesion. Involvement of vital structures and adjacent tissues are the deciding factors in limiting local spread and survival rates.[9]

CONCLUSION

EES of the maxillofacial region is claimed to have better prognosis region in comparison to those arising elsewhere as per many authors. Yet, these lesions are worrisome as they pose dilemmas in clinical diagnosis, metastatic tendencies, and locally aggressive behavior. Although a rare occurrence in head and neck, EES needs to be treated with adept clinical acumen.

Financial support and sponsorship
Nil.

Conflicts of interest
The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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