Ewing’s sarcoma of the mandible with multilocular radiolucency

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Abstract

Ewing’s sarcoma (ES) is a small blue round cell tumor, malignant in nature typically affecting long bones and pelvis. Occurrence of ES in the head and neck region is rare and is reported to be 2%–3%, of which the chances of having primary lesion are rare. In the head and neck region, it has been reported to strike skull, supraclavicular region, parotid region, orbital floor, nasal cavity, maxilla, mandible and zygoma. We present a case of primary ES of the mandible in a 22-year-old female who reported with a palpable swelling on the lower left part of the face; and intraorally, there was a growth in the molar region. Orthopantomogram showed multilocular radiolucency in the molar–ramus region. The diagnosis was made after surgical resection, histopathology and immunohistochemistry profiling. The patient was treated by cortical segmental resection of mandible combined with chemotherapy and a follow-up was done for 2 years.

Keywords: Ewing’s sarcoma, mandible, multilocular radiolucency, round cell

INTRODUCTION

Ewing’s sarcoma (ES) is a small blue round cell tumor that arises most often in the medullary cavity. ESs are aggressive tumors with a tendency toward recurrence following resection and early metastasis. ES is the second most common bone cancer after osteosarcoma commonly occurring in Caucasian children and young adults. It represents the most undifferentiated form of a primitive neuroectodermal tumor (PNET). With Askin’s tumor, it forms ES family of tumors (ESFTs) [1]. Pathognomonic hallmark of ESFTs is chromosomal translocations between chromosomes 11 and 22.

CASE REPORT

A 22-year-old female patient reported to the department of oral surgery, with a chief complaint of pain and swelling in the lower left part of the face that had progressed over the last 6 months. She was moderately built and nourished with no relevant medical history. No history of recent trauma was there. Intraoral examination revealed a hard swelling in the left mandible extending from distal surface of first molar till the third molar. Second molar was displaced lingually. Remaining part of the oral cavity was unremarkable. Left submandibular lymph nodes were palpable, nontender and mobile. Routine blood investigation report was normal.

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Conventional orthopantomogram revealed a multilocular radiolucency starting from second molar and extending till the posterior border of ramus of the mandible involving coronoid and condylar processes measuring approximately 4.5 cm × 2.5 cm [Figure 1]. Hard swelling in the mandibular molar region in a young patient depicting multilocular radiolucency in molar–ramus region led us to consider differential diagnoses of ameloblastoma, keratocyst odontogenic tumor, aneurysmal bone cyst (ABC) and osteosarcoma.

A written informed consent was obtained from the patient after explaining the procedure and its risks and benefits. In the per-operative examination, peristomeum was not intact and tumor was infiltrating to adjacent tissues. A hemimandibulectomy including the condyle was performed along with the excision of submental and submandibular lymph nodes. A titanium reconstruction plate with a condylar replacement was fixed to the mandible anteriorly while the condyle segment was stabilized by suturing the articular disc and temporomandibular joint capsule to the condylar segment. Gross examination of the primary resected specimen showed extent involving coronoid and condyle posteriorly and symphysis menti anteriorly measuring approximately 3.5 cm × 7 cm. Superiorly, it was up to the level of crown of molar teeth and inferiorly till the lower alveolar margin of the body of the mandible. Medially, it was till lingual cortical plate, and laterally, it was involving buccal cortical plate. Along with the hard tissue specimen, soft tissue specimens including salivary gland and submandibular lymph nodes were sent for microscopic analysis [Figure 2]. Histopathological examination was suggestive of small blue round cell tumor. Anterior and posterior margins of the resected specimen were free from tumor infiltration. Round cell tumor is distinct and vast entity. It is always a challenge to find cell of origin in round cell tumors. Immediately, PAS stain was done and it came out to be positive. Immunohistochemistry (IHC) profiling was done for definitive diagnosis. CD99 marker, which is seen in most of the cases of ESs, was found to be positive. Patchy positivity for friend leukemia virus integration site 1 (FLI1) was noted with intense nuclear reactivity [Figure 3]. On the basis of clinical, histological and IHC profile, a definitive diagnosis of ES of the mandible was justified.

The histopathological report showed no evidence of metastasis in the excised lymph nodes. Consultation with the oncologist postsurgery warranted the start of chemotherapy. Two cycles of vincristine, doxorubicin and cyclophosphamide were administered to the patient. The patient responded well to the chemotherapy. The patient was followed up on monthly basis for 2 years. Figure 2d shows a well-formed scar of the surgery in the neck region,
and Figure 1d shows orthopantomogram of the same. The patient did not show any abnormal sign in the operated region during the course of follow-up.

**DISCUSSION**

As this young patient had displayed an asymptomatic swelling in the posterior mandible with a multilocular radiolucency, ameloblastoma was considered as the most probable diagnosis.[8] Keratocystic odontogenic tumor (KCOT) is also commonly found in mandible in molar–ramus region. Hence, this entity was included in the differential diagnoses for the present case.[9] The characteristic radiological feature of ES is “onion skin” appearance, which is normally seen in long bones. In ES of bone, plain radiographs exhibit permeative and infiltrative destruction. The present case demonstrated multilocular radiolucency in angle–ramus region of the mandible. This is a trademark feature of ameloblastoma and KCOT [Figure 1b]. Thence, it is stated that roentgenographic appearance of ES in the head and neck region is certainly variable [Table 1].

ABC is an intraosseous osteolytic lesion which is nonodontogenic and nonepithelial cystic lesion most commonly found in the mandible. Of all the ABCs reported till date, only 1.9% have been in the jaws. Radiographically, there is cystic bone expansion resembling a honeycomb or soap bubble appearance with destruction of cortical plates. Since the patient was of younger age group and a multilocular radiolucency of mandible was present, this lesion was taken into account for differential diagnosis.[10] Osteosarcoma of the jaws is rare that too involving mandible. However, it accounts for 8% of all the osteosarcomas. Osteosarcoma shows varied radiographic appearance ranging from osteolytic to mixed and osteogenic pattern. Because of the patient’s age and site of the lesion, a possible diagnosis of osteosarcoma was contemplated too.[10]

ES and PNET affect primarily white young people of Central and South America and are uncommon in individuals of African or Asian origin.[6] It usually involves long bones, pelvis and ribs. Only 2%–3% of osseous lesions occur in the head and neck region. In the head and neck region, it involves skull, clavicle, maxillary sinus, infraorbital region and mandible. This patient was aged 22 years and presented with pain and swelling in the mandible. These findings were in congruence with most of the literature available; however, there is a slight male predilection for this tumor.[7] Earlier, it was thought that ESs are derived from primitive neuroectodermal cells; however, there is much wrangle over its provenance. In this regard, endothelial, mesodermal, epithelial, neural and mesenchymal cells have all been hypothesized as cell of origin, but there is substantial research indicating that mesenchymal stem cells may be original progenitor of ES proliferation.[8] The pathognomonic hallmark of ES is chromosomal translocations of the EWS RNA binding protein 1 (EWSR1) gene on chromosome 22 and any one of the erythroblastosis virus-transforming sequence (ETS) family genes. EWSR1 is from TET family of genes. The most common translocation is with FLI1 gene on chromosome 11.[9] In 85% of cases, it is derived from FLI1 [t(11;22) (q24q12)], and in 10% of cases, it is from ETS-related gene t(21;22) (q22q12). In rare instances, EWS is fused to the ET5 domains of ETS translocation variant 1; t(7;22) (p22;q12), E1A factor; t(17;22) (q12q12) or fifth Ewing variant; t(2;22) (q33q12).[10]

Histologically, ES is composed of sheets of homogenous round tumor cells with hyperchromatic nuclei and scanty cytoplasm. The photomicrograph of the present case showed proliferation of tumor cells round to oval in shape with minimal cytoplasm [Figure 3]. Nuclei were uniform with distinct nuclear membrane and 1–2 nucleoli. Increased mitotic activity was also seen. Other histopathological differentials for small blue round cell tumors are lymphoma, rhabdomyosarcoma and neuroblastoma. However, IHC profiling and in situ hybridization plays a significant role in arriving at diagnosis. In this case, IHC profiling assisted in deducing the diagnosis.

**CONCLUSION**

Round cell tumor presenting as multilocular radiolucency in the mandible has never been reported as ES as per our literature search, so the aim of our case report was to update the clinicians about this unique radiographic presentation of ES and the disputes came across in arriving at cell of origin.

| Table 1: Differential diagnoses of multilocular radiolucency in mandible |
|--------------------------|----------------------|-----------------|------------------|
| Lesion                  | Radiological appearance | Site            | Incidence        |
| KCOT                    | Soap bubble           | Molar-ramus region | Most common     |
| Ameloblastoma           | Soap bubble           | Molar-ramus region | Most common     |
| ABC                     | Soap bubble/honeycomb | Angle of the mandible | Common       |
| Osteosarcoma            | Variable              | Mandible        | Not so common   |
| Ewing's sarcoma         | Onion skin/variable   | Mandible (uncommon) | Rare           |

KCOT: Keratocystic odontogenic tumor, ABC: Aneurysmal bone cyst
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patients understand that her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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