Osteosarcoma of the mandible - A case report of a rare variant

Ajay Prakash P1, Shyam Prasad Reddy D2, Madhusudan Rao T3, Jeevan Kumar4

ABSTRACT:
Osteosarcoma (OS), third most common cancer in adolescence, occurs less frequently than only lymphomas & brain tumours. Osteosarcoma is a highly malignant bone forming tumor characterized by frankly to subtly anaplastic stromal cells with evidence of direct formation of osteoid and/or primitive bone by these cells. Bone or osteoid formation within tumor is characteristic of osteosarcoma. OS of the head and neck are considered by most clinicians to be distinct from OS that arise in the long bones. OS of the jaws is an exceptionally rare entity with an incidence of 0.7 per million. Jaw osteosarcoma presents a wide spectrum of clinical and radiological features along with highly variable histopathology. Small cell OS, a rare histological subtype, has very infrequently been reported in mandible. In the present case report, a case of small cell OS in a young male patient is described along with its clinical, radiological, histological features, genetic aspects and treatment modalities.

Key words: Osteosarcoma, jaw tumor, malignant bone tumor.

INTRODUCTION
Osteosarcoma (OS), most common primary tumor of bone, is a malignant mesenchymal tumor characterized frankly to subtly anaplastic stromal cells with evidence of direct formation of osteoid and/or primitive bone by these cells. Bone or osteoid formation within tumor is characteristic of osteosarcoma. It accounts for approximately 20% of sarcomas, 19% of all malignant tumors of bone but only 5% osteosarcomas occur in jaws. OS of the jaws is an exceptionally rare entity with an incidence of 0.7 per million.1,2 Despite its histopathologic similarities with long bones osteosarcoma, OS of the jaws is biologically different. Jaw osteosarcoma presents a wide spectrum of clinical and radiological features along with highly variable histopathology.

Jaw osteosarcomas usually present in third & fourth decades of life, almost a decade after their presentation in long bone tumors. Males are slightly more commonly affected than females. Maxilla & Mandible are equally involved. Mandibular tumors arise more frequently in posterior body and horizontal ramus, whereas maxillary tumours are discovered more commonly in alveolar ridge, sinus floor, and palate.4
The most common presenting features are increase tumour volume, pain, ulceration and neurological disorders. Radiological appearances manifest as mixed radiolucent/radiopaque lesion, periodontal ligament widening, radiopaque masses with moth eaten appearance, codman triangle and sunburst appearance. Osteosarcomas arise in several clinical settings, including pre-existing bone abnormalities such as Paget’s disease, fibrous dysplasia, giant cell tumor, multiple osteochondroma, bone infarct, chronic osteomyelitis, osteogenesis imperfecta, and with history of radiation exposure.

WHO lists several variants that differ in location, clinical behaviour and level of cellular atypia. The classical osteosarcoma is the most frequent variant which develops in medullary region of bone & can be subdivided into osteoblastic, chondroblastic and fibroblastic histologic types depending upon the type of extracellular matrix produced by tumor cells. Other histological variants include telangiectatic type, small cell osteosarcoma, giant cell and large cell predominant type etc. Here we describe a case of small cell OS in a young male patient who is 23yrs old, along with its clinical, radiological, histological features and treatment modalities.

Case Report

A 23 year old male patient reported to the institution with the chief complaint of pain and swelling in the right posterior mandibular region. The swelling was present since two months which was slowly grown to the present size, measuring about 4 x 5 cms in size. Medical, surgical, dental, family and personnel histories were not noteworthy.

There were no abnormalities detected on physical examination. Extra-oral examination revealed a diffuse, smooth surfaced, hard swelling in the mandible, extending anteriorly from the body of the mandible to first molar and posteriorly to the angle of the mandible. It was found to be hard, non tender and firm in consistency on palpation. Intra-ora, the swelling extended from right mandibular second molar to the angle of the mandible. Clinical differential diagnosis included ameloblastoma.

The radiographic findings (OPG) showed a large radiolucency extending from right mandibular second molar to the angle of the mandible (figure 1). The inferior border of the mandible was intact. Incisal biopsy was performed for the histopathological diagnosis. The slides were stained with routine H&E stain. The histopathology showed dense infiltration of soft tissue by small round cells with scanty cytoplasm that were not arranged in any particular pattern (figure 2, 3). Spindle cells were also present in few areas (figure 4). Areas of tumor osteoid with bizarre osteocytes were present very similar to those seen in conventional OS (figure 5). The above histological features in relation to the radiographic findings were suggestive of small cell osteosarcoma. Mandibular resection was performed and there is no evidence of recurrence of the lesion.

Discussion

Small cell osteosarcoma, a rare histological subtype of OS, was first described in 1979 by Sim et al as resembling Ewing’s tumor, being made up of small round cells. Small cell osteosarcomas have been reported from almost every part of the skeleton, including extragnathic craniofacial bones as well as extraskeletal locations. However small cell osteosarcomas of the jaws are extremely rare with very few cases published in the literature. The most common clinical presentation of small cell osteosarcoma is pain and swelling with durations varying from few days to several months. Sometimes patient may also present with numbness and pathologic fractures. In the present case, patient complained of pain and swelling in the right posterior mandibular region since 2 months.

Radiographically small cell osteosarcoma usually shows a poorly demarcated radiolucency which may be purely lytic or may be mixed lytic-blastic. Destruction of the cortex with elevation of the periosteum - Codman’s triangle - periosteal new bone formation and soft tissue extension has been described. The classic ‘sunburst’ appearance of osteosarcoma also occurs. In the biopsy, the presence of calcified matrix in the tumor especially with no osteoid is an important clue to the diagnosis of small cell osteosarcoma which can otherwise look like any small round cell tumor especially Ewing’s sarcoma.

The histologic picture of small cell osteosarcoma consists of small round cells arranged in islands or sheets, sometimes separated by septae of dense fibrous tissue. In some cases, areas of myxoid tissue may be present in association with chondroid tissue along with areas of necrosis. In some cases, the cells may be arranged in strands and cords. The present case showed sheets of round cells with areas of dense fibrous tissue. The cells were round to oval in shape with scanty cytoplasm. Some areas of spindled cells have also been noted. The nuclei were usually round or oval showing variability in size. Mitotic figures were present and varied widely.

Ayala et al have classified the tumor into three histological types based on cell morphology:

a. Ewing’s sarcoma - like in which the histology closely resembled, Ewing’s sarcoma, with cells showing scanty cytoplasm and round nuclei with fine chromatin and inconspicuous nuclei;
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b. Lymphoma - like pattern resembling large cell lymphoma showing large cells with abundant cytoplasm, round to oval nuclei, finely dispersed chromatin and prominent nucleoli;

c. Spindle cell pattern showed cells with scanty cytoplasm and short ovoid or spindle shaped nuclei with inconspicuous or no nucleoli.

In tumors with multiple patterns, the predominant pattern determined the type. According to this classification the present case fits the Ewing's sarcoma like pattern as it predominantly shows round cells with scanty cytoplasm that were not arranged in any particular pattern and few areas of spindle cells. The defining histologic feature of small cell osteosarcoma is the presence of osteoid which has been described in each and every case reported so far. It varies from fine, lace-like deposits around the tumor cells to larger areas or calcified matrix. The present case showed calcified osteoid in one area, and a smaller area of uncalcified osteoid with bizarre osteocytes, quite similar to that seen in conventional osteosarcoma.

Though the histologic differential diagnosis of small cell osteosarcoma includes several round cell tumors, it can be most easily mistaken for either Ewing's sarcoma or mesenchymal chondrosarcoma. Ewing's sarcoma can be considered when the biopsy specimen does not include any osteoid and mesenchymal chondrosarcoma when there is presence of cartilage. The cells and nuclei in Ewing's sarcoma are more uniform than in small cell osteosarcoma. There is no osteoid formation, though on occasion, fibrin present between tumor cells may be mistaken for lacy osteoid. The presence of tumor cartilage may lead one to think of mesenchymal chondrosarcoma. But most of the cases of small cell osteosarcoma show the presence of cartilage along with osteoid. Mesenchymal chondrosarcoma does not show any osteoid; also, the cartilage formed is usually of low-grade malignancy, whereas high-grade malignant cartilage is seen in small cell osteosarcoma.12

Genetic & Molecular Aspects:

Osteosarcoma tumorigenesis has been linked to alterations in several genes. The first association of osteosarcoma with an inherited predisposition was the observation by Kitchin and Ellsworth that patients with bilateral retinoblastoma had an unusually high incidence of osteosarcomas regardless of whether the patient had been treated with radiation. They concluded that as patients with bilateral disease had the inherited form of retinoblastoma that there must be a pleiotropic effect of the gene for retinoblastoma that resulted in an increased predisposition for secondary osteosarcomas. This predisposition was further demonstrated by the observation that osteosarcoma tumors from patients with bilateral retinoblastoma underwent tumor-specific loss of constitutional heterozygosity (LoH) for the same region of chromosome 13 that occurred in the retinoblastoma tumors. This association was confirmed by the identification of the retinoblastoma susceptibility gene (RB1) on human chromosome 13 which permitted several groups to demonstrate that mutations in the RB1 gene occurred in a high percentage of osteosarcomas.1

The second gene associated with osteosarcoma was the p53 gene. Mutations in the p53 gene were first observed in sporadic osteosarcoma. Genes other than p53 and RB1 have also been associated with osteosarcoma. High frequencies of allelic loss have been detected at 3q and 18q, suggesting that at least two other tumor suppressor genes important in osteosarcoma may exist. HER2/neu (c-erbB-2) overexpression has been observed in approximately 40% of cases and has been associated with early pulmonary metastases and decreased survival.3

Pellin et al. in a study of several round cell tumors for the translocation (11:22) (q24;q 12), found it to be present in Ewing's sarcomas and PNETs, and absent in other round cell tumors including small cell osteosarcoma.13 A recent study by Lee et al on Fli-1 expression in round cell tumors found that it is expressed in Ewing's sarcoma and lymphoblastic lymphoma and negative in mesenchymal chondrosarcoma and small cell osteosarcoma.14 Further studies are needed in this area.

While a review of treatment methods is beyond the scope of this article, it appears that adjuvant chemotherapy improves the prognosis as compared to only surgery. Mandibular resection was performed in the present case and there is no evidence of recurrence of the lesion. The treatment should be in correlation with the histologic and clinical behavior of the lesion. Furthermore, recurrence of small cell osteosarcoma may be long delayed, and a long term postoperative follow up is essential to the proper management of these patients.

In summary, osteosarcomas of the jaws have different behavior than those of the long bones. Early diagnosis and radical surgery with wide surgical margins are the keys to a good outcome. The diagnosis of this small cell osteosarcoma if not obvious from histology, can be made using adjunctive molecular genetic techniques. A better prognosis is achieved if diagnosed and treated at an early stage.
REFERENCES


