Chondroblastic and Fibroblastic Osteosarcoma of the Jaws: Report of Two Cases and Review of Literature

Abstract
This study aims to report of two variants of gnathic osteosarcoma with highlights on the varied histopathological presentation of osteosarcomas (OS). OS present with diverse histological appearances. Despite significant advances in molecular pathogenesis and biomarkers, clinicopathologic correlation is still considered as the important criteria in diagnosis. Chondroblastic osteosarcoma in a 52-year-old female and fibroblastic osteosarcoma in a 35-year-old female. Osteosarcoma is a relatively rare disease of the oral and maxillofacial region. Regular screening and follow-up is highly recommended, as recurrence rates are higher. Thorough understanding of the histologic spectrum of osteosarcoma reduces the diagnostic difficulties in categorizing the OS and separating these neoplasms from benign bone diseases.

Keywords: Chondroblastic type, fibroblastic type, osteosarcoma

Introduction
Osteosarcoma is the most common malignancy of mesenchymal cells after hematopoietic neoplasms. Most originate within bones, but the occurrence of this malignancy in the jaw bones is rare.[1] Osteosarcoma can be found as part of some rare inherited syndromes, such as hereditary retinoblastoma, Li-Fraumeni syndrome, Paget's disease of bone, Rothmund-Thomson syndrome, RAPADALINO syndrome, and Werner syndrome or as sporadic osteosarcoma. Sporadic osteosarcoma is far more frequent than the inherited forms of Osteosarcoma.[2] It is characterized by the direct formation of bone or osteoid by tumor cells.[3] Osteosarcoma of the jaw accounts for 10% of primary malignant and aggressive tumors of the jaw, and 8% of all malignant lesions of the jaw.[4]

Gnathic osteosarcoma is usually regarded as a separate specific entity, due to the difference in age of occurrence and the severity of the disease. Osteosarcomas (OS) of the jaws mainly occur at older ages, whereas the most prominent sites, that is, the long bones, are more affected at ages below twenty. Jaw-localized tumors are less malignant and have lower metastatic spread rates.[5][6] Unlike skull lesions, jaw lesions are rarely associated with Paget's disease although some may be associated with postirradiation of fibrous dysplasia.[7]

Swelling and pain are the most common symptoms. Loosening of teeth, paresthesia and nasal obstruction may also be present.[8] The essential microscopic criterion is the direct production of osteoid by malignant mesenchymal cells. In addition to osteoid, the cells of the tumor may produce chondroid material and fibrous connective tissue. Depending on predominant type of matrix, the osteoid, cartilage, or collagen fibers produced by the tumor; OS are subclassified into osteoblastic, chondroblastic, and fibroblastic types.[9] 50% are osteoblastic, 17% are fibroblastic, and 33% are chondroblastic.[10]

Numerous studies have reported the molecular pathogenesis of osteosarcoma and related biomarkers. Although the studies are highly promising, there has been no improvement in the recurrence and survival rates of osteosarcoma. Till date, clinical and histopathological findings are considered to be given the utmost importance in diagnosis and decision on treatment strategies. This paper discusses two variants of osteosarcoma with highlights on the varied histopathological presentation of OS.
Case Reports

Case report 1

A 52-year-old female patient reported with a complaint of pain in the left lower back tooth region of 1-week duration. Clinical examination revealed mild facial asymmetry with diffuse extraoral swelling in the left side of the face. Intraorally, swelling was present in relation to missing 36 measuring 3 cm × 4.5 cm, extending from the mesial aspect of 35 to mesial aspect of 38. The overlying mucosa was erythematous in appearance with well-defined borders obliterating the mucobuccal fold. On palpation, the swelling was hard in consistency [Figure 1]. Submental and left submandibular lymph node measuring 1 cm × 1 cm were tender on palpation. Except for her facial asymmetry, her physical examination was unremarkable, and routine laboratory tests were within normal limits. Diagnostic orthopantomograph [Figure 2] and intraoral periapical [Figure 3] radiograph revealed poorly defined mixed radiolucent and opaque areas in relation to 36 regions. Asymmetric periodontal ligament space widening was noted in the distal aspect of the root of 35 and mesial aspect of root of 37. Correlating the clinical and radiographic features a malignant bone lesion was thought of and a provisional diagnosis of osteosarcoma was made.

Incisional biopsy was done [Figure 4], and histological examination revealed malignant mesenchymal cells with osteoid production. Masses of chondroid with atypical chondroblasts, abundant pleomorphism, and hyperchromatism were found. The neoplastic osteoblasts were typically angular and hyperchromatic [Figures 5 and 6]. Intralesional chicken-wire calcifications were observed. Some areas showed bicellular strands of tissue separated by filmy vascular stroma suggestive of filigree pattern. Based on the clinicopathologic correlation, the diagnosis of chondroblastic osteosarcoma was given.

Case report 2

A 35-year-old female reported with the chief complaint of swelling in the right side of the lower jaw of 2 days duration. Extraoral examination revealed the presence of a diffuse swelling on the right side of the face. The overlying skin was normal in color and texture. Mouth opening was found to be normal. Intraoral examination revealed a diffuse swelling in the retromolar area in relation to missing 48, measuring approximately 2.5 cm × 3.5 cm. The overlying mucosa was normal in color and texture. The swelling seemed to obliterate the mucobuccal...
fold. The swelling was mildly tender and firm in consistency [Figure 7]. Orthopantomogram revealed diffuse osteolytic region involving a major portion of the ramus of the mandible [Figure 8]. Correlating the clinical and radiographic features, a malignant bone lesion was thought of and a provisional diagnosis of osteosarcoma was made for this patient also.

Incisional biopsy of the lesion was performed [Figure 9], and histopathological examination revealed highly cellular areas of malignant spindle-shaped cells with an enlarged nucleus. The spindle-shaped fibroblasts were densely packed and atypical with a minimal amount of tumor osteoid. Storiform arrangement of fibroblasts was seen in few areas [Figure 10]. Based on the clinicopathologic correlation, the diagnosis of fibroblastic osteosarcoma was given.

**Discussion**

OS account for approximately 40%-60% of primary malignant bone tumors. About 10% of OS occur in the head and neck; most are located in the mandible or maxilla.[9] Extragnathic osteosarcoma presents with a bimodal age distribution, most of the cases occur in the first and second decade of life and few in old age. Osteosarcoma occurring earlier than the second decade or after the cessation of skeletal growth is often associated with other osseous abnormalities such as Paget's disease or fibrous dysplasia or previous radiation of the bone involved.[10]

Jaw lesions are diagnosed about two decades later than their long bone counterparts, which have a peak incidence between the ages of 10 and 14 years. Head and neck OS are associated with a lower metastatic rate than long bone OS, and they have a better 5-year survival rate, ranging between 27% and 84%.[9] The maxilla and mandible are involved with about equal frequency. Mandibular tumors arise more frequently in the posterior body and horizontal ramus rather than the ascending ramus. Maxillary lesions are found in the inferior portion near the alveolar ridge, sinus floor, palate than the superior aspects such as the zygoma and the orbital rim.[9] The common presenting symptoms of osteosarcoma are swelling and pain. Other features include facial deformity, loose teeth, paresthesia, toothache, bleeding and nasal obstruction.[11]
Radiographic findings vary from dense sclerotic or mixed sclerotic radiolucent lesion to an entirely radiolucent lesion. Resorption of roots adjacent to the tumor tissue is noted in few cases. Classic sunburst appearance due to the production of bone spurs or osteophytes on the surface of the lesion is seen in only 25% of the jaw OS.

Classification of OS is based on their histological presentation and anatomical location. Jaw OS present with diverse histological presentation. The pathognomonic feature of osteosarcoma is the presence of malignant osteoid. In addition to the basic neoplastic cell the osteoblast-like tumor cell, seven tumor cell types have been reported in OS. They are chondroblast-like, fibroblast-like, histiococyte-like, myofibroblast, osteoclast-like, and angioblast-like cells. Depending on the cells present and the type of matrix, OS are subdivided into osteoblastic, chondroblastic, fibroblastic, telangiectatic, low-grade osteosarcoma, small-cell osteosarcoma, parosteal osteosarcoma, and periosteal osteosarcoma.

Histogenesis of such multifarious presentation is due to the potential of differentiation of the stromal mesenchymal cells into different lineages. Mesenchymal stem cells can give rise to several lineages, such as myocytes, adipocytes, chondrocytes, and osteocytes, with appropriate stimuli by activating proper lineage-specific regulators. Disruption of osteogenic differentiation may lead to OS development. The defects caused by genetic and epigenetic alterations may occur at different stages of osteogenic differentiation. Defects at the early stages of osteogenesis may lead to the development of more aggressive OS.

The diagnosis of osteosarcoma is based on the demonstration of radiographic findings and cellular morphological features. Immunohistochemical characterization of the various histological subtypes has been attempted by earlier studies. Osteonectin and osteocalcin have been widely used to study osteosarcoma. Osteocalcin is specific for osteoblasts, whereas osteonectin is not specific for osteoblasts but consistently immunostained other cell types such as fibroblasts, pericytes, endothelial cells, chondrocytes, basal layer of skin epithelium; nerves, and osteoblastic giant cells. Other markers used as a panel to delineate the histological variants in addition to osteocalcin and osteonectin are cytokeratin, S100, Sox-9, Ki-67, Bel-2, p53, p16, survivin, CD99, and caveolin-1. However, due to the heterogeneous presentation conclusive evidence to differentiate the histological subtypes has not been achieved so far and histological evaluation is still considered the gold standard.

Prognosis of OS is usually determined by the Enneking system which assesses the histological grade of the tumor (G), extent of the primary tumor (T), and metastasis to nearby lymph nodes or other organs (M). Among the histological subtypes, chondroblastic type is more resistant to treatment exhibits adverse prognosis, fibroblastic type has a better prognosis as it responds well to treatment.

The two main prognostic criteria of gnathic OS are the tumor size and the resectability at presentation. Wide surgical resection is the primary treatment modality for jaw bone OS, but obtaining clear surgical margins is difficult because of anatomic constraints. Complete resection of tumors involving the maxillary bone is especially difficult and local recurrence is more frequent than mandibular ones. Local recurrence is more common than distant
metastasis in jaw bone OS, and positive margins were strongly associated with poor prognosis.[17]

OS are relatively radioresistant, and hence doses in excess of 60 Gy in the conventional fractionation of 2 Gy per fraction are commonly used.[15] Chemotherapy improves the survival in nonmetastatic osteosarcoma of the long bones; this improvement does not occur in osteosarcoma of jaws. However, neoadjuvant chemotherapy helps by improving local control and decreasing incidence of pulmonary metastases.

Conclusion
Osteosarcoma is a relatively rare disease of the oral and maxillofacial region. Regular screening and follow-up is highly recommended, as recurrence rates are higher. Thorough understanding of the histologic spectrum of osteosarcoma reduces the diagnostic difficulties in categorizing the OS and separating these neoplasms from benign bone diseases.

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Conflicts of interest
There are no conflicts of interest.

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