Fibroblastic variant of Osteosarcoma: A Diagnostic Challenge

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Abstract

Fibroblastic Osteosarcoma is a rare histopathological entity with unpredictable prognosis. Osteosarcoma(OS) of jaw bones have some distinct features such as older age at presentation, longer median survival, rare metastases but local recurrences.The pathogenesis is unknown and the treatment still remains controversial. Depending on predominant type of matrix, the osteoid, chondroid or collagen fibers produced by the tumor cells the osteosarcoma are subclassified into osteoblastic, chondroblastic, and fibroblastic types. The diagnoses is mainly done on the basis of clinical, radiological, histological and immunohistochemical features.

Keywords: Bone, chondroblastic, fibroblastic, mandible, osteoblastic osteosarcoma.

INTRODUCTION

Osteosarcoma (OS) arising from the jaw comprises 2.1% of all malignant oral and maxillofacial tumors. OS of jaw differs from the OS of the long bones in its biological behavior, presenting a lower incidence of metastasis and a better prognosis with approximately 40% of patients showing a 5 year survival rate as compared to 20% for long bone lesions.[1] It arises in bone during periods of rapid growth and primarily affects the adolescents and young. OS of jaw is classified into two types such as primary and secondary. The etiology of primary type is unknown; may be due to genetic influence or other environmental factors.Secondary craniofacial osteogenic sarcomas occur in older patients of skeletal Paget's disease, fibrous dysplasia of bone, and as a late sequel to craniofacial irradiation.[2]

Majority of craniofacial OS occur in skeletally mature patients in contrast to those that affect the appendicular skeleton. OS of jaw bones have some distinct features such as older age at presentation, longer median survival, rare metastases, and local recurrences.[2] They comprise only 6.5% of all OSs. Men seem to be more commonly affected. Maxillary OS occurred in females with the ratio of 4:1, whereas mandibular lesions occurred more in males.

Radiographs typically demonstrate a poorly marginated or moth eaten appearance of the bone with mixed amounts of cloudy mineralized matrix and areas of bone resorption. If the lesion has an associated soft tissue mass, a discontinuous or broken periosteal reaction is usually seen. The widening of periodontal ligament space and inferior dental canal,together with sunburst effect are almost pathognomonic of OS of jaw bone. Codman's triangle may be identified sometimes.

The essential microscopic criterion is the direct production of osteoid by malignant mesenchymal cells. In addition to the basic neoplastic cell, the osteoblast like tumor cell the seven other tumor cell types have been reported in OS. Osteoblastic OS is the most common subtype. Nearly, 60% of gnathic OS are osteoblastic, 34% fibroblastic, and less than 10% are chondroblastic.[3]

We present here an extremely rare case of fibroblastic variant of osteosarcoma in the mandible of a 14 year old female. The immunohistochemical analysis of neoplastic cells showed strong immunopositivity for osteocalcin and vimentin. The tumor cells were found to be negative for S100 protein thus ruling out neural tumours. The aim of this article is to describe a case of fibroblastic variant of osteosarcoma with immunohistochemical analysis that was useful in making the final diagnosis.

CASE REPORT

A 14 year old female reported with swelling in left lower third of face. Extraorally the swelling was about 3 x 2 cm. (FIGURE1). Intraorally, the swelling extended from distal aspect of 35 to 38.(FIGURE 2).Provisional diagnosis of ossifying fibroma was given. An excisional biopsy was performed under general anasthesia. The specimen was fixed in formalin, paraffin embedded and stained by hematoxylin and eosin.The patient had a normal postoperative course of healing. Microscopic feature revealed highly cellular lesion comprising of proliferating fibroblasts in the form of fascicles and storiform pattern along with bundles of collagen fibers(FIGURE 3). At high power, spindle to few ovoid shaped cells were seen with indistinct cytoplasmic membranes.Cells exihibited increased nuclear-cytoplasmic ratio, hyperchromatic nuclei and abnormal mitosis. Osteoid formation was prominently seen in one portion of the section with osteocytes within the lacunae (FIGURE 4).

On Immunohistochemical analysis, neoplastic cells expressed strong immunopositivity for osteocalcin and vimentin (FIGURE 5 and FIGURE 6). The tumor cells were found to be negative for S-100 protein, thus ruling out neural tumours. These findings were consistent with fibroblastic variant of osteosarcoma.

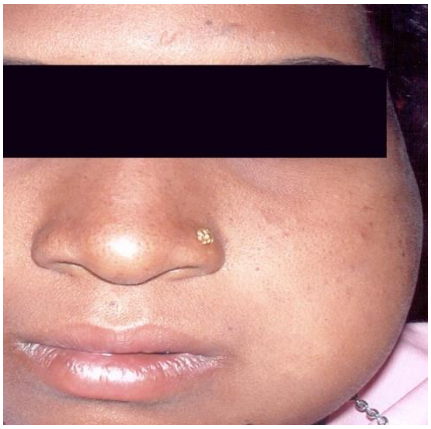

Fig.1

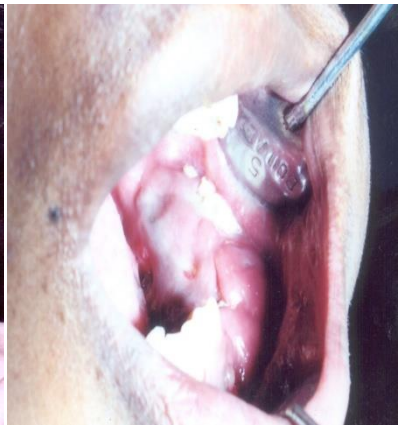

Fig. 2

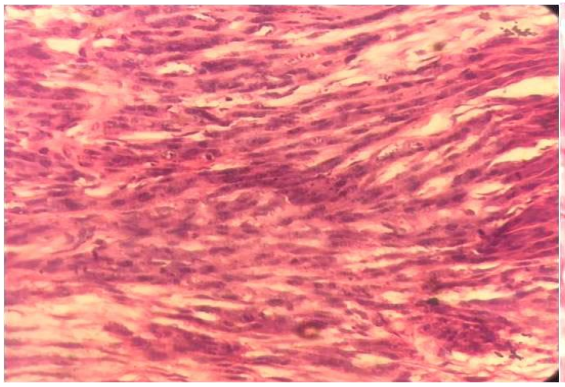

Fig: 3 H& E at 4x

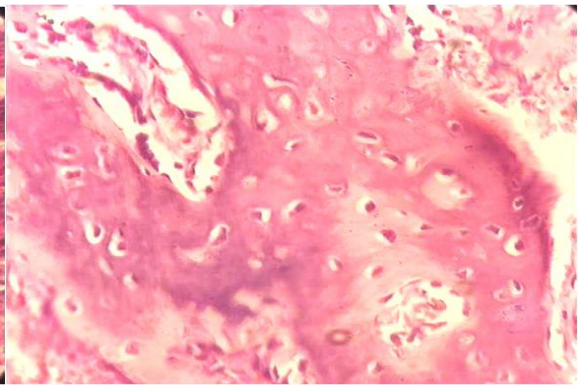

Fig:4 H& E at 10x

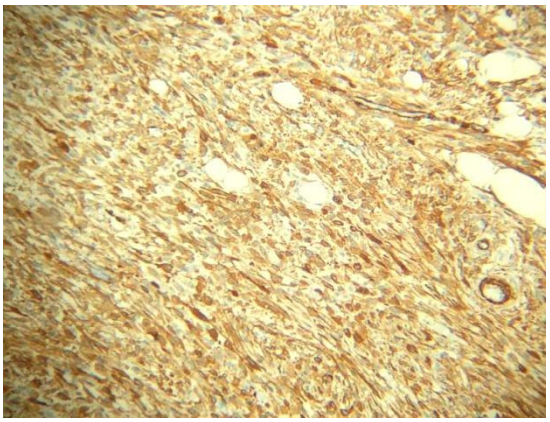

Fig 5: Tumor cells positive for osteocalcin

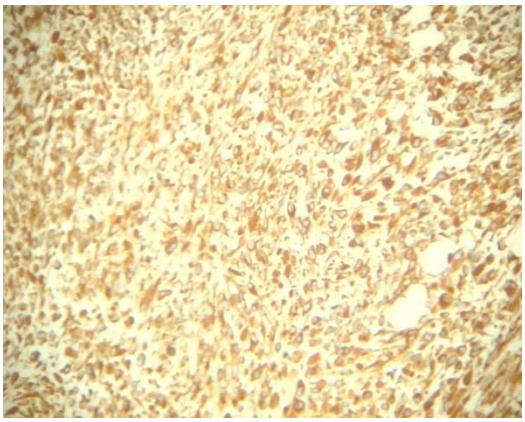

Fig 6: Tumor cells positive for vimentin

DISCUSSION

Osteosarcoma is a disease of mesenchymal cell origin characterized by the proliferation of osteoblastic precursors and the production of osteoid or immature bone. According to the 2013 WHO classification, OS can be classified into high-grade, intermediate-grade, and low-grade lesions. Jaw osteosarcoma (JOS) develops mainly in the mandible and it differs from long-bone osteosarcomas (LBOS) in several important ways.

JOS tends to be diagnosed approximately two decades later than LBOS at an average age of 35 years. There is a lower risk of lung metastases, reported to be 20–25 % for JOS versus 44 %–49 % for LBOS. There is 25 % of patients having primary metastases at the time of the diagnosis in case of LBOS, whereas metastases occur in 17–20% of patients within two years in case of JOS. The overall survival rate is better for JOS, with 77 % survival at 5 years for localised disease and after complete resection.OS has a predilection for developing in rapidly growing bone. However, the OS of jaws peaks one or two decades after adolescence which excludes rapid bone growth as the major etiologic factor.[2] Physical, chemical, and biological agents have been suggested as carcinogens for OS. Among these,the role of ultraviolet and ionizing radiation is the best established. Physical examination findings may reveal a palpable mass, restricted joint motion, pain with weight bearing bones,or localized warmth and erythema.[4] In OS of jaw bones, where swelling rather than pain is the most common finding.[2] Loosening of teeth, paresthesia, and nasal obstruction may also be present.

Radiographically, if the tumor invades the periosteum, many thin irregular spicules of new bone may develop outward and perpendicular to the surface of the lesion producing the so called “sunray appearance.” The widening of periodontal ligament space and inferior dental canal, together with sunburst effect are almost pathognomonic of OS of jaw bone.[5] Advanced imaging is best accomplished with magnetic resonance imaging (MRI) and should be performed for the entire bone [6].

The system used most often to formally stage bone sarcomas is known as the Enneking system[2]. It is based on the grade (G) of the tumor, the local extent of the primary tumor (T), and whether or not it has metastasized to the regional lymph nodes or other organs (M). The grade is divided into low grade (G1) and high grade (G2). The extent of the primary tumor is classified as either intracompartmental (T1), meaning it has basically remained in place, or extracompartmental (T2), meaning it has extended into other nearby structures.[3]

In addition to the basic neoplastic cell, the osteoblast like tumor cell and seven other tumor cell types have been reported in OS. They are chondroblast like,fibroblast- like, histiocyte- like, myofibroblast,osteoclast like, and angioblast like cells.[7] Depending on predominant type of matrix, the osteoid, chondroid or collagen fibers produced by the tumor; the OS are subclassified into osteoblastic, chondroblastic, and fibroblastic types.[2] Also are hemangiopericytomatous, and osteoblastoma like OS variant.[8] OS subtypes can be grouped into three categories: high grade, intermediate grade, and low grade.[3]

Immunohistochemistry (IHC) plays an important role in the diagnosis of sarcomas. Osteonectin and osteocalcin have been widely used to study OS. Osteocalcin is specific for osteoblasts, whereas the osteonectin is not specific for osteoblasts, but consistently immunostained other cell types such as fibroblasts, pericytes, endothelial cells. Chondroblastic OS will be positive for vimentin, EMA, S100, and rarely cytokeratin.[9] Fibroblastic OS will be positive for vimentin and negative for S-100 thus ruling out the neural tumors.

Differential diagnosis for OS depends on the histologic variant. Mostly, it includes osteoblastoma, chondrosarcoma, malignant fibrous histiocytoma, and fibrosarcoma, but the presence of osteoid produced directly by the tumor cells clinched the diagnosis.

The two main prognostic criteria of gnathic OS are the tumor size and the resectability at presentation.[7] The prognosis is more favorable for mandibular OS in comparison to those arising in the maxilla,with the maxillary antral tumors having the worst prognosis.[3] Among the histological subtypes, the chondroblastic type is more resistant to treatment exhibits adverse prognosis,fibroblastic type has a better prognosis as it responds well to treatment.[10]

In our case, the lesion was found in the mandible of a young female where as in the literature the OS of jaws are more common in older adults. Most of the OS are osteoblastic type and the fibrblastic variant is very rare which was found in this case which makes the case unique.

CONCLUSION

The infrequent exposure of oral pathologists to sarcomas coupled with overlapping histologic patterns can often make diagnosis challenging as undifferentiated malignant neoplasms are a daunting diagnostic problem for anatomical pathologists, calling for a tour de force in morphological skill, clinicopathologic correlation, and application of adjunctive laboratory studies. Early and accurate diagnosis followed by radical treatment is of utmost importance for improving the prognosis of these tumors. Given the limitations of histopathologic examination in precisely predicting the clinical behavior and prognosis of sarcoma, identification of new molecular markers emerges as a necessity.

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