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Malignant mandibular tumors: two case reports of rare mandibular tumors in a single institution

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ABSTRACT

Mandibular lesions can be benign or malignant, malignant being less common. The most common malignant tumor of mandible is squamous cell carcinoma. Others are ameloblastic carcinoma, osteosarcoma, chondrosarcoma, fibrosarcoma, malignant fibrous histiocytoma and metastasis. Osteosarcoma is a bone tumor. It can occur in any bone, usually in the long bones of the extremities, but osteosarcoma of mandible is rare. In the initial phase, they may present as nondescript bony swellings with an indolent growth, only to become malignant towards the later stages. Osteosarcomas of the jaw are rare and they differ from osteosarcomas of the long bones in their biological behavior, even though they have the same histological appearance. Malignant fibrous histiocytoma (MFH) is the most common soft-tissue sarcoma, but relatively uncommon in head and neck region with only 30 reported cases till date. The purpose of this report is to present two cases of rare malignant mandibular tumors in a single institution.

KEY WORDS: ***Osteosarcoma; Malignant fibrous histiocytoma; Mandible***

INTRODUCTION

Malignant tumours of the mandible and maxilla are grouped into primary tumours that originate within the mandible and secondary lesions, predominantly oral cancers and metastatic lesions, that involve the mandible secondarily.[1] The most common symptoms of jaw lesions are swelling and pain. Depending on the location of the lesion, patients may also experience paresthesia, loosening of teeth, nasal obstruction, epistaxis, proptosis, or diplopia.[2]

The osteogenic sarcoma is the most common sarcomatous lesion in the mandible and is suggested when a bone-forming matrix with sclerosis is found within the tumor on CT images. Lesions involving the jaws account for 5% to 7% of all osteosarcomas and most commonly affect patients in their third and fourth decades of life, with slight male predilection[2].

The importance of radiography in the diagnosis of mandibular osteosarcoma is stressed because the widening of the periodontal membrane spaces, the sunray effect and the widening of the mandibular canal are considered as pathognomonic features of osteosarcoma[3].

Malignant fibrous histiocytoma (MFH) is considered to be a primitive mesenchymal tumor showing both fibroblastic and histiocytic differentiation[4]. This tumor was originally described as a soft tissue sarcoma, but it is also a well-recognized primary tumor of bone, which may occur in the jaws[5]. MFH has a predilection for the extremities and the incidence of head and neck MFH is relatively low[6]. MFH of the maxilla and mandible is a highly malignant tumor that recurs and metastasizes resulting in death despite aggressive surgical management[7].

The etiology of most osteosarcomas and MFH remains unknown but seems to be multifactorial[8,9]. The treatment protocols for sarcomas include radical or conservative surgery complemented by radiotherapy and/or chemotherapy[10,11].

We report here two rare cases of malignant mandibular tumors with their relevant clinical, pathological and radiographic features, and the treatment as well.

CASE 1

A 20-year old male patient reported to the Department of Surgery, GSVM Medical College, Kanpur, India, with chief complaint of swelling in the lower half of the left side of his face for 4 months. According to the patient, the swelling was evident extra-orally for 2 months. The patient also expressed inability to chew food at the time of presentation.

Clinical Examination

His extra-oral examination revealed an ill-defined swelling, 5 x 4 cm in size, at the lower half of the left side of the face, which extended superoinferiorly, 1 cm from the right zygoma to the inferior mandibular border and anteroposteriorly, 1 cm from the angle of the mouth to 2 cm from the angle of the mandible (**Figure 1**). On palpation, the swelling was smooth, warm, tender, bony hard and immobile in both the anteroposterior and the lateral directions. The left sub-mandibular lymph nodes were palpable, soft to firm and mobile. Intra-orally, a well-defined irregular swelling of size 3 x 3 cm extending from the free gingival groove to the vestibule was found to obliterate the buccal vestibule. The swelling had distinct margins, irregular and ulcerated surface with focal areas of hyperaemia in the overlying mucosa. On palpation, the swelling was found to be tender, bony hard and immobile with evident buccal and lingual cortical plate expansion.

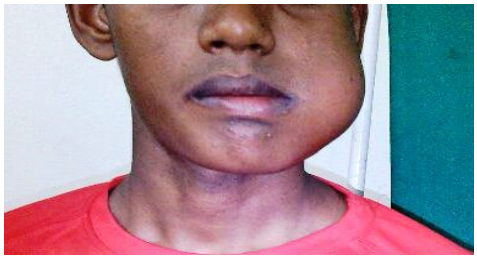

Figure 1: Jaw swelling in the mandible.
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Radiographic Examination

Mandibular cross-sectional radiograph showed bicortical expansion and the presence of radial spicules spreading outside the jawbone on the lingual side, giving a “sunray appearance”. The non-contrast multislice spiral CT scan of the mandible and face revealed an ill-defined lesion arising from the left ramus of the mandible with large soft tissue involvement (**Figure 2**).

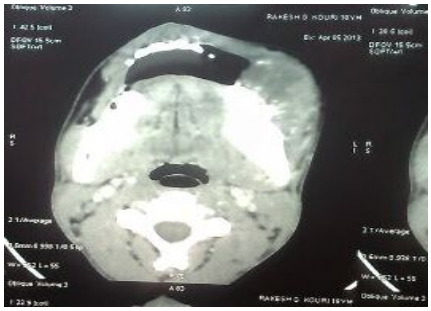

Figure 2: CT scan of left mandible.
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Areas of bone mineralization were seen within the mass. Spiculated osteoblastic periosteal reaction was noted with mild and heterogenous contrast enhancement.

Histopathology

Excisional biopsy revealed fibroblastic tumor cells grouping diffusely with atypical big nuclei and the eosinophilic irregular contours of glassy appearing osteoid rimmed by osteoblasts. Foci of chondroblast components were also present with densely infiltrated mixed inflammatory cells. Tumor cells were spindle, oval or round in shape with size varying from small to giant type with occasional osteoclast-like giant cells.

Diagnosis

Based on the clinical and radiological findings, a provisional diagnosis of malignancy of the left body of the mandible was made. Histopathology examination was suggestive of left sided osteosarcoma mandible (chondroblastic type) with superadded infection.

Treatment

According to sandwich treatment of osteosarcoma, we had given three cycles of chemotherapy of cisplatin and doxorubicin followed by wide excision with left segmental mandibulectomy and intermaxillary fixation. Postoperative recovery was uneventful (**Figure 3**).

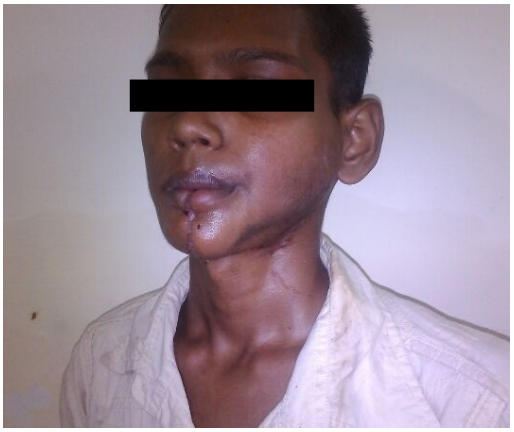

Figure 3: Postoperative photograph. © AMBR

Follow up

Adjuvant chemotherapy was started after three weeks of surgery. The patient completed the adjuvant treatment and responded well.

CASE 2

A 22-year old male complaining of a swelling on the right mandibular alveolar ridge for two months reported to the Department of Surgery, GSVM Medical College, Kanpur, India. The swelling kept on gradually increasing in size since then. Ulceration led to the generation of algesia. There was no history of alcohol, tobacco or any other drug intake.

Clinical Examination

Clinical examination showed a mass of approx. 5.5 x 3.5 cm in size on the right side of alveolar ridge of mandible extending between 2nd premolar and 2nd molar teeth (**Figure 4**). It was hard in consistency without any tenderness or parasthesia with two ulcers on the mass probably due to occlusion trauma. The mass had implicated the alveolar ridge buccolingual region and extended to the adjacent mandibular vestibule. There was no palpable cervical lymphadenopathy.

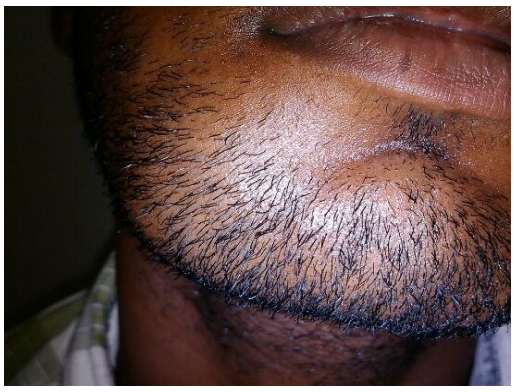

Figure 4: Swelling on right side of mandible. © AMBR

Radiographic Examination

Panoramic radiography revealed an area of radiolucency with ill-defined borders on the right side of the mandible. Mild displacement of right 2nd premolar and 2nd molar teeth were noticed. The non-

contrast CT scan of the mandible and the face revealed a large, ill-defined, osteolytic and expansile lesion involving the right angle of mandible with cortical breach and soft tissue involvement (**Figure 5**).

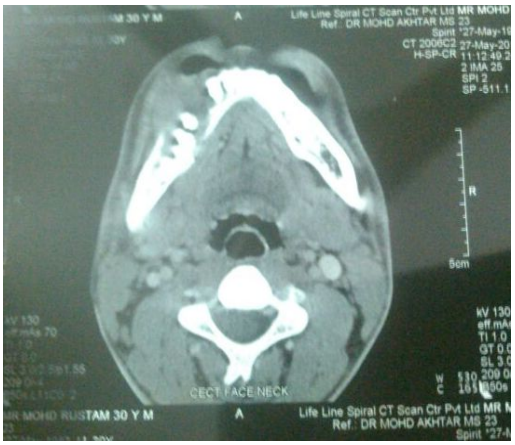

Figure 5: CT scan of mandible. © AMBR

Histopathology

Biopsy showed storiform areas consisting of plump spindle cells arranged in short fascicles and storiform pattern. There were foci of haphazardly arranged pleomorphic zones showing atypical anaplastic tumor cells with multinucleated giant cells invading and destroying the bony trabeculae. Intervening areas of myxoid changes were also seen.

Immunohistochemistry

The tumor cells of storiform pleomorphic malignant fibrous histiocytoma (MFH) showed diffuse and strong cytoplasmic immunoreactivity to vimentin.

Diagnosis

The lesion was diagnosed as malignant fibrous histiocytoma on the basis of histopathologic, radiographic and clinical examination of the patient.

Treatment

The patient underwent wide local excision with right segmental mandibulectomy and reconstruction with avascular fibular grafting and plating (**Figure 6**). Postoperative recovery was uneventful (**Figure 7**). Adjuvant chemotherapy (CyADIC regime) was started after 3 weeks of surgery.

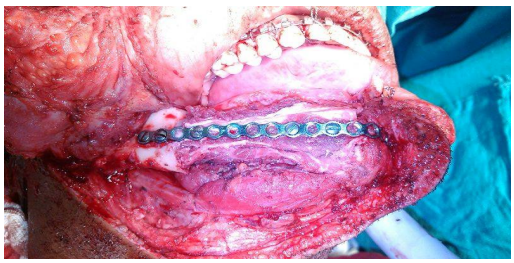

Figure 6: Fibular grafting with plating after segmental mandibular resection. © AMBR

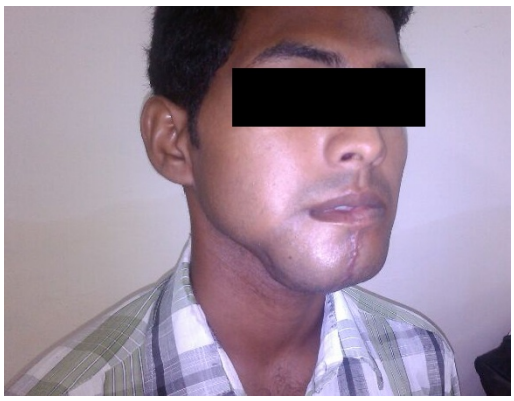

Figure 7: Postoperative photograph. © AMBR

Follow up

The patient completed the adjuvant treatment and was sent for radiotherapy to avoid local recurrence.

DISCUSSION

Oral sarcomas include osteosarcoma, MFH, fibrosarcoma, liposarcoma, leiomyosarcoma, rhabdomyosarcoma, angiosarcoma, alveolar soft-part sarcoma and solitary plasmacytoma. The most common histological subtype is osteosarcoma (chondroblastic type more common than osteoblastic type) followed by MFH[12]. Our case was diagnosed as chondroblastic type of osteosarcoma.

Although osteosarcoma is generally the most common malignant bone tumor, its incidence in the mandible is rare[13], and despite its histopathologic similarities with osteosarcoma of the long bones, it is biologically different[14].

The WHO has listed several variants that differ in the location, clinical behavior and the level of cellular atypia. Classical osteosarcoma is the most frequent variant, which develops in the medullary region of the bone. It can be subdivided into osteoblastic, chondroblastic and fibroblastic histologic types depending upon the type of the extracellular matrix produced by the tumor cells. The other histological variants include the telangiectatic type, the small cell osteosarcoma, the giant cell and the large cell predominant type.[10,11,14]

Lesions involving the jaws account for 5% to 7% of all osteosarcoma and most commonly affect patients in their third and fourth decades of life with a mean age of approximately 35 years. There is a slight male predilection. The mandible is affected more frequently than the maxilla. The most common symptoms of jaw lesions are swelling and pain. Depending on the location of the lesion, patients may also experience paresthesia, loosening of teeth, nasal obstruction, epistaxis, proptosis, or diplopia[1]. Osteosarcomas arise in several clinical settings but most often the etiology remains unknown.

Radiography in the diagnosis of mandibular osteosarcoma is important because of the widening of the periodontal membrane spaces, the sunray effect and the widening of the mandibular canal as pathognomonic features for osteosarcoma[3]. In the present case, mandibular cross-sectional radiograph showed bicortical expansion and the presence of radial spicules, which spread outside the jawbone on the lingual side, giving a “sunray appearance”. The extent of the tumor in both the bone and soft tissue is best appreciated as was shown by cross-sectional imaging techniques such as computerized tomography (CT). This is particularly important prior to definitive surgery. A CT scan of an osteosarcoma often shows formation of irregular endosteal and extracortical bone with a destroyed or obliterated cortex. CT scan cannot differentiate between osteosarcoma and fibrous dysplasia, but the typical sunray spiculations were seen in the soft tissue in this case, which is highly suggestive of osteosarcoma[11].

Although MRI is generally accepted to be superior to CT scanning in the evaluation of the local tumor spread, Panicek and colleagues showed that CT scanning and MRI were equally accurate in the staging of the local disease in bone tumors[15]. However, in the present case, MRI was not done due to financial limitations. In the present case, it was observed that the lesion was mixed (radiolucent-radiopaque) in appearance, which was in accordance with the finding of the Clark *et al* classification[16].

Histologically, osteosarcomas can be classified according to their cellular differentiation as osteoblastic and chondroblastic. In the osteoblastic type, the atypical neoplastic osteoblasts exhibit considerable variation in their shapes and sizes, showing large deeply staining nuclei arranged in a disorderly fashion. It constitutes 60% of the jaw lesions. The chondroblastic type occurs predominantly in the head and neck region and consists of atypical chondroid areas composed of pleomorphic and atypical binucleate cells, which have large hyperchromatic nuclei and prominent nucleoli[14,17]. The fibroblastic type is rare especially in the jaws. In our case, histologically, the tumor revealed fibroblastic tumor cells grouping diffusely with atypical big nuclei and surrounded by the eosinophilic irregular contours of glassy appearing osteoid, which was rimmed by osteoblasts. Foci of chondroblast component were also present with densely infiltrated mixed inflammatory cells. Tumors cells were spindle, oval or round in shape with size varying from small to giant type with occasional osteoclast like giant cells suggestive of chondroblastic osteosarcoma[15,16].

The treatment for osteosarcoma has been well established for long bones, but it is not well understood when the condition

involves the mandible or the maxilla[16,18]. It is clear that chemotherapy is beneficial for osteosarcoma of the long bones, leading to significant changes in the disease-free survival rate (from 20% in the 1960s to 70% in the 1980s). This improvement did not include osteosarcoma of the jaw, due to its rare occurrence and lack of standardized chemotherapy protocols, which made it difficult to evaluate the efficiency of the adjuvant therapy[13]. In most cases, the therapy of choice is radical surgical excision, since it provides a 5-year survival rate of over 80%. As for chemotherapy, it does not seem to have much impact on the survival rates of the patients with osteosarcoma of the jaws. This can be explained on the basis of the fact that metastases were rare and late, occurring only in 18% cases and local recurrence of the lesion is still considered the leading cause of death[13]. In this case, the patient underwent radical surgical resection along with the margin of surrounding normal tissue and adjuvant chemotherapy. The prognosis of jaw osteosarcoma is better than that of long bone osteosarcoma. This could be due to the histologically better differentiation of jaw osteosarcoma than that of long bone osteosarcoma[19].

Malignant fibrous histiocytoma (MFH) is the most common soft tissue sarcoma of late adulthood and was first described by O'Brien and Stout in the 1960s[20]. Its incidence in young people is less than 5%[21]. Feldman and Norman[11] for the first time in the 1970s described primary malignant tumour of bone that satisfied the histopathologic criteria of MFH[22]. MFH of the bone constitutes approximately 5% of primary bone tumors and less than 1% of malignant tumors of bone. MFH is very rare in the head and neck region[21]. MFH of the jaws is a highly malignant tumor that recurs, metastasizes, and commonly results in death despite of aggressive surgical therapy[7].

The most common presenting symptom of MFH is a painless, gradually progressing mass without any mucosal ulceration similar to that of osteosarcoma[23]. Clinical symptoms are usually present from 2 weeks to 6 months before diagnosis. The age distribution at diagnosis varies from 1.5 to 69 years, but is more common in the latter half of life with a mean age of 41 years. These data are consistent with MFH of other bones[24].

Histologically MFH is a sarcoma composed of a bimodal cell population, fibroblasts and histiocyte-like cells arranged in a cartwheel or storiform pattern[25]. It has been divided into the following five subclasses: storiform-pleomorphic type, myxoid type, giant cell type, angiomatoid type and inflammatory type[26,27]. Our findings show that the MFH of the present patient belongs to the storiform-pleomorphic type, which is the most frequent one.

MFH of bone is differentiated histologically from osteosarcoma by the presence of histiocytic cells and fibroblastic cells by contrast. The predominant cell type in osteosarcoma is the neoplastic osteoblast characterized by abundant rough endoplasmic reticulum. Signs of matrix calcification in the intercellular matrix between the collagen fibrils are regularly observed in osteosarcoma, but not in malignant histiocytoma[28].

Typical X-ray features included aggressive and destructive tumor centrally located in the metaphysis of long bones. Periosteal reactions and expansive growth are rarely seen. CT scan of the mandible and the face reveal a large ill-defined osteolytic expansile lesion with cortical breach and soft tissue involvement.

With respect to the differential diagnosis of MFH from other malignant tumors in the head and neck region, squamous cell carcinomas, malignant lymphomas, malignant giant cell tumors, fibrosarcomas, and osteolytic osteosarcomas must be considered[6].

The treatment of choice for MFH is extended surgical resection with adequate margins of normal surrounding

tissue[27]. Many researchers have reported that radiotherapy for MFH was less effective[29]. Yamaguchi et al revealed that local recurrence was less common in patients with adjuvant therapy (radiation therapy and/or chemotherapy) comparing with patients treated by surgery alone[12]. MFH is often resistant to chemotherapy, however, use of vincristin, cyclophosphamide, dactiomycin, adriamycin, cisplatin (cisdiaminedichloro platinum), tyrosine kinase inhibitors and dacarbazine (DTIC—Dimethyl Triazeno Imidazole Carboxamide) have been reported[21,30]. Due to poor prognosis and high recurrence rate adjuvant chemotherapy with continuous infusion CyADIC regime until an 800mg/sq.m cumulative doxorubicin dose is recommended.

The prognosis of MFH lesions is influenced by the size, anatomic location and the extent of tumor infiltration into the surrounding tissues. The prognosis of this tumor is often unfavorable and recurrence rate is approximately 44–48%. Metastases more commonly occur in the lung (90% of metastasis) followed by lymph nodes (12%), bone (8%) and liver (1%). About 5% of cases already revealed metastasis when the primary tumor is diagnosed[21]. Aggressive infiltration to the adjacent tissues or muscle fibers can be responsible for a high recurrence rate. The 5-year survival rate of MFH of bone is reported to be 36.5-53%[27]. Close follow-up and monitoring after treatment is required because of its frequent recurrence and early metastasis to the lungs.

CONCLUSION

Sarcomas are often difficult to distinguish from many of the common tumors in the oral cavity. Although osteosarcoma of mandible and MFH of mandible are rare, they should be included in the differential diagnosis of the oral cavity lesions because early diagnosis and adequate surgical resection are the keys to high survival rates.

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