Periosteal Osteosarcoma with Diabetes Mellitus in a 20 year old female

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ABSTRACT:
Osteosarcomas of jaws is a rare lesion as compared to osteosarcomas of other parts of body. Osteosarcomas are more commonly seen in long bones of young adults with male predilection. We present a case of a 20 year old female patient reported to us with a chief complaint of swelling in lower right jaw region since 5 months, diagnosed with osteosarcoma of mandible in right posterior region. Patient was also found to be diabetic during routine investigations. Relation between oral malignancy and diabetes is always been found in various literatures but has never gained much importance. This article provides information about the pattern and regularity and treatment of osteosarcoma in jaw bone as well as enlightens the relation of presence of diabetes along with oral malignancies.

Key words: Osteosarcoma, Periosteal, Parosteal.

INTRODUCTION
Osteosarcoma of the jaws is an unusual lesion representing less than 4% of all recorded osteogenic sarcomas. The relative paucity of jaw lesions makes their analysis difficult in several respects. Osteosarcoma occur in the jaws at an average of 37 years, whereas osteosarcomas occur in long bones at an average age of 25 years. However, numerous jaw osteosarcomas occur in the teen years and early 20s as well.

Osteosarcoma occurs evenly among males and females. Osteosarcomas represent malignant neoplasms arising from mesenchymal stem cells and/or their early progeny. Their partial differentiation leading to the production of tumor bone from a malignant cellular stroma is what defines them as osteosarcomas rather than any other malignant mesenchymal tumor that can arise from a mesenchymal stem cell. Recent genetic findings indicated that osteosarcoma development is related to loss of the p53 tumor suppressor gene, loss of retinoblastoma tumor suppressor gene, and development of independence from regulation by platelet-derived growth factor (PDGF). Osteosarcoma may present with an expansion of bone, an incidental radiographic finding of a radiopacity, a widened periodontal ligament space (garrington sign), a mobile tooth, a numb lip or other paraesthesia and/or pain. Because some of these signs and symptoms can be produced by a number of different developmental, infectious, benign neoplastic diseases or malignancies, an osteosarcoma often goes undiagnosed for a significant period of time.

We report a case of a periosteal osteosarcoma in a young Indian female whose initial complaint was “a growing mass” on the right side of the mandible.

REPORT OF A CASE:
A 20 year old female was referred by a private practitioner from agra for evaluation and treatment of an asymptomatic enlarging mass in the right mandible. The tumor had been present and slowly growing for approximately 5 months. (Fig 1a)
Oral examination disclosed a 3 x 2 x 2 cm sessile growth with ulcerated surface showing pinkish – red like hard mass on the right buccal and lingual mucosal surface extending from first molar region to the retromolar trigone ,anteroposteriorly and from buccal and lingual vestibule to the occlusal surfaces of mandibular right posterior tooth ,superoinferiorly. The growth was impinging between the occlusal surfaces of maxillary and mandibular molar teeth. The patient presented with no paraesthesia, tenderness or trismus. (Fig 1b) (Fig 1c)

Orthopantomograph shows a non-healing extraction wound in mandibular right posterior region, distal to first molar. Isolated area of radiolucency is observed in the same region involving the ascending ramus approaching the inferior alveolar canal. The extraoral radiograph also reveals irregularity in bone pattern with the concerned area resembling new bone formation. (Fig 2a). Axial CT scans along with 3D images reveals large expansile lytic lesion approximately measuring 3.5 x 2.2 cm in size at junction of ramus and body of right mandible. Lesion is causing cortical thinning and mild destruction of lingual and buccal cortex with minimal extension to the alveolar margin corresponding to region of third molar which is otherwise missing. Lesion is involving pterygoid muscles and muscles of floor of mouth medially. Extension to retromolar trigone and to the buccal space is also noted anterolaterally. (Fig 2b) (Fig 2c)

Incisonal biopsy was taken twice: 4 months and 3 months back at a clinic in Agra and was diagnosed as chronic granulation tissue and pyogenic granuloma respectively. Then a biopsy was repeated in our oral surgery department and sent for examination which was reported as peripheral giant cell tumour of bone. Later the tumor was resected by our operating team under general anaesthesia followed by a routine marginal mandibulectomy and the specimen was sent again in-toto for histopathological examination. The specimen sent was diagnosed as Aggressive ossifying fibroma and the reason for it was the linear behaviour of the tumor border with the surrounding normal tissue as shown (Fig 4a). However it was finally diagnosed as Osteogenic sarcoma of mandible at Tata memorial centre, Mumbai on our referral. She was additionally diagnosed with Juvenile diabetes during routine investigations which were performed prior to surgery. Her pre-operative diabetes level was 387 gm/dl along with sufficient amount of sugar seen positive in urine examination. The tumour was resected completely with a safe margin of 2-3 cm, the gross specimen revealed a fleshy lesion measuring 4 x 3.5 x 2.5 cm in cut section as shown (Fig 3b). The tumor was responsible for focal destruction of the buccal alveolar bone and emerging through it in the oral cavity. The adjacent bone cortex seems relatively free of tumour (Fig 3a).

Microscopic examination of the specimen revealed a cellular lesion composed of polygonal to elongated cells. The surface of lesion shows ulceration with overlying exuberant granulation tissue. The margins of the lesion surprisingly were not encroaching and were rounded with the surrounding tissue (Fig 4a). There was focal cellular pleomorphism observed at different areas along with mitosis which appeared interspersed among the tumor cells (Fig 4b). Multinucleated cells were also noted occasionally. Extracellular matrix was eosinophilic with osteoid tissue laid down at various areas along with lamellar bone formation seen (Fig 4c).

**DISCUSSION:**

Osteogenic sarcoma (O.S.) can be divided into more typical intramedullary, parosteal and periosteal forms according to its particular clinical, radiographic and histologic characteristics. The parosteal and periosteal forms of osteogenic sarcoma initially grow outwards from the surface and do not involve the underlying bone. Osteogenic sarcoma arising on the surface of bone exhibit distinct radiographic and histologic features and is also classified into one more type: as High grade surface O.S. However parosteal and periosteal types tend to have better prognosis then conventional O.S or High grade surface O.S. Both parosteal and periosteal O.S are uncommon neoplasm and comprise only approximately 5% of all O.S. They are confined to the jaws exclusively.

Koyama et al described a tumor that spread into bone marrow by way of the periodontal ligament similar to what we observed in our case. The C.T images in our case fulfill the criteria established for periosteal O.S, namely an erosive change in the cortical layer with no/minimal involvement of the marrow cavity which is associated with periosteal new bone formation. These findings suggested that the tumor originated from the periosteal cambium layer which lies between the periosteal fibrous tissue and the cortex of the mandible.2
The case of periosteal O.S presented here can be separated on the grounds of clinical and histological features from periosteal O.S. and intramedullary O.S. Periosteal O.S can be distinguished from parosteal type by its unique clinical, histological and behavioural differences as follows: periosteal O.S behaves more favourably than does conventional intramedullary O.S but not as well as the parosteal type. In contrast to typical parosteal O.S our patients lesion presented as a sessile mass that arose within the bone cortex and elevated the overlying periosteum. This in turn stimulated production of conspicuous periosteal new bone formation. Also it is significant that the tumor in our case included foci of osteoid material as compared to parosteal type which consists more of a chondroid tissue. In our case an intramedullary O.S was ruled out because the tumor originated and initially proliferated outward from the osseous surface. It exhibited an intact cortex with only minimal destruction of the alveolar crestal bone with extension to the bone marrow as a consequence of its apparent proliferation within the periodontal ligament space. Moreover the C.T images of this case revealed significant new bone formation with minimal involvement of the marrow cavity.

With addition of the case reported here few cases of periosteal O.S of the jaws are also been summarized (Table 1). The average age of patient was, with a male to female ratio of 4:5. The most frequent site of origin was the posterior mandible. Conservative local excision is believed to be an inadequate form of treatment for this malignancy. Preferred a surgical intervention includes a clearly tumor-free resection margin, hemimandibulectomy, or when indicated, a wide maxillary resection. With the exception of one case, others have no recurrence of tumor. In the exceptional described by Piatelli and Favia, tumor metastasize to the lung and patient consequently died. Because the number of reported cases of periosteal O.S is relatively small, the prognosis remains uncertain.4

Marta Ujpal, Orsolya Matos et al conducted a study regarding relation between oral cancers and diabetes. According to the study, benign tumors were found in 14.5% and precancerous lesions in 8% of diabetic patients compared to lower rate in control group. He concluded as diabetes may be a risk factor for oral malignancy.5 L.Goutzanis, E.Vairaktaris et al also found that diabetes may increase risk for oral cancer through the insulin receptor substrate-1 and focal adhesion kinase pathway.6 Maliyannar Itagappa and Shrinivas B. Rao suggests a suppression of cellular regenerative activity by sugar and sugar phosphates which is well known to be a prerequisite factor for cancer in the body.7

CONCLUSION:

Additional cases of periosteal O.S must be analysed before meaningful conclusion about the tumors prognosis can be drawn and newer researches on relation between Diabetes and Oral Malignancy must be conducted for better understanding the behaviour of the lesion and for improving quality of treatment and prognosis for the patient.

REFERENCES

5) Marta Ujpal, Orsolya Matos, Gyorgy Bibok, Aniko Somogyi, Gyorgy Szabo, Zsuzsanna Suba Diabetes and Oral Tumors in Hungary: Epidemiological correlations Diabetes Care March 2004 27:770-74; doi:10.2337/diacare.27.3.770
Figure 1a: Straight Profile view, Pretreatment.

Figure 1b: Occlusal aspect showing extension of tumor

Figure 1c: Lateral aspect with teeth in occlusion showing lateral extent of lesion

Figure 2a: Extraoral radiograph showing radiopaque as well as radiolucent areas resembling the tumor in mandibular right posterior region

Table 1: Shows various cases of OS reported in literature referred from Yoon et al article.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age(yr)/Gender</th>
<th>Site</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patterson et al</td>
<td>65/F</td>
<td>Rt Mx</td>
<td>Partial Maxillectomy</td>
<td>1yr, no recur and no mets</td>
</tr>
<tr>
<td>Millar et al</td>
<td>60/m</td>
<td>Midline Mx</td>
<td>Wide excision</td>
<td>2yrs, no recur and no mets</td>
</tr>
<tr>
<td>Zarbo et al</td>
<td>57/F</td>
<td>Lt Mn</td>
<td>Hemimandibulectomy</td>
<td>1yr, no recur and no mets</td>
</tr>
<tr>
<td>Sorensen et al</td>
<td>20/m</td>
<td>Rt Mn</td>
<td>Partial Mandibulectomy</td>
<td>Not available</td>
</tr>
<tr>
<td>Piatelli et al</td>
<td>45/M 16/M</td>
<td>Rt Mn</td>
<td>Radical en bloc resection</td>
<td>6yr, no recur and no mets</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rt Mx</td>
<td>Radical maxillectomy and 7 cycles of chemotherapy</td>
<td>Lung mets, died 5 yr after the first diagnosis</td>
</tr>
<tr>
<td>Koyama et al</td>
<td>15/F</td>
<td>Rt Mn</td>
<td>Partial mandibulectomy</td>
<td>8yr, no recur and no mets</td>
</tr>
<tr>
<td>Yoon et al</td>
<td>27/F</td>
<td>Rt Mn</td>
<td>Marginal mandibulectomy</td>
<td>3yr, no recur and no mets</td>
</tr>
<tr>
<td>Minic</td>
<td>20/F</td>
<td>Rt Mn</td>
<td>Partial mandibulectomy</td>
<td>5yr, no recur and no mets</td>
</tr>
<tr>
<td>Present case</td>
<td>20/F</td>
<td>Rt Mn</td>
<td>Excision of lesion in toto</td>
<td>Follow up required</td>
</tr>
</tbody>
</table>
Figure 2b: 3D image showing the breach in the buccal cortex of mandible near ascending ramus region.

Figure 2c: Axial CT Contrast scan showing the extent of lesion measuring approximately 3.5 x 2.2 cm.

Figure 3a: Showing the affected area after resection of the tumor.

Figure 3b: Showing resected tumor from the affected site.

Figure 3c: Showing formation and deposition of tumor Osteoid tissue.

Figure 4a: Histopathologically showing the interface between tumor border with the adjacent normal oral tissues.

Figure 4b: Histopathological slide showing Extracellular eosinophilic matrix with focal cellular pleomorphism and interspersed mitosis.

Figure 4c: Histopathological view showing formation and deposition of tumor Osteoid tissue.