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CLINICOPATHOLOGICAL STUDY ON OSTEOSARCOMA MANDIBLE AND LITERATURE REVIEW

Oncology

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ABSTRACT

Osteosarcoma is the most common bone malignancy and it is rarely studied in head and neck. In head and neck, the most common sites are maxilla, mandible and skull bones. The treatment strategies are based on metanalysis on osteosarcoma of extremities. The prognosis and survival depend on the surgical margins. Due to complexities in anatomy, local recurrence is the most common pattern of failure in head and neck. This study outlines the management protocol of osteosarcoma mandible at our institute and a review of literature on osteosarcoma mandible is discussed.

KEYWORDS

Osteosarcoma (OS), Osteoblastic , Margin, mandible, chemotherapy

1. INTRODUCTION

Osteosarcoma is the most common primary, non-haematopoeitic malignant neoplasm of the bone. About 6-10% cases involve the jaws, with 40% occurring in maxilla and 35% in mandible. OS typically occurs in the body of the mandible and the alveolar ridge or antral area of the maxilla.[1] Other than jaw bones other sites in head and neck where OS occurs are skull bones (20%), cervical vertebrae (<5%) and in soft tissues (<5%).[2]

OS is characterized by direct formation of osteoid or primitive woven bone by malignant cells.

OS can be classified in the following ways:

1. **Primary or secondary**

Primary arises denovo.

Secondary OS occurs post radiation, in conditions like Paget's disease, fibrous dysplasia, bone infarction and some genetic syndromes (LiFraumeni syndrome, hereditary retinoblastoma, Rothmund-Thomson syndrome and Werner syndrome). Secondary tumors are usually high grade.

2. Based on anatomical location – craniofacial and appendicular
3. Clinicopathological types- conventional (intra-medullary), parosteal and periosteal
4. Histological variants- chondroblastic, osteoblastic, fibroblastic and others.[3]

The tumour biology and natural history of OS of jaws is different compared with the same in other sites. Surgery with negative margins is the mainstay of treatment. The prognosis of OS jaw is better than the long bones (5-year survival- 40% vs 20%). The role of neoadjuvant / adjuvant chemotherapy still needs to be defined.

In our study, we are outlining our experience on OS cases of mandible, analysis of the clinicopathological features and a comprehensive literature review of OS mandible.

2.MATERIALS AND METHODS

Cases of osteosarcoma mandible treated during the time period 2018 to 2020 were reviewed. All the relevant information regarding the cases like clinical features, imaging, histopathology report, type of resection and adjuvant treatment were collected and analyzed.

2.1 Patient and tumour characteristics

Five cases of OS mandible presented to our institution during the above said period. The average age of our patients was 38 years (30-45years) which included three females and two males. None of the patients had any family history of malignancy, prior history of radiation or any bony disease. One patient had a history of previous surgery for the same for which she underwent corticotomy with enucleation and curettage with dental implant placement. All the cases presented with a common symptom of swelling and paraesthesia. Radiological evaluation was done with contrast enhanced CT scan for all cases which revealed the extent of the lesion and any associated lymphadenopathy.

Table 1 Characteristics Of Patient And Lesion

Age (years)	Gender	Size of lesion	Histology	Site of lesion
36	M	11.5cm	Osteoblastic	Body
45	F	8.2cm	Osteoblastic	Body
36	F	9cm	Osteoblastic	Body + arch
30	F	7.5cm	Osteoblastic	Alveolus+body
19	M	6.5cm	Osteoblastic	Body

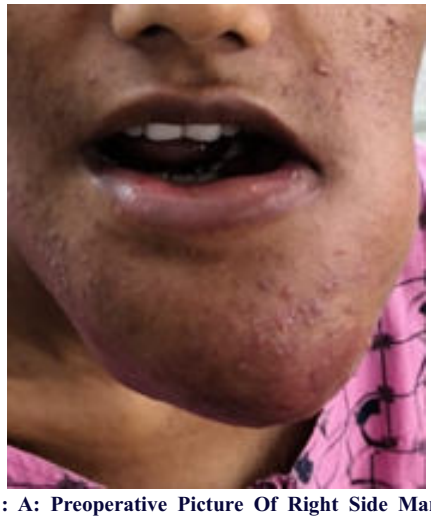

Figure 1: A: Preoperative Picture Of Right Side Mandibular Swelling , B: Intraoral Swelling

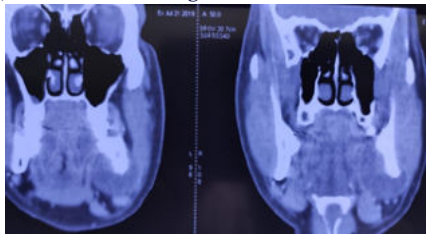

Figure 2: Preoperative Picture Of Lesion Involving The Left Side Body And Arch Of Mandible

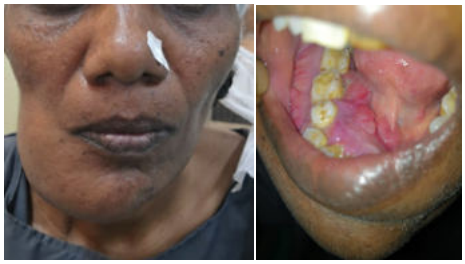

Figure 3: Cect Coronal Images Showing Tumour Involving The Left Body Of Mandible

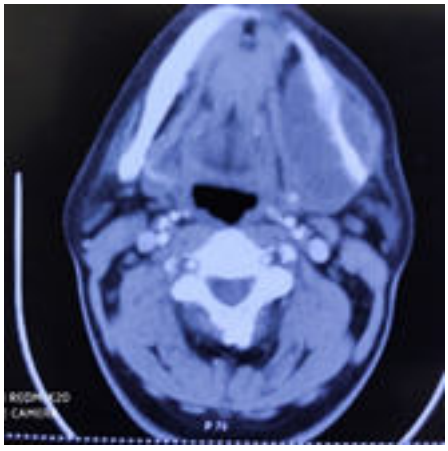

Figure 4: Axial Image Showing Tumour Invading The Left Body Of Mandible

2.2 Management details

All the five patients underwent surgical modality of treatment with composite resection followed by adjuvant treatment.

Table 2: Showing Extent Of Resection And Pathological Features.

TYPE OF RESECTION	MARGINS	GRADE	ADJUVANT TREATMENT
LEFT CONDYLE + CORONOID BODY OF MANDIBLE CROSSING MIDLINE	NEGATIVE	HIGH	RT+CT
RIGHT RAMUS AND BODY OF MANDIBLE CROSSING MIDLINE	NEGATIVE	HIGH	RT+CT
LEFT POSTERIOR SEGMENT	NEGATIVE	LOW	RT
LEFT RAMUS +CONDYLE+CORONOID	CLOSE SOFT TISSUE MARGIN	HIGH	-
RIGHT POSTERIOR SEGMENT	NEGATIVE	HIGH	RT+CT

All the cases with the histopathology features suggestive of high grade tumors, larger size (>5cm), positive or close margins were offered adjuvant treatment. One patient refused to take adjuvant treatment, rest all patients with high grade lesions were planned for CTRT. Two patients received three cycles of chemotherapy while one patient developed chemotherapy induced toxicity and stopped after two cycles. The low grade OS case was managed only with definitive surgery. The chemotherapy drugs used were cisplatin (100mg) and Adriamycin (40mg). One patient took neoadjuvant chemotherapy two cycles of cisplatin and Adriamycin.

Figure 5: A: Intraoperative Picture Showing Pectoralismajor Musculocutaneous Flap Reconstruction Following Resection Of Mandible. B: Showing 2 Weeks Postoperative Picture

Figure 6: Pmmc Flap With Reconstruction Plate Following Resection Of Tumor Involving Mandibular arch

2.3 Outcomes

All the patients were on monthly follow-up during the first year and every three months in the second year. The median follow up duration was 17 months. At the time of last follow up, two patients were disease free, other two cases had local recurrence and managed with palliative care. One patient had chemotherapy induced leukopenia and died of sepsis.

3. DISCUSSION

Osteosarcoma in the head and neck region is extremely rare. It has a distinct biology and natural history compared to the one that affects trunk and extremities.[4] The main symptoms include swelling over the mandible or intraoral swelling, pain, paraesthesia and ulceration.[5] In craniofacial OS, it has a bimodal age distribution with peaks in the third – fourth decades and sixth decade. In our case cohort, the median age of patients was 33.2years which is similar to other studies. The mean age at diagnosis of head and neck OS is at least 10- 15 years higher than appendicular OS. The male to female ratio is 1:1 in head and neck, while there is a slight female predominance in the appendicular OS. In our study we had a slight female predominance with a ratio of 2:3. But most of the studies report either equal distribution or male predominance. The longer period of skeletal growth and additional volume of bone in men are the reasons these studies quote. Krishnamurthy A et al, showed a result similar to us with a slight female dominance in their case series of 14 patients.[6] In another study by Forteza et al, the incidence of maxillary OS was higher in females and mandibular OS was seen only in males.[7]

The most common site of head and neck OS is the jaw bones and our series is exclusively on OS of mandible.

The pattern of spread is through the marrow spaces. In mandible the possible route is the mandibular canal and the structures which connect the intraosseous and soft tissue components like periodontal ligament and inferior alveolar canal. Another possible route is the dental sockets and through perforation of cortical plates.[8] Clinicopathological groups in OS are: conventional, periosteal and paraosteal. The diagnosis of OS relies on the presence of neoplastic immature woven bone. The most common forms of conventional OS are classified based on the predominant type of matrix: osteoblastic, chondroblastic or fibroblastic. All the five cases in our case series were conventional OS with neoplastic bone and osteoid as the predominant matrix component. In most of the studies on OS, osteoblastic variant was more than 50%, while there were few studies showing chondroblastic OS as the commonest one.[9,10,11,12] Hence literature review shows a mixed observation and chondroblastic is associated with unfavorable outcome. The surface variants of OS are parosteal and periosteal types. Parosteal OS is a low-grade tumor with spindle cells in parallel. The periosteal OS is an intermediate grade tumor with malignant bone and cartilage essentially with a subperiosteal base. These are rare in the head and neck region. Other rare variants include telangiectatic OS, small cell, giant cell rich etc.[2]

Head and neck OS fails at the primary causing local recurrence while appendicular OS fails mostly at the distant metastatic sites. This is the reason for neoadjuvant therapy prior to surgery in appendicular OS while for OS of head and neck, surgery with negative margins is of prime importance. The local recurrence rate in head and neck OS is 17 to 70% compared to 5-7% in the extremities. Local recurrence is the

cause of death in head and neck OS rather than metastasis.[13,14] Hence metastatectomy has no role in head and neck while it can possibly impact survival in other parts. The prognosis of head and neck OS lies midway as compared to the other sites. The postoperative adjuvant radiotherapy is indicated in patients with positive margins. In our study adjuvant treatment was advocated for all high-grade tumors irrespective of margin status. All patients except one received adjuvant treatment with concurrent CT and RT. The role of chemotherapy in head and neck is a debatable topic. In a metanalysis by Liang et al they found that chemotherapy improved the overall and disease-free survival in patients who had tumors in maxilla, positive margins, high grade tumour and recurrent tumour.[15]

The role of neoadjuvant chemotherapy also is not clear until now. The arguments against neoadjuvant therapy still stand strong as it is evident that the rate of distant metastasis is very less in head and neck OS and moreover the response assessment of neoadjuvant treatment is very difficult both clinically and radiologically in head and neck.

According to the National Cancer database report on OS of head and neck by Smith R et al, there is no significant difference in the 5-year survival rate between surgery alone and surgery with adjuvant chemotherapy.[16] In another study by Boon E et al, it was observed that in younger patients with surgically resected high and intermediate grade tumors, neoadjuvant chemotherapy resulted in smaller risk of local recurrence.[17] The single meta-analysis by Kasser RR et al and a systemic review by Smeele LE et al revealed that the overall survival and disease-free survival improved with the neoadjuvant.[18,19]

Macke T et al, found that the 5 year survival rate with neoadjuvant was 66.7% versus 41.7% without chemotherapy. It also showed improvement in local control, decreased the incidence of lung metastasis and prolonged the time taken for distant spread.[20] In our study, three of the five cases were high grade tumors, and out of which one had a close resection margin. Adjuvant radiotherapy of 60Gy was advised for all three cases. One patient who developed recurrence received neoadjuvant chemotherapy prior to surgery due to extensive soft tissue involvement including infratemporal fossa.

The 5-year DFS and OS for OS head and neck are 50% and 65% respectively. Complete surgical resection with clear margins is the strongest prognostic factor. Other prognostic risk factors include age, stage, tumour size, osteoblastic variant, non-surgical initial treatment, non-mandibular location and soft tissue in the extremities.

4.CONCLUSION

Head and neck OS is a rare malignant bone tumour mainly affects the jaw bones.They are aggressive tumours and biologically distinct from its counterparts in the extremities. The optimal treatment strategy is surgical excision with a clear negative margin. The role of adjuvant radiotherapy is now restricted to close or positive margins. The role of chemotherapy is ill defined and need further studies. In our series, chemotherapy in adjuvant setting gave a good treatment response. Even Though our series was a small study we highlighted the importance of negative margins in OS. Considering the rarity of the disease and paucity of data, further studies are required to conclude on the role of adjuvant and neoadjuvant treatments.

5. REFERENCES

1. Woolgar JA, Hall GL , Cysts and tumours of the bony facial skeleton, chapter 25,Scott-Brown's Otorhinolaryngology Head and neck surgery, volume3, Watkinson JC.8th edition, 2018, p399-421.
2. El Mofty S et al. Bone lesions of the head and neck,Surgical pathology 4 (2011) 1273-1328.
3. Purgina B et al, Distinctive head and neck bone and soft tissue neoplasams, surgical pathology 10 (2017) 223-279.
4. Chaudhary M et al, Osteosarcoma of jaws, Journal of oral and maxillofacial pathology,2012 May-aug;16(2):233-238
5. Baumhoer D et al , Bone related lesions of the jaws,Surgical pathology,2017, p 1-12.
6. Krishnamurthy A et al.Osteosarcomas of head and neck region: A case series with review of literature,J Maxillofac Oral Surg.2018 Mar:17(1):38-43.
7. Forteza G et al,Osteogenic sarcoma of maxilla and mandible, Oral surg oral med oral oathol,1986;62:179-84.
8. Kalburge JV et al, Osteosarcoma of the mandible,Journal of clinical and diagnostic research,2012 November, vol-6(9): 1597-1599.
9. Nissanka E et al, Clinicopathological analysis of osteosarcoma jaw bones. Oral Dis.2007;13:82-87
10. Clark JL et al, Osteosarcoma of the jaw. Cancer.1983;51:2311-2316
11. Bennett JH et al, Osreosarcoma of the jaws: a30 year reteospective review. Oral Surg Oral Med Oral Pathol .2000;90:323-333
12. Laskar S et al, Osteosarcoma of the head and neck region: lessons learned from a single institution experience of 50 patients. Head and neck.2009;30:1020-1026.
13. Guadagnolo BA et al, Osteosarcoma jaws/craniofacial region. Cancer.2009;115:3262-3270.
14. Canadian society of otolaryngology- Head and neck surgery oncology study group osteogenic sarcoma of the mandible and maxilla: a Canadian review (1980-2000)J Otolaryngol.2004;33:139-144.
15. Liang L et al,An individual patient data metaanalysis on the effect of chemotherapy on survival in patients with craniofacial osteosarcoma,Head and neck.2019 jun;41(6):2016-2023.
16. Smith RB et al, National cancer data base report on osteosarcoma of the head and neck. Cancer. 2003;98:1670-1680.
17. Boon E etal, Impact of chemotherapy on the outcome of osteosarcoma of the head and neck in adults, Head and neck,volume 39,issue1,p 140-146.
18. Kassir RR et al, Osteosarcoma of the head and neck; metaanalysis of nonrandomized studies, Laryngoscope.1997;107:56-61
19. Smeele LE et al, Effect of chemotherapy on survival of craniofacial osteosarcoma: A systemic review of 201 patients, J Clin Oncol.1997;15:363-7.
20. Mucke T et al, Effect of neoadjuvant chemotherapy treatment in the management of osteosarcomas of the head and neck, J Cancer Res Clin Oncol.2014 Jan:140(1):127-31.