

HISTOPATHOLOGICAL ASSESSMENT OF ORAL SQUAMOUS CELL CARCINOMA OF THE MANDIBULAR REGION

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ABSTRACT

BACKGROUND

Oral cancer accounts for 30% of cancers in India.¹ Of these, the tumours that abut on mandible show a greater local recurrence. This includes the tumours on mandibular alveolar ridge, lower buccal sulcus, sublingual sulcus and mandibular retromolar area.^{2,3} So, it is important to assess the histopathological features of these tumours to identify the factors related to prognosis and plan the surgical resection accordingly.

The aims of the study-

1. Histopathological characterisation of oral squamous cell carcinoma of the mandibular region.
2. Evaluation of the underlying mandible for marrow invasion and perineural tumour invasion.

MATERIALS AND METHODS

50 resection specimens of squamous cell carcinoma of the mandibular region received in Department of Pathology, Medical College, Thiruvananthapuram, and sent from the Department of Surgical Oncology, Regional Cancer Centre, Thiruvananthapuram, from May 2000 to August 2001 were included. The clinical factors like site, size of tumour, proximity and fixity to the mandible, history of radiation and evidence of bone invasion were checked. Hemimandibulectomy specimens were cut buccolingually and representative bits were processed after decalcification.

RESULTS

72% of the tumours in the lower alveolus showed mandibular bone invasion while those in buccal mucosa and tongue did not. The infiltrative pattern was associated with deeper invasion of the bone. Perineural and intraneural infiltration of inferior alveolar nerve occurred in 16.7% and 5%. Marrow fibrosis was the commonest tissue response to tumour invasion.

CONCLUSION

Mandibular resection is essential for large tumours, which are located on the alveolar ridge with clinical fixity to the mandible. An infiltrative pattern of bone invasion and perineural involvement are seen in more aggressive tumours.

KEYWORDS

Oral Squamous Cell Carcinoma, Mandibular Region, Histopathological Characterisation.

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BACKGROUND

Oral cancer is one of the 10 most common human cancers worldwide and accounts for over 30% of all cancers reported in India.¹ Oral carcinoma of the mandibular region is defined as carcinoma of the mandibular alveolar ridge, lower buccal sulcus, sublingual sulcus and mandibular retromolar area. These tumours have the ability to invade mandible usually by direct extension.^{2,3} The incidence of tumours with mandibular involvement ranges from 30-33%.³ Once within

the medullary cavity of mandibular bone, local spread of the tumour can occur both anteriorly and posteriorly. Perineural tumour spread along the inferior alveolar nerve is also an important pathway of tumour spread.^{4,5,6} Tumours of the mandibular region present the lowest survival rates among those of oral squamous cell carcinomas. These tumours are usually large, locally aggressive and are unlikely to be cured by radiation therapy alone. They require partial or total mandibulectomy.

It is also important to identify the oral tumours that show a lesser propensity to invade the mandible since a less extensive surgical treatment can be offered in such cases. Exact evaluation of mandibular invasion by oral cancers is of paramount importance for staging, treatment planning and assessing the prognosis. The gold standard for this is histopathological assessment of the tumour and the underlying mandible.

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Aims of the Study

- 1. Histopathological characterisation of oral squamous cell carcinoma of the mandibular region.
- 2. Evaluation of the underlying mandible for marrow invasion and assessment of perineural tumour invasion.

MATERIALS AND METHODS

50 consecutive surgical resection specimens of biopsy-proven squamous cell carcinoma of the mandibular region received in Department of Pathology, Medical College, Thiruvananthapuram, during the period of May 2000 to August 2001 were included in this study.

The specimens were received from the Department of Surgical Oncology, Regional Cancer Centre, Thiruvananthapuram. The tumours selected were all within 1.5 cms of the mandible. The important clinical factors like site and size of tumour, proximity and fixity to the mandible and prior history of radiation were noted. Evidence of bone invasion, nature and depth of invasion were checked clinically and intraoperatively.

All specimens received were grossed after checking the site of tumour, exact measurement and any macroscopic evidence of bone involvement. All the hemimandibulectomy specimens were cut buccolingually into slices of 0.5-1 cm thickness. Representative bits were taken and processed after decalcification.

OBSERVATIONS AND RESULTS

Of the 50 cases of oral squamous cell carcinomas of the mandibular region included in our study, 28 cases were in the lower alveolus, 12 were on buccal mucosa and 10 were on the tongue (Figure 1).

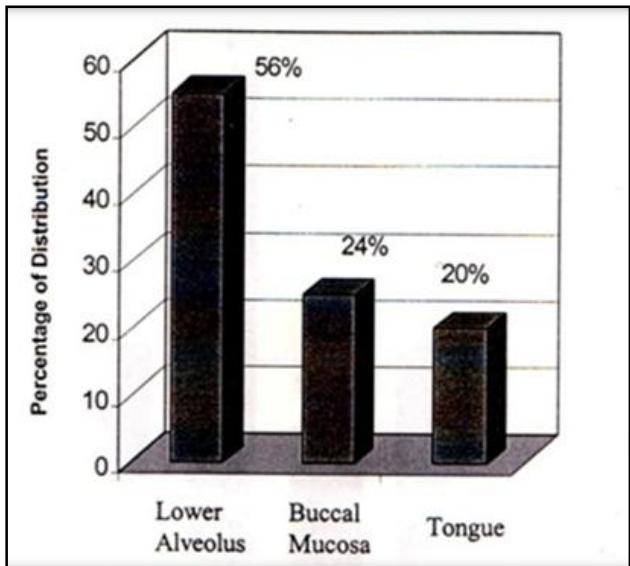


Figure 1. Distribution of Cases by Site of Tumour

Lesions of buccal mucosa and tongue were at a distance of more than 1 cm from the mandible. Of those involving the lower alveolus, 21 (75%) were within a distance of 0.5 cms, while 7 cases (25%) were at a distance of 0.5 to 1 cm from the mandible. The size of tumour in greatest diameter ranged between 35-45 mm in 40 (80%) cases.



Figure 2. Resected Hemimandibulectomy Specimen-Tumour Involving Buccal Mucosa

On clinical assessment, 25 of 28 cases (89.2%) of lower alveolar tumours were fixed to the mandible indicating a positive bone involvement. Peroperatively, also these 25 cases of carcinoma of lower alveolus showed cortical irregularity, cortical thickening, erosion or discontinuity, which were suspicious of a mandibular involvement. Cases of buccal mucosa and tongue did not show any clinical evidence of mandibular involvement.

Of these 25 cases of lower alveolar tumours clinically suspicious of invasion, only 18 (72%) showed a positive bone involvement histologically (Table 1).

Site	Histological Evidence of Mandibular Invasion		
	Yes	No	Total
Lower alveolus	18	10	28
Tongue	0	12	12
Buccal mucosa	0	10	10

Table 1. Histological Evidence of Mandibular Invasion in Tumours of Mandibular Region

8 cases (44.4%) of the squamous cell carcinomas that invaded mandible were well differentiated, 9 cases (50%) were moderately differentiated and 1 case (5%) was poorly differentiated.

Histologically, the pattern of invasion of bone was typically of two types- infiltrative or erosive (Figures 5 and 6). While the infiltrative pattern is defined by nests and cords of tumour cells with an irregular advancing tumour front, erosive pattern is characterised by a broad pushing margin with a layer of connective tissue in the actual tumour bone interface. In our study, 10 cases were infiltrative and 8 cases were erosive in type. (Figure 3)

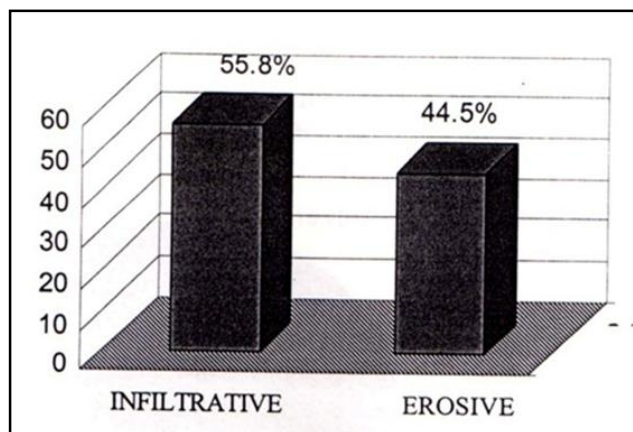


Figure 3. Bar Chart Showing Histological Pattern of Bone Invasion

Bone invasion was categorised as cortical when limited to the cortex or medullary when extension into marrow was present. Figure 4 shows pie chart displaying manner of bone invasion in various tumours in our study. Bony invasion can involve the inferior alveolar canal with or without perineural invasion. Spread of tumour through cortical bone alone was seen in 3 cases (16.7%) and spread beyond the cortical bone into the medullary cavity was noted in 6 cases (33.3%). Involvement of inferior alveolar canal with extension to perineural space occurred in 3 cases (16.7%), and of these, 1 case had intraneural infiltration (Figures 7 and 8). Table 2 displays the status of bone invasion and the histological type of invasion. The tumours with infiltrative pattern of invasion showed a deeper invasion of bone and nerve infiltration.

Pattern of Bone Invasion	Spread				
	Cortical	Cortical + Medullary	Inferior Alveolar Canal without Perineural	Inferior Alveolar Canal with Perineural Involvement	Total
Erosive	3	5	-	-	8
Infiltrative	-	1	6	3	10
Total	3	6	6	3	18

Table 2. Pattern of Invasion vs. Spread within Bone

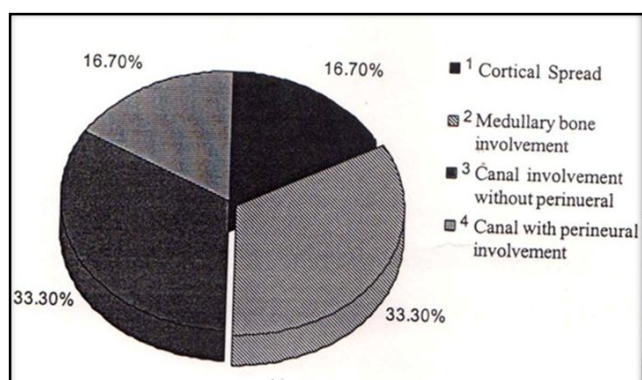
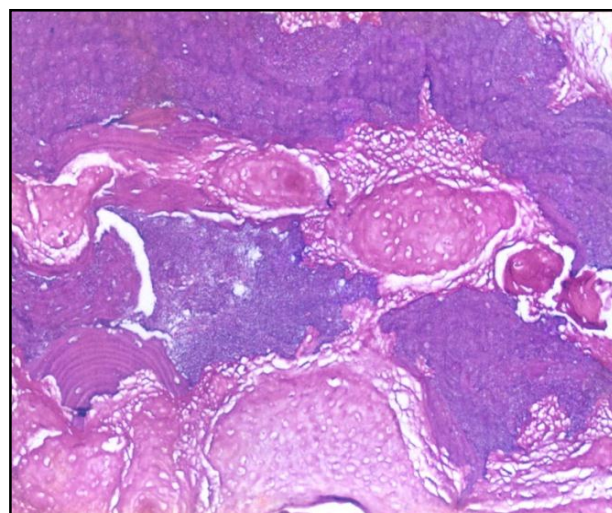


Figure 4. Pie Chart Showing Distribution of Cases by Manner of Bone Involvement

study, marrow fibrosis was the predominant finding in 13 cases (83.3%). 34 cases (68%) who had received prior radiotherapy showed fatty infiltration of the marrow.



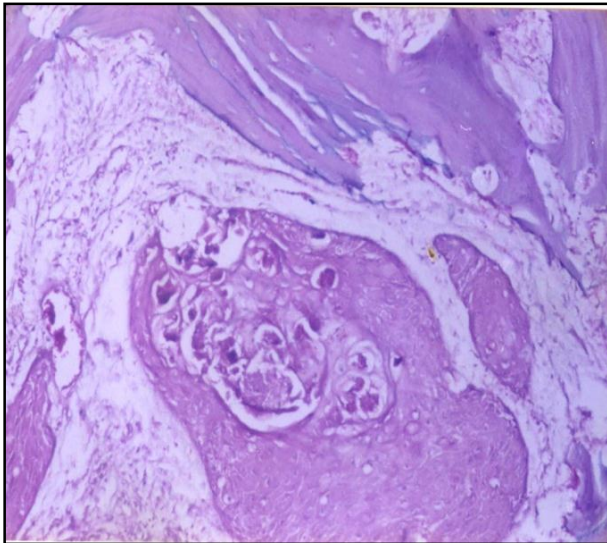
(Haematoxylin and Eosin x200)
Figure 5. Infiltrative Pattern of Tumour Invasion with Irregular Nests and Islands Invading Mandibular Bone

The maximum dimension of tumour within the bone histologically ranged from 30-45 mm in 80% of cases. In none of the 18 cases, which showed mandibular invasion, the greatest diameter of tumour within the bone did not exceed that of the corresponding mucosal tumour anteriorly or posteriorly as given in Table 3.

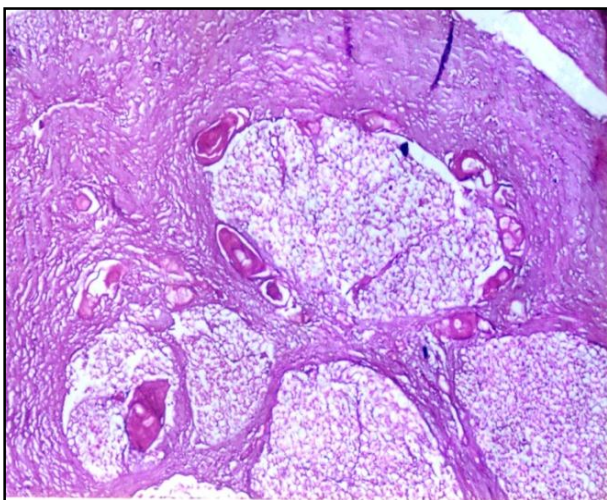
Histological Extent (mm)	Extent of Mucosal Tumour (mm)					
	30	35	40	45	50	Total
20	-	1	-	-	-	1
25	1	2	-	-	-	3
30	2	3	-	-	-	3
35	1	2	2	1	-	6
40	-	1	2	-	1	4
45	-	-	-	-	1	1
Total	4	7	4	1	2	18

Table 3. Histological Extent vs. Extent of Mucosal Tumour

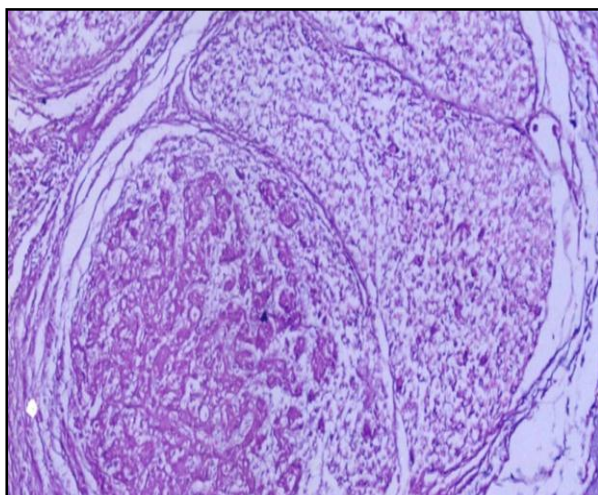
Marrow reaction seen were fibrosis, fatty infiltration, inflammation, increased osteoclastic activity and reactive new bone formation (Figures 9 and 10). In the present



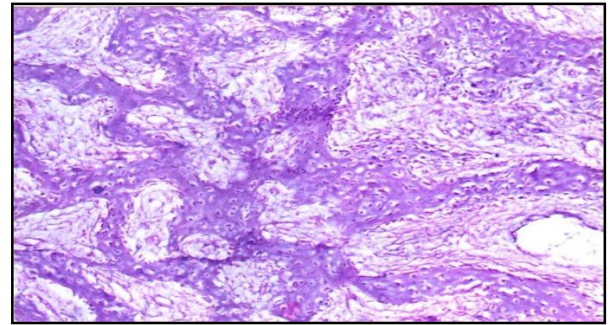
(Haematoxylin and Eosin x200)
Figure 6. Tumour Eroding Bone with Broad and Smooth Pushing Margins



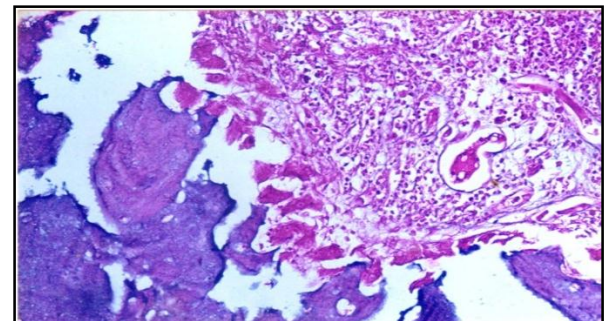
(Haematoxylin and Eosin 200x)
Figure 7. Perineural Tumour Infiltration of Inferior Alveolar Nerve



(Haematoxylin and Eosin x 200)
Figure 8. Endoneurial Tumour Infiltration of Inferior Alveolar Nerve



(Haematoxylin and Eosin x200)
Figure 9. Reactive New Bone Formation and Marrow Fibrosis Associated with Tumour Invasion



(Haematoxylin and Eosin x200)
Figure 10. Marrow Inflammation and Increased Osteoclastic Activity Associated with Tumour Infiltration

DISCUSSION

A total of fifty biopsy-proven cases of oral squamous cell carcinoma of the mandibular region were studied. The commonest site of involvement by these tumours in our study was the lower alveolus.

In this study, 80% of cases that showed bone involvement were the tumours with greatest diameter between 35-50 mm. This supported the earlier reports on the positive correlation between increased clinical 'T' stage and bony invasion.^{7,8} Another study has identified that size of tumour did not correlate with bone invasion, but both increase in size and marrow invasion were identified as independent risk factors for the tumour morbidity.⁹

None of the primary lesions located on the tongue and buccal mucosa invaded the mandible. But, tumours involving lower alveolus had a 64.2% incidence of mandibular invasion, which is comparable with earlier studies.² Tumours abutting into cortical bone like carcinoma of buccal mucosa and tongue, unless very extensive, rarely infiltrate bone unlike their alveolar counterpart.^{2,10}

85% of tumours with clinical fixity to mandible showed histological evidence of bone involvement especially when they were within 1 cm of the mandible. Present study suggests that clinical appearance of tumour in relation to bone is an important predictor of mandibular invasion.¹¹

The histopathological pattern of bone invasion was also found to be important. In the present study, tumours, which exhibited an infiltrative pattern of tumour invasion in histology progressed deeper into the marrow spaces involving the mandibular canal. Erosive pattern was restricted to upper part of marrow in 80%, whereas the

infiltrative pattern known for its diffuse and extensive spread involved mandibular canal in 64% cases. This is in accordance with previous studies.^{4,7,8,12}

Perineural invasion of tumour was seen in 6% tumours of mandibular region in the present study. A high incidence of perineural tumour invasion was reported in earlier studies.^{5,6} Tumours of buccal mucosa and tongue did not show evidence of nerve-related spread histologically, whereas 10.7% of tumours of lower alveolus showed perineural infiltration.¹³ This is in contrast to the earlier studies by Zupi et al (1998)⁵ where they found the highest incidence of perineural invasion with squamous cell carcinoma of the lower lip.

The incidence of perineural and intraneural invasion in carcinomas of lower alveolus shows that neural diffusion has occurred by direct extension through the mandibular bone to the inferior alveolar nerve rather than by preferential spread without mandibular involvement.¹³

Nerve-related spread beyond the posterior margins of tumour in the medullary cavity was not seen in any of the cases in the present study. This is in contrast to the earlier studies¹⁴ where tumour invasion in the perineural space was seen about 1-2 cms beyond the posterior margin of tumour. In the present study, involvement of canal alone without perineural involvement was noted in 6 cases in contrast to the reports in literature.

Tumour spread within the bone never exceeded beyond the margin of tumour in the soft tissue also. McGregor and McDonald (1989)¹⁵ has reported that this was seen infrequently in their study. Lukinmaa et al (1992) has reported in four cases, the distal extension of bone infiltration markedly (1 cm or more) exceeded the dimension of tumour in the overlying mucosa.

The predominant marrow reaction included bone marrow fibrosis in the present study.¹⁶ History of previous irradiation correlated with the host cell reaction in marrow. Over half of patients with prior radiotherapy showed a fibrofatty marrow with no inflammatory response to the tumour extension into bone. This is similar to the study by McGregor and McDonald¹⁵ who reported a peculiar pattern of tumour spread in irradiated mandible in relation to haversian system to a variable and unpredictable extent with no bone reaction or bone resorption in the surrounding cortical bone.¹³

The grade of tumour differentiation did not show significant correlation with presence, pattern or extent of bone invasion. This is in good agreement with earlier studies.^{13,16}

CONCLUSION

- Mandibular resection is essential for large tumours, which are located on the alveolar ridge with clinical fixity to the mandible. Extensive surgical measures can be withheld in tumours of the buccal mucosa and tongue.
- Infiltrative pattern of marrow involvement and perineural involvement are seen in more aggressive tumours.
- Perineural involvement occurs more by direct extension of tumour through the bone rather than by preferential spread along the inferior alveolar nerve.

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