

# Infiltrative Type of Bone Invasion in Oral Squamous Cell Carcinoma – Case Report

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## Abstract

Oral squamous cell carcinoma (OSCC) is a well known malignancy which accounts for more than 90% of all oral cancers. OSCC are malignant tumors that frequently invade bone and bone invasion is a common clinical problem. Bone invasion by oral squamous cell carcinoma may progress by either an infiltrative or an erosive histological pattern. The pattern of bone invasion co-relates with the clinical behavior of OSCC thus having a potential prognostic value. The present case report is of a 35-year-old female patient presenting with a lesion in the lower right buccal vestibule which was histopathologically confirmed as OSCC. The type of bony invasion was also assessed microscopically. The objective of this paper was to define the characteristics associated with each histological pattern of invasion and its significance when reviewing oral squamous cell carcinoma with mandibular invasion.

**Key Words:** Oral cancers, Osteoclastogenesis, Osteoprotegerin

## Introduction

OSCC is the sixth most common cancer and more than 3,00,000 new cases are diagnosed each year world wide.<sup>1</sup> Oral carcinoma of the mandibular region has been defined as carcinoma of the mandibular alveolar ridge, lower buccal sulcus, sublingual sulcus and mandibular retro molar trigone.<sup>2</sup> Carcinoma at this site may eventually progress to directly invade the mandible, a feature associated with a worse prognosis. Mandibular invasion is one criterion of the American Joint Committee on Cancer classification for the most advanced primary stage (T4) and overall stage (IV) for these tumors. The 5-year determinate survival of patients with stage IV oral lesions has been demonstrated to be 39%, as compared with 53%, 68%, and 70% for stages III, II, and I disease, respectively.<sup>3</sup>

OSCC invades the mandibular bone through an erosive, infiltrative or mixed pattern that correlates with clinical behavior. The erosive pattern is characterized by a broad, expansive tumor front with a sharp interface between tumor and bone. In contrast, the infiltrative pattern is composed of nests of tumor cells with fingerlike projections along an irregular tumor front. The recent distinction between these two histological patterns challenges the previously held

assumption that mandible invasion universally presents a poor prognosis. The erosive pattern of bone invasion has been hypothesized to extend in a more predictable fashion than the infiltrative pattern. Infiltrative pattern of bone invasion is associated with a higher recurrence rate of about 53% compared with the erosive pattern which is about 17%.<sup>4</sup> The present case report describes about the infiltrative pattern of bony invasion by squamous cell carcinoma originating from the buccal vestibule in a middle aged woman.

## Case report

A 35-year-old female patient reported in MGM dental college and hospital with a chief complaint of a non healing cut in lower right cheek since the past 3-4 months. Past medical history was non contributory. The patient had habit of chewing tobacco since the past 20 years. She also had history of Misheri application on teeth and gums since the past 20-25 years. There was no history of trauma, sinus or pus discharge. Extraoral examination revealed a very mild facial deformity with a diffuse swelling in the right side of the face. Ipsilateral cervical lymphadenopathy (level IB) was also noticed. Intraorally there was presence of a linear endophytic lesion extending from lower right first premolar to lower right third molar region in the gingivo-buccal sulcus region. (Fig. 1) Additional feature i.e. Grade II mobility of teeth from mandibular right third molar to mandibular left canine was seen. On radiological examination, Orthopantomogram (OPG) revealed an ill-defined radiolucency extending from mandibular right third molar (48) to mandibular right canine (43). Computed tomography (C.T scan) showed an osteolytic lesion involving the right side of the mandible crossing the midline. (Fig.2) A provisional diagnosis of Squamous Cell Carcinoma involving the bone was given. Incisional biopsy was taken. The histopathological report of well differentiated SCC was

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Fig. 1- An endophytic lesion extending from 44 to 48 in the gingivo- buccal sulcus region.



Fig. 2 - C.T scan showing an osteolytic lesion involving the right side of the mandible crossing the midline.

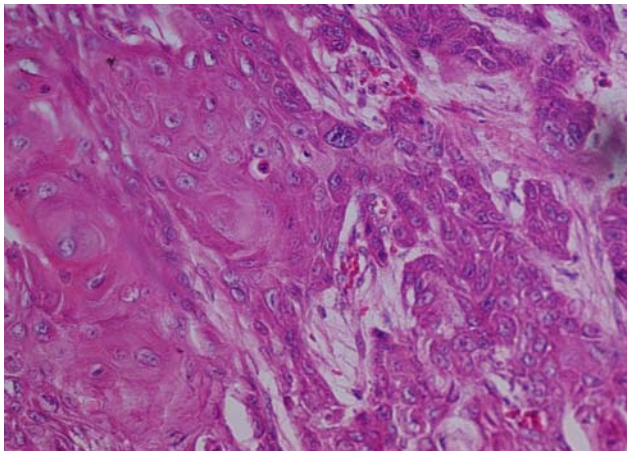


Fig. 3 - H & E Section showing islands of malignant epithelial cells with moderate amount of keratin pearl formation(40X)

confirmed. Excisional biopsy was done which included hemimandibulectomy extending from 48 to 34 with supra-omohyoid neck dissection (SOND). Histopathological examination revealed dysplastic stratified squamous epithelium. The underlying connective tissue showed infiltration by nests & small islands of malignant epithelial cells. Some of the larger islands showed keratin pearl formation. (Fig. 3). Also seen was moderate degree of chronic inflammatory cell infiltration and prominent stromal activity at the tumour invasion front. In some areas perivascular and muscular invasion of tumour islands was also noticed. There was no evidence of perineural

invasion. Level IB lymph nodes were positive for tumour with extra capsular spread. Serial sectioning of the mandible was done. The anterior bony margin representing socket of mandibular left first premolar (34) and lower border of the mandible microscopically

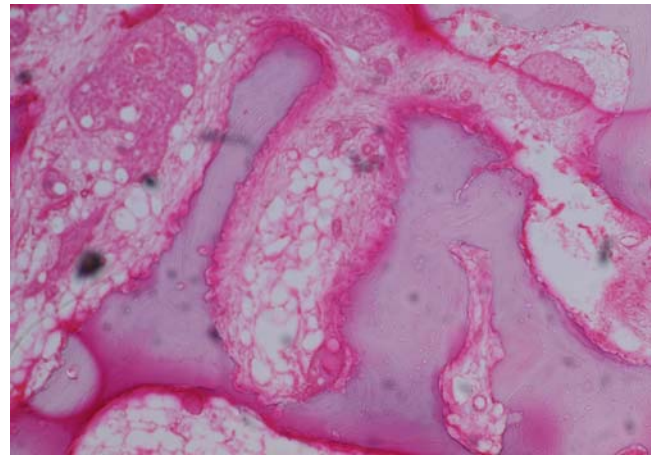


Fig. 4 - H & E Section showing intramedullary invasion of tumour islands (10X)

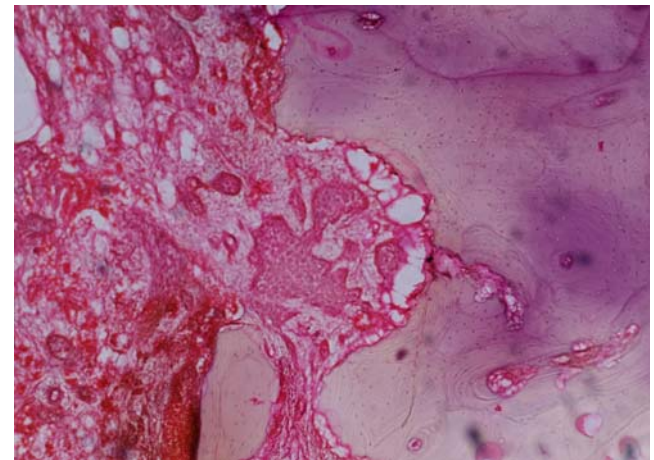


Fig. 5 - H & E Section showing tumour islands resorbing the cortical bone (10X)

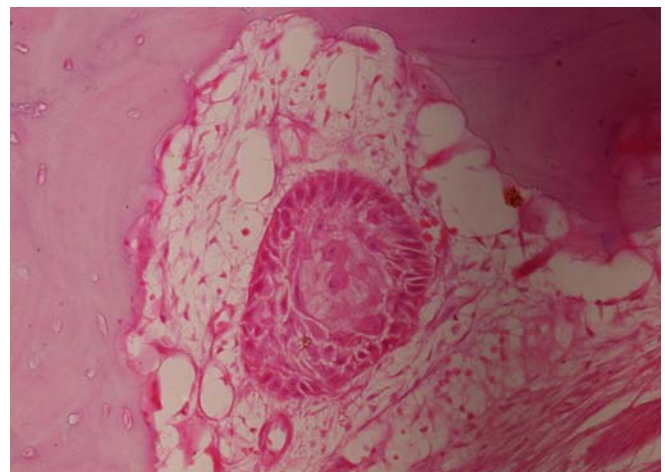
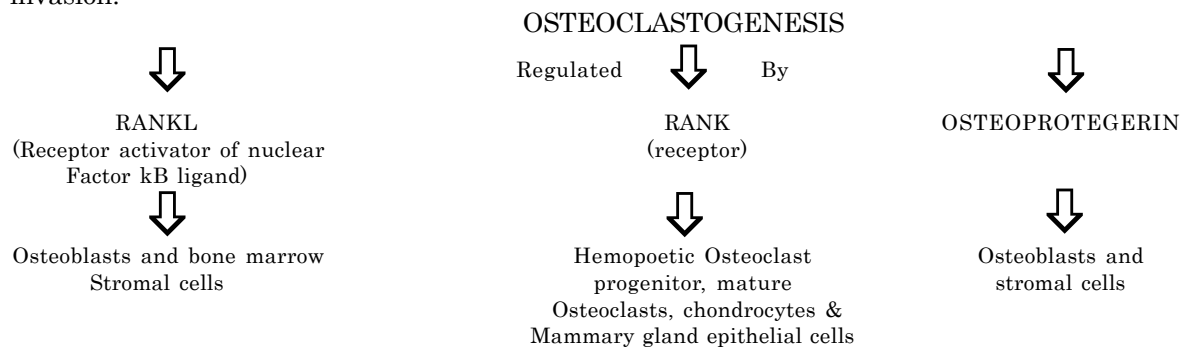


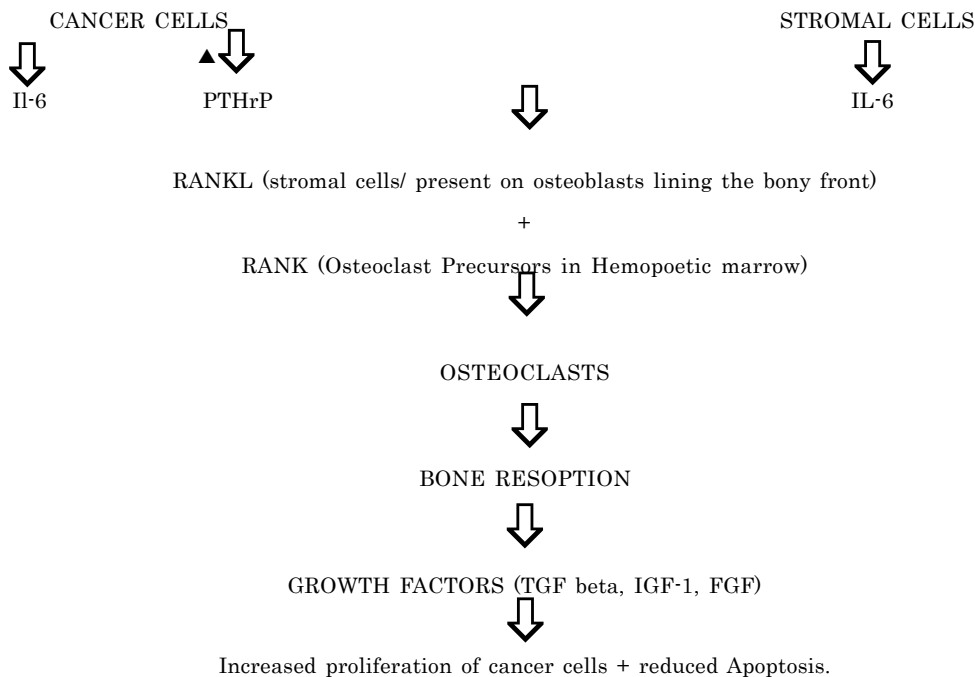
Fig. 6 - H & E Section showing tumor island resorbing the cortical bone. (40X)

showed intramedullary invasion of tumour cells. Extensive and deep invasion by small groups and islands of tumor cells was seen in the mandible (Fig. 4) with irregular resorption of cortical bone (Fig. 5 and 6). H & E section of the tissue excavated from the bony margin also proved positive for tumour showing sheets of keratin with few islands of malignant cells. The overall impression was consistent with Moderately Differentiated Squamous Cell Carcinoma. Anneroth's histological classification also showed Grade II SCC. (Table 1) with level IB lymph nodes being positive for tumor and apparently safe anterior bony margin also involved (not free) showing infiltrative pattern of bony invasion.

men and may contribute up to 25% of all new cases of cancer. At least 95% of OSCC cases occur in individuals aged 40 years or older and is twice as often in men as in women. In the present case report the female patient is 35 years old which is a relatively younger age group. Most important risk factors are tobacco use, increased consumption of alcohol and betel quid usage all of which act separately and synergistically together. Oral cancer risk due to consumption of tobacco and alcohol combined is estimated to be more than 80%. In our case the patient had history of chewing tobacco and applying Misheri on the teeth and gums since the past 20-25 years. This well correlates the association of tobacco and OSCC.<sup>5</sup>



Thus a balance between expression levels of RANKL and OSTEOPROTEGERIN is crucial because both are produced by the same cells.



## Discussion

OSCC is a well known malignancy which accounts for more than 90% of all oral cancers. The annual estimated incidence is around 275000 for oral and 130300 for pharyngeal cancers excluding nasopharynx. In high risk countries like Sri Lanka, India, Pakistan and Bangladesh, OSCC is the most common cancer in

Clinical examination requires an imaging correlation. Various imaging techniques (i.e.: Orthopantomogram, Bone Scintigraphy, Computed Tomography, Magnetic Resonance Imaging and Positron emission tomography) are used to make a diagnosis of mandibular invasion by tumour of the oral cavity<sup>6</sup>. In the present report, OPG and C.T scan were used to detect the extent of mandibular invasion. On the CT scan the lesion seemed

to be crossing the midline. This was initially suspected clinically as the teeth showed mobility from 48 to 33.

As tumor cells grow and mitosis increases, they invade the basement membrane, destroy the surrounding tissue regionally, resist the immune system, and secrete certain proteins and angiogenic factors that will facilitate lymphovascular invasion and metastasize regionally or distantly. OSCC tends to invade the adjacent bone due to its close anatomical proximity, so higher bone invasion will occur in the OSCC that lies in direct contact with the bone. The size and proximity of the primary tumor to the jaw bone will determine the degree of bone invasion. Prognosis is affected by the pattern of bone invasion, which could be either an erosive, infiltrative or mixed<sup>7</sup>. The erosive pattern of bone invasion is marked by a broad pushing front, a sharp interface between tumour and bone, osteoclastic bone resorption and fibrosis along the tumour front and an absence of bone islands within the tumour mass. In contrast, the infiltrative pattern is characterized by nests and projections of tumour cells along an irregular front, residual bone islands within the tumour and Haversian system penetration. The histological pattern of mandibular invasion seems to correlate with the clinical behavior. Infact the infiltrative lesions are more likely to have primary, regional and distant recurrence<sup>8</sup>. The 3 year disease free survival in the infiltrative pattern is reported as 30% as against that in erosive pattern is 73%<sup>4</sup>. The present case showed an infiltrative pattern of bone invasion suggesting that it was an aggressive lesion. It is seen that cellular and molecular mechanisms regulate osteoclast differentiation.

Thus, it can be deduced that stromal cells regulate osteoclast formation induced by OSCC. Also IL-6 and PTHrP released from oral cancer cells induce Osteoclastogenesis through RANKL expression in stromal cells.<sup>8</sup>

Patients with mandibular invasion should be treated surgically but the extent of mandibular resection required remains controversial<sup>8</sup>. Histological pattern of mandibular invasion has prognostic significance. Poor clinical outcome is highly correlated with the infiltrative histological pattern of invasion. Infiltrative pattern has a 4-fold increased risk of death as compared to erosive pattern. In the present case hemimandibulectomy was performed and considering a 1 cm safe margin, the mandible was resected up to Lower left first premolar.(34) However, on histopathology of the resected mandible, the margin considered to be safe showed infiltrative pattern of bone invasion, thus being positive for tumor. Therefore the patient was informed about the prognosis, advised radiotherapy and explained about the need of another surgical intervention.

A recent study has demonstrated that tumour invasion of the mandible is not significantly correlated with the

survival of the patient with OSCC and if bone invasion is identified histologically, the prognosis is not worsened and additional surgery need not be undertaken.<sup>9</sup>

However, more studies are required with more number of cases to prove the prognostic value of the pattern of bony invasion in OSCC.

## Conclusion

The infiltrative pattern intuitively appears to be an aggressive tumor that is difficult to resect surgically. The intraoperative and preoperative determination of invasion pattern remains problematic. If the preoperative imaging studies do show radiographic characteristics suggesting an infiltrative pattern such as an irregular front or bone spicules, a wide surgical margin should be taken around the grossly apparent tumor. Pattern of invasion provides important prognostic information and therefore should be routinely commented on by pathologists reviewing cases with mandibular bone invasion.

In addition, new approaches have been developed to examine cellular and molecular mechanisms of bone invasion by OSCC. Inhibition of osteoclast differentiation and function by blocking RANKL and RANK by inhibitor antibody constitutes a novel approach to development of target therapy.

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