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Post Operative Histological Evaluation of Perineural Invasion in Patients Diagnosed with Oral Squamous Cell Carcinoma with No Clinical Signs and Symptoms of Nerve Involvement Pre-Operatively at a Tertiary Care Hospital

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ABSTRACT

Oral Squamous cell carcinoma (OSCC) has highest incidence of morbidity and mortality globally. Perineural invasion (PNI) is the main histological feature linked to poor prognosis of OSCC, however, it is usually missed in those patients who do not have any neurological symptoms prior to surgery. Therefore, the aim of this study was to evaluate histological characteristics of perineural invasion in oral squamous cell carcinoma patients who has no sign and symptoms of nerve involvement pre-operatively at tertiary care hospital. This was a cross—sectional study with total population of fifty-five (55) patients, conducted from July 2024 to December 2024 at Abbasi Shaheed Hospital, Karachi. The tissue sample from perineural space, post-surgery was collected from the participants who gives consent to participate and was then sent for histopathologic examination. All the histological information with the demographics and history of patients were recorded and the data was analyzed using SPSS version 23. The mean age of participants was 57.4±10.1 years with more males having 67.3% habit of tobacco chewing and 54.5% habit of smoking. Based on histopathological evaluation, 15 patients were positive for perineural invasion, among which 46.7% experience recurrence. We can conclude that PNI can be present in OSCC patients without pre-operative neurological symptoms therefore, early detection of PNI may improve prognostic accuracy and adjuvant treatment strategies.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the sixth most common type of cancer worldwide and most common type of malignancy in oral cavity(1). The prognosis of OSCC is generally poor, (2) and the prognosis of oral tongue squamous cell carcinoma (OTSCC) is even poorer(3). Perineural invasion (PNI) is the result of a complex interaction between invading tumor cells and the particular perineural niche, which has been noted to affect outcomes in many cancers(4). This PNI not only indicates aggressiveness of the disease but is also associated with increase rates of recurrence, reduced survival and higher risk of metastasis(5). Perineural invasion is observed in many cancers and is independently associated with poorer prognosis and clinical local and regional recurrence(4). PNI is also associated with the depth of invasion of OTSCC and cervical lymph node involvement and might suggest consideration for elective neck dissection, even in stage 1 and 2 diseases(6). A significant number of recently published research has outlined the contribution of PNI to clinical outcomes in OTSCC. Some authors advocate incorporating PNI in the staging systems for OTSCC(7).

Treatment decisions in OSCC are mostly dependent on tumor site, TNM classification, pathologic parameters and patient's clinical status and preferences. Several studies have showed the significance of pathologic findings, such as the type of invasive edge, inflammatory response, stromal component, tissue eosinophilia, and PNI(8). The pre-operative histological evaluation serves as corner stone in identifying extend of tumor invasion. This histological detection should be done without pre-operative nerve related symptoms as well. Therefore, this study was conducted to access the incidence of PNI in patients diagnosed with OSCC, with no signs and symptoms of neurological pain pre-operatively, at a tertiary care hospital. By correlating these histological findings, the research aims to highlight

the clinical relevance of PNI detection in OSCC management and its impact on therapeutic decision making.

Objective

To assess post-operative histological evaluation of perineural invasion in patients diagnosed with oral squamous cell carcinoma with no clinical signs and symptoms of nerve involvement pre operatively in patients presenting to Abbasi Shaheed Hospital, Karachi.

MATERIAL AND METHODS

This study was cross-sectional conducted at Department of Oral and Maxillofacial Surgery, Abbasi Shaheed Hospital Karachi. The study duration from July 2024 to December 2024. The sample size was calculated using WHO calculator keeping 10% absolute precision. The calculated sample size was fifty—five (55). All the samples collected were through non-probability consecutive sampling technique.

Inclusion criteria

- Patients of either gender aged 25—80 years.
- Patients with histopathological confirmation of primary oral squamous cell carcinoma (OSCC).
- Patients that is undergoing OSCC surgery at Abbasi Shaheed Hospital.

Exclusion criteria

- Patient with secondary tumors.
- Patients of OSCC with pre-operative signs of trigeminal neuralgia, facial palsy, numbness or tingling.
- Pregnant patients.

The approval from ethical review committee from College of Physicians and Surgeons Pakistan was taken (CPSP/REU/DSG-2021-174-3711). Informed consent was secured from all the participants, who meet the inclusive criteria, explaining the procedure, risks and benefits of the study. All the demographic data and systemic disease with clinical history of tumor was recorded. The surgery was preform by experienced Oral and Maxillofacial Consultant. The post-surgery specimen from perineural space were collected and sent for histopathological examination. The tumor cells exhibiting brown cytoplasmic, nuclear, or surface membrane staining light microscope at low power is considered PNI positive. All the histopathologic information was recorded and analyzed further. The data was analyzed using SPSS version 23.

RESULT

A total fifty—five (55) patients who are diagnosed with oral squamous cell carcinoma (OSCC) were included in the study with mean age of participants 57.4±10.1 years. Most of the study participants were males (n=34, 61.8%) with positive history of tobacco chewing (67.3%) and smoking (54.5%) [Table 1]. Out of these 55 patients, 15 (27.3%) were positive for perineural invasion (PNI), of which 73.3% have advance-stage tumor, and only 26.7% has poorly differentiated tumor. All these clinicopathological parameters showed statistically significant results [Table 2]. Table 3 showed the correlation between PNI and post-operative recurrence. From all 15 PNI positive patients, 53.3% showed no recurrence whereas 33.3% showed local recurrence. Both of these showed statistically significant results. To assess whether tumor location influences PNI prevalence, an analysis of primary tumor sites was performed. PNI was most frequently observed in tongue (40%) and buccal mucosa (33.3%) [Table 4].

Table 1

Frequency Distribution of demographics of study participants (n=55)

Variable	Classification	n (%)
Gender	Male	34 (61.8)
	Female	21 (38.2)
Diabetes Mellitus	Yes	22 (40)
	No	33 (60)
Cardiovascular Disease	Yes	9 (16.4)
	No	46 (83.6)
Hypertension	Yes	17 (30.9)
	No	38 (69.1)
Smoking	Yes	30 (54.5)
	No	25 (45.5)
Tobacco Chewing	Yes	37 (67.3)
	No	18 (32.7)

Table 2

Association of PNI with clinicopathological parameters (n=55)

Parameter	PNI positive (n=15) n (%)	PNI negative (n=40) n (%)	p-value[a]
Tumor size (>4 cm)	9 (60)	10 (25)	0.012*
Depth of invasion (>10 mm)	12 (80)	18 (45)	0.020*
Lymphovascular Invasion	10 (66.7)	14 (35)	0.028*
Advance Tumor Stage (III/IV)	11 (73.3)	16 (40)	0.015*
Poorly differentiated Tumor	4 (26.7%)	2 (5)	0.009*

a: Chi-Square was applied

*: p-value <0.05 is statistically significant

Table 3

Correlation between PNI and Post-operative Recurrence (n=55)

Recurrence	PNI positive (n=15) n (%)	PNI negative (n=40) n (%)	p-value[a]
Local Recurrence	5 (33.3)	3 (7.5)	0.014*
Regional Recurrence	2 (13.3)	3 (7.5)	0.440
No Recurrence	8 (53.3)	34 (85)	0.008*

a: Fisher's exact test was applied

*: p-value <0.05 is statistically significant

Table 4
Correlation between PNI and Tumor site (n=55)

Tumor Site	PNI positive (n=15) n (%)	PNI negative (n=40) n (%)	p-value[a]
Tongue	6 (40)	9 (22.5)	0.018*
Buccal Mucosa	5 (33.3)	10 (25)	0.120
Gingiva	2 (13.3)	8 (20)	0.300
Floor of Mouth	2 (13.3)	13 (32.5)	0.250

a: Chi-Square was applied
*: p-value <0.05 is statistically significant

DISCUSSION

This study showed that perineural invasion (PNI) is most important histopathological feature of oral squamous cell carcinoma (OSCC). Increased recurrence rate, poorly differentiation of tumor with advanced stage and larger tumor size are key findings that showed association with perineural invasion. Even there were no neurological symptoms prior to the surgery, this study results showed 27.3% oral squamous cell carcinoma patients having PNI. This aligns with the case series had in 2015 by Varsha et al. which showed 40.5% of OSCC patients with PNI. This case series also showed strong correlation between PNI and advance tumor stage which is similar to our study findings(8).

PNI identification should be incorporated in histological analysis of OSCC and patients with presence of PNI should be considered as high-risk and need intensive post-operative care due to its tendency for recurrence. The site of tumor should also be considered, as tumor on tongue and buccal mucosa has higher chance of invasion then on any other site(9). PNI positive individuals were more likely to smoke and has habit of tobacco chewing. This implies the development of PNI in OSCC may be influenced by environmental factors. There is a huge variation in the incidence of reported PNI in OSCC, from a low frequency between 2% to a high of 82%, specifically when neural stains were used(10). At sites, such as the tongue and floor of mouth, PNI was detected in up to 70% of OSCC, whereas cancer of lower lip has a lower rate of PNI at 5.2%(11). In another study Perineural invasion was identified in 17.4% of oral squamous cell carcinomas(12).

This is a single-center study design with small sample size of fifty-five participants only is the limitation of this study which may affect the generalization of the finding. The selection bias may also be introduced by study's retrospective design. Future research should be focused on prospective, multi-center studies to validate these findings. Exploring the molecular mechanism underlying PNI in OSCC may also identify potential therapeutic targets.

CONCLUSION

Perineural invasion (PNI) is a significant histopathological feature of oral squamous cell carcinoma (OSCC) that give idea about disease progression and treatment outcomes. It is associated with large tumor size, higher recurrence rate and poorly differentiation of tumors. Routine assessment of PNI in biopsy report should be emphasized which would help in better treatment planning of these patients. From the results of this study we can confirm that PNI has an important implication for disease progression and prognosis.

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