ORIGINAL ARTICLE

Frequency of Cervical Lymph Node Extracapsular Spread in Oral Squamous Cell Carcinoma Patients

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ABSTRACT

Aim: To estimate the frequency of cervical lymph node extracapsular spread in oral squamous cell carcinoma patients.
Methodology: This prospective study was conducted in the Department of Oral and Maxillofacial Surgery, The University of Lahore from 1st December 2021 to 30th November 2022 and 50 diagnosed cases of oral squamous cell carcinoma were enrolled. Computed tomography scan was conducted for the diagnosis in addition to the histopathology of the samples. The CT scan images were used for identification of lymph node size, shape, and central necrosis. The frequency of the extracapsular extension of lymph nodes with the central necrosis was correlated with histopathology.
Results: The mean age of the patients was 60.5± 11.1 years with 60% of the cases were males and 40% of the cases were females. 36% of those patients were having a history of smoking, 22% were having a history of taking pan, 14% supari & chalia, 8% alcoholics and 6% consuming gutka. The primary tumor site identified through clinical and diagnostic imaging was anterior 2/3rd of tongue in 38% followed by posterior 1/3rd of tongue in 20%, buccal mucosa 14%, mandible and lip each as 10%, maxilla 4%, floor of mouth and retromolar trigone region each as 2%. It was observed that T3 and T4 cases had more ECS than T1 and T2 with a percentage of 20% and 30% respectively.
Practical implication: Knowledge of frequency and burden of this disease in Pakistan will assist in generating more efficient management and treatment protocols with early detection strategies of oral squamous cell carcinoma through association analysis and biomarker role of cervical lymph node extracapsular spread.
Conclusion: Extracapsular spread is observed more in patients having advanced stage tumor or having advanced grade of oral squamous cell carcinoma.
Key words: Extracapsular spread, Oral squamous cell carcinoma, Recurrence, Histopathological examination

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common cancer type for oral cavity with a very low survival rate. OSCC is the second highest carcinoma after breast carcinoma in females and bronchogenic carcinoma in males. OSCC of oral cavity is nearly 90% of total head & neck cancers. Various predisposing factors have been investigated that are the root cause of this lethal disease. This includes tobacco smoking, alcohol, pan, supari, chalia and gutka use. Extracapsular spread (ECS) of tumor occurs when tumor cells reach the capsule of lymph node. Different mechanisms are documented for the metastasis in regional lymph nodes. Nearby lymph nodes are considered as the anatomic barriers or primary cause of metastasis. Likewise, lymphatic shunts bypass the tumor regions (lymph nodes) and provide the site for the dissemination of malignant cells to lymphatic systems[1-4].

Extracapsular extension inside the lymph nodes of the patients with head cancer has been identified as a deprived prognosis factor of the disease as mentioned in multiple researches. Various studies have been conducted for assessing the predictive factors of ECS on computer-tomography (CT) imaging for cases undergoing surgical interventions[5].

Another study also mentioned extracapsular spread to be present in 33.6 to 75.6%the cases with presence of metastases in the cervical nodes. Thus making its frequency identification as highly significance for proper management of the disease at appropriate period[6.]

Presence of ECS further worsen the disease condition and reduce the 5-year survival rate of patients to 27% as compared to much higher rate up to 70% when ECS is not present[7,8]. Extracapsular spread is significantly correlated with higher chances of contralateral recurrence, metastasis and recurrence of tumor cells at unusual sites[9,10]. It has proved that ECS is found in majority of the oral squamous cell carcinoma cases. Histopathological

examination is considered to be the standard diagnostic method for the identification of ECS in these cancer patients. Severity of the metastatic state can be determined on the basis of histopathological assessment[11-13].

Present study was designed to estimate the frequency of ECS in oral squamous carcinoma patients.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Oral and Maxillofacial Surgery, The University of Lahore from 1st December 2021 to 30th November 2022 after approval of the Institutional Review of the Study for ethical concerns and clearances. The patient' informed consent was taken prior to the study enrolment. The present study was a prospective design where 50 diagnosed cases of squamous cell carcinoma were enrolled. The sample size was taken as 50 after complete assessment about the frequency of squamous cell carcinoma in Pakistan which turned around 3-6%. Squamous cell carcinoma of oral cavity subsites included: anterior 2/3rd of tongue, posterior 1/3rd of tongue, buccal mucosa, maxilla, mandible, floor of mouth, retromolar trigone region, lip. The Inclusion criteria for this study was including male and females of all age groups and races, biopsy proven cases of OSCC of oral cavity and its subsites only. While the Exclusion criteria was already operated cases of OSCC of oral cavity (recurrent/residual disease), patients who have completed or were undergoing chemotherapy/ radiotherapy, patients diagnosed for secondary or any other malignancy, patients who refused to be included in the study were excluded. Computed tomography was conducted for the diagnosis in addition to the histopathology of the samples. The CT scan images were used for identification of size, shape, and central necrosis after the clinical diagnosis and radiological imaging all the cases underwent surgical resection for their primary carcinoma. The frequency of the extracapsular extension of lymph nodes with the central necrosis was correlated with histopathology. Demographic and clinical details of all the patients were entered. Data was analyzed using

SPSS version 25.0 where frequency and percentages and mean and standard deviations were determined. Chi square test was used for analysis where p value <0.05 was taken as significant.

RESULTS

The mean age of the patients was 60.5± 11.1 years with 60% of the cases were males and 40% were females. There were 36% those patients who were having a history of tobacco smoking, 22% were having a history of taking pan, 14% supari & chalia, 8% consuming alcohol and 6% consuming gutka. The primary tumor site identified through diagnostic imaging was anterior tongue as 38% and posterior tongue 20%, buccal mucosa 14%, mandible and lip each as 10%, maxilla 4%, floor of mouth and retromola r trigone region each as 2% (Table 1).

The nodal stage was detected as N1 in 18% of the patients while N2a in 6% of the patients. N2b and N2c was prevalently seen in various cases with a percentage of 32 and 30 respectively (p<0.05) [Table 2].

The tumor site was observed as having higher positive cases of ECS in T3 and T4 lesions than T1 and T2 lesions with a percentage of 20% and 30% respectively. The difference of ECS positive between tumor sizes was significant (Fig. 1). There was a raised frequency of extracapsular extension of tumor occurring when tumor cells reach the capsule of lymph node among the squamous cell carcinoma patients. The extracapsular extensions of lymph nodes were assessed, and their presence was visualized on post-operative pathology at a magnification of 10x power (Fig. 2).

Inter-observer agreement in context with the complete assessment of individual imaging was conducted and it was observed that Cohen's Kappa inter-observer agreement for ECS was in moderate range with a value of 0.60. Highest agreements of imaging were presented in central necrosis cases with a value of 0.74 (Table 3). Distant failure was significantly higher in ECS +ve group as compared to ECS –ve group. Similarly, disease free survival was also higher in ECS +ve group in contrast to ECS-ve group (Table 4).

Table 1: Demographic characteristics of patients (n=50)

Parameter	No. (%)
Mean age (years)	60.5± 11.1
Males	30 (60%)
Females	20 (40%)
Smokers	18 (36%)
Pan	11 (22%)
Supari & chalia	7 (14%)
Alcoholics	4 (8%)
Gutka	3 (6%)
Primary tumor-site	
Anterior tongue	19 (38%)
Posterior tongue	10 (20%)
Buccal mucosa	7 (14%)
Mandible	5 (10%)
Maxilla	2 (4%)
Floor of mouth	1 (2%)
Retromolar trigone region	1 (2%)
Lip	5 (10%)

Table 2: Frequency of extracapsular spread (ECS) of tumor occur when tumor cells reach the capsule of lymph node (n=50)

Parameter	No. (%)
N1	9 (18%)
N2a	3 (6%)
N2b	16 (32%)
N2c	15 (30%)
N3	7 (14%)

Table 3: Criteria of integrated agreement

	Kappa
Radiological ECS assessment	0.60 (0.44–0.75)
Indistinct nodal margins	0.12 (0.3–0.24)
Infiltration into adjacent tissues	0.52 (0.33–0.70)
Irregular nodal enhancement	0.38 (0.19–0.57)
Matted nodes	0.51 (0.28–0.73)
Central necrosis	0.74 (0.62–0.88)

Table 4: Outcomes comparison on the basis of ECS

Outcomes	ECS (-ve)	ECS (+ve)	P value
Loco-Regional Failure	15.9 %	16.9 %	0.82
Distant-Failure	8.4 %	34 %	0.04
Disease Free-Survival	75.9 %	50 %	0.05
Overall-Survival	87.9 %	58.9 %	0.01

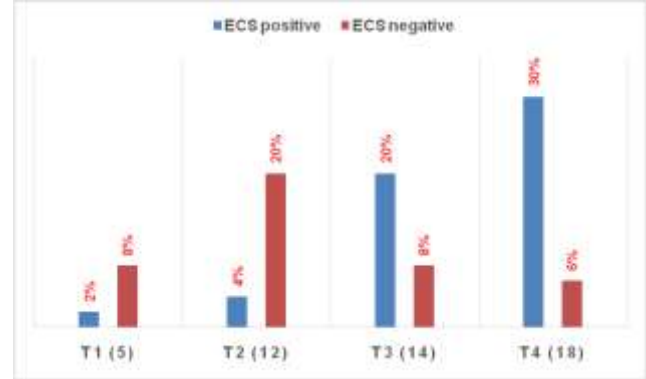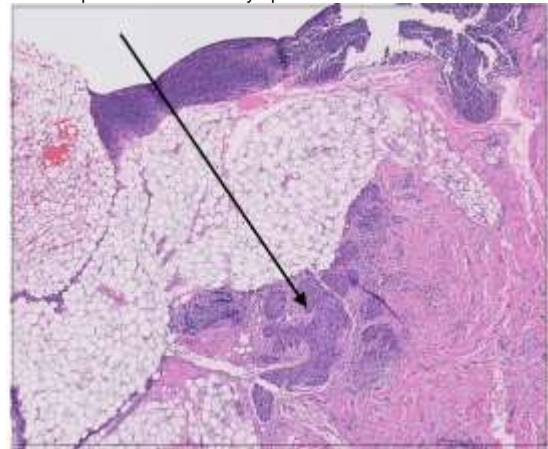Fig. 1: ECS positive cases in various tumor sizes (p<0.05)

Fig. 2: Extracapsular extension in lymph nodes

DISCUSSION

Oral squamous cell carcinoma is a fatal disease, having worst outcomes and very low survival chances in patients. In US, 2% of the women and 3% of men had oral squamous cell carcinoma among all cancer types.[14] In Pakistan, HNSCC is among the most diagnosed cancers in both males and females. Extra-capsular spread in case of oral squamous cell carcinoma further worsens the disease outcome and management. ECS status can be determined in carcinoma patients with the help of histopathological findings.[15-17] Purpose of the present study was to estimate the incidence and survival rate of oral squamous cell carcinoma patients with extracapsular spread to lymph nodes.

In the present study, radiological assessments were made to get the better representation of nodal metastasis. Specificity and sensitivity of the results were carefully taken into consideration for ensuring accurate and validate results. If a patient satisfies more than three ECS imaging criteria, then the patient was said to be positive for ECS. Histopathological findings showed that more than 50% of the study participants had extracapsular spread. Various studies have already proved the diagnostic accuracy of CT and histopathological examinations[18-20].

Prabhu et al[21] and King et al[10] have already documented that extracapsular spread is a common event in case of oral squamous cell carcinoma patients. It aggravates the disease condition and reduced the survival rate of the patient. Histopathological

assessment concluded that these results will prove helpful for ensuring adjuvant treatment success rate, management guidance and informing patient about their success and survival chances after the surgery and chemotherapy[22,23].

Metastasis is defined as invasion of tumor cells in another healthy cell and these tumor cells will not remain localized in a single region. It involves invasion in plasma membrane, bursting and swelling in groups of cells as compared to a single cell. Nodal metastasis represents and allows the tumor to break through capsule of lymph nodes and become more aggressive and invasive. In the present study, disease free survival was significantly higher in ECS-ve patients as compared to ECS+ve patients. These results were similar with already available data[24-29].

The limitations of the present study was that it included a small sample size and the nature of the study being concentrated on a single region/centre and therefore does not provide a complete picture of the population.

CONCLUSION

Extracapsular spread was observed more in patients having advanced stage tumor i.e., T3 & T4 lesions along with N2b & N2c lesions and having advanced grade of oral squamous cell carcinoma (moderate to poorly differentiated).

Significance of study: Knowledge of frequency and burden of this disease in Pakistan will assist in generating more efficient management and treatment protocols with early detection strategies of oral squamous cell carcinoma through association analysis and biomarker role of cervical lymph node extracapsular spread.

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