

## Unmasking the Silent Threat: The Enigma of Head and Neck Squamous Cell Carcinoma

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Received: 13-12-2023 / Revised: 04-01-2024 / Accepted: 30-01-2024

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Conflict of interest: Nil

### Abstract:

**Introduction:** Head and neck squamous cell carcinoma (HNSCC) is one of the most common malignancy throughout the world. It represents a significant global health burden due to its high morbidity and mortality rates. HNSCC exhibits varying degree of differentiation, invasion and lymph node involvement impacting its prognosis and treatment.

**Objectives:** We aim to delve into microscopic characteristics of HNSCC, grading system and their prognostic significance providing foundation for accurate histological diagnosis and tailored treatment approaches.

**Materials and Methods:** Study was conducted for 18 months and included 80 cases of histopathologically confirmed squamous cell carcinoma of head and neck. Clinical and histopathological features of each case were analysed. In radical resection cases, according to College of American Pathologists (CAP) guidelines TNM staging and histologic grading was done.

**Results:** A total of 80 (51 biopsy and 29 radical resection) cases were included, among which 65(81.25%) were men, with a mean age of 54.8 years. Commonest risk factor was tobacco chewing seen among 64 cases (80%). 63 cases (78.75%) presented with an exophytic mass, followed by ulcer with leukoerythroplakia 4(5%). Most frequent site involved was buccal mucosa 34(42.5%) followed by tongue 12(15%). In radical resections 16 cases (55.1%) were showing lymph node metastasis, lymphovascular invasion and perineural invasion was seen in 6(20.6%) cases 8(27.58%) cases respectively. Most of them were of grade II accounting for 49 cases (61.25%), followed by grade I which totalled to 30 cases (37.5%) and a solitary(1.25%) case of grade III. A statistically significant correlation was obtained between age and grade of the tumour. Worst pattern of invasion, depth of invasion showed significant correlation with lymphovascular invasion, perineural invasion and lymph node metastasis.

**Conclusions:** Our data reflect the histopathological characteristics of HNSCC. The intricate understanding of the pathological features of HNSCC is essential for optimizing diagnostic accuracy, prognostication and development of therapeutic strategies for improved patient outcome.

**Keywords:** Head and Neck Squamous Cell Carcinoma, Worst Pattern Of Invasion, Depth Of Invasion.

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### Introduction

Head and neck squamous cell carcinoma (HNSCC) develop from mucosal epithelium in the oral cavity, pharynx, larynx and are the most common malignancies that arise in the head and neck [1]

The burden of HNSCC varies across countries/regions has generally been correlated with exposure to tobacco derived carcinogenesis, excessive alcohol consumption or both [1,2]

There are many developing biomarkers for HNSCC with prognostic potential which require equipment,

kits or special training specific for research lab that rarely can be implemented in a standard clinical setting. [2]

Clinical and histopathological assessments are still the main prognostic tools routinely used in medical process.

In squamous cell carcinoma(SCC) histopathological assessment can provide more valuable information regarding prognostic potential. Features such as degree of differentiation, tumour depth of invasion

(DOI), worst pattern of invasion(WPOI), perineural and vascular invasion and lymph node metastasis carry additional prognostic potential in patient assessment. [2]

**Objective:** In this study we delve into the histopathological features available in standard haematoxylin eosin (HE)staining and their prognostic potential which helps in providing tailored treatment approaches to HNSCC.

### Materials and Methods

This cross sectional study conducted for 18 months included 80 cases of histopathologically confirmed diagnosis of HNSCC.

Inclusion criteria for our study were patients with biopsies and radically operated cases of HNSCC.

We excluded the HNSCC patients with previous treatment or recurrent tumour or metastatic tumour.

Relevant clinical and radiological details for each cases were recorded.

All specimens were fixed in 10% formalin and were grossed according to AJCC protocol applied with the particularities of each case.

Paraffin blocks were cut at 5µm and stained in HE using Leica histopathology system.

Sections from paraffin blocks were taken such that the slides included the deepest portion in terms of invasive front.

Representative slides were selected for examination and were evaluated according to 8<sup>th</sup> AJCC CAP protocol.[3,4]

Tumour grading was done as per WHO definition based on the degree of differentiation, cellular pleomorphism and mitotic activity as recommended in CAP guidelines.[5]

### Statistical analysis

Statistical analysis was conducted with SPSS version 23.

We used chi square test for the analysis of categorical data in order to identify potential relations between histological features and clinicopathological characteristics of tumour.

Statistical significance was considered for  $p < 0.05$

### Results

Totally 80 cases were evaluated among them 51 were biopsy cases and 29 were radical resection cases.

The maximum number of patients were under the age group of 41-60 years with 38 patients and mean age was 54.8 years (Table-1). There were 65 males and 15 females affected in total(Table-2). The buccal mucosa being the most common site with 34 patients with lesion in buccal mucosa followed by lateral surface of tongue 8 cases being second most common site (Table-3). Clinically 47 of the patients presented within 6 months of onset of symptoms. Majority of them ie. 63 cases presented with exophytic mass, 11 cases with ulcer, 4 with ulcer with leukoerythroplakia and 2 cases with stridor at the time of presentation. (Table- 4).

49 patients presented with grade 2 followed by 30 patients with grade1 and a single case of grade 3. Among the resection specimens the size of tumor was 2-4 cm in majority of the cases ie. 14 cases.. when evaluated under microscope 16 cases had depth of invasion of 6-10 mm , 9 cases with > 10 mm and 4 cases with 1-5 mm. 19 cases showed WPOI of I-III and 10 cases with WPOI IV- V. Lymph node metastasis was seen in 16 cases, lymphovascular invasion in 6 cases and perineural invasion in 8 cases. There were 5 cases in which surgical resected margins were positive for tumor cells( Table-5)

**Table 1: Age distribution**

Age group(years)	No. of patients	Percentage
20-40	11	13.75
<b>41-60</b>	<b>38</b>	<b>47.5</b>
61-80	31	38.75
Ttal	80	
<b>Mean age-54.8</b>		

**Table 2: Gender distribution**

Sex	No. of patients	Percentage
<b>Male</b>	<b>65</b>	<b>81.25</b>
Female	15	18.75
Total	80	

**Table 3: Primary site**

Site	No. of patients	Percentage%
<b>Buccal mucosa</b>	<b>34</b>	<b>42.5</b>
lateral surface of tongue	8	10
vocal cords	5	6.25

lower lip	5	6.25
gingiva/ retromolar area	5	6.25
alveolar mucosa	4	5
pyriform fossa	4	5
dorsal surface of tongue	4	5
Larynx	4	5
Upper lip	3	3.75
Epiglottis	2	2.5
Pharynx	1	1.25
Palate	1	1.25

**Table 4: Clinical characteristics of cases**

Parameters	Number of cases	Percentage
<b>Duration of symptoms</b>		
< 6 months	47	58.75
6-12 months	23	28.75
> 12 months	10	12.5
<b>Clinical presentation</b>		
exophytic mass	63	78.75
Ulcer	11	13.75
ulcer with leukoerythroplakia	4	5
stridor	2	2.5

**Table 5: Histological characteristics of tumours**

<b>Tumour differentiation</b>		
Grade 1	30	37.5
<b>Grade 2</b>	<b>49</b>	<b>61.25</b>
Grade 3	01	1.25
<b>Greatest dimension of specimens of radical resections (n-29)</b>		
2cm or less	5	17.2
<b>2-4cm</b>	<b>14</b>	<b>48.2</b>
>4cm	10	34.4
<b>Depth of invasion</b>		
1-5mm	4	13.79
<b>6-10mm</b>	<b>16</b>	<b>55.17</b>
>10mm	9	31.03
<b>Worst pattern of invasion</b>		
<b>I-III</b>	<b>19</b>	<b>65.51</b>
<b>IV- V</b>	<b>10</b>	<b>34.48</b>
<b>Lymph node metastasis</b>		
<b>Present</b>	<b>16</b>	<b>55.17</b>
Absent	13	44.82
<b>Lymphovascular invasion</b>		
<b>Present</b>	<b>6</b>	<b>20.68</b>
Absent	23	79.31
<b>Perineural invasion</b>		
<b>Present</b>	<b>8</b>	<b>27.58</b>
Absent	21	72.41
<b>Status of surgical resected margin</b>		
Involved	5	17.24
Uninvolved	24	82.75

Correlation between histopathological grade with age, site, duration. chi square test was significant in the correlation of grade and age ( $p < 0.05$ ) Table-6

**Table 6: Correlation between histopathological grade with age, site, duration.**

Parameter	Grade I	Grade II	Grade III	P
<b>Age(years)</b>				
<50	16	11	0	<b>0.015</b>
>50	14	38	1	
<b>Anatomic site</b>				
Buccal mucosa	11	22	1	0.439
Other site	18	28	0	
<b>Duration(months)</b>				
<6	16	38	1	0.382
6-12	10	9	0	
>12	3	3	0	

Correlation between WPOI and DOI with lymphovascular invasion, perineural invasion and lymph node involvement was significant  $p < 0.05$ . as the WPOI and DOI increased there was increase in lymphovascular , perineural and lymph node invasion.(Table -7). There were 9 cases each in stage T2 and T4 , 4 cases in T1 and 7 cases in stage T4(Table-8)

**Table 7: Correlation between WPOI and DOI with lymphovascular invasion, perineural invasion and lymph node involvement**

	Lymphovascular Invasion	Perineural invasion	Lymph node involvement
WPOI I –III(19)	1 (16.67%)	2(25%)	6(37.5%)
WPOI IV –V(10)	<b>5(83.33%)</b>	<b>6(75%)</b>	<b>10(62.5%)</b>
P value	<0.001	<0.001	0.013
<b>DOI</b>			
	Lymphovascular Invasion	Perineural invasion	Lymph node involvement
1-5mm(4)	1	1	2
6-10mm(16)	2	3	4
<b>&gt;10mm(9)</b>	<b>3</b>	<b>4</b>	<b>10</b>
P value	< 0.001	<0.001	<0.001

**Table 8: No. of cases in different stages.**

Stage	No. of cases
T1	4
T2	9
T3	7
T4	9

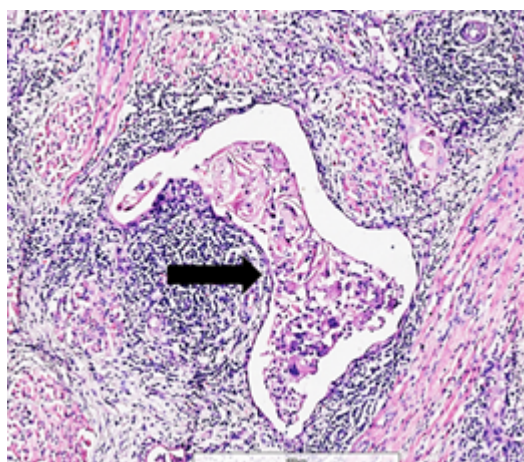


Figure. 1: Lymphovascular invasion(H &E 40x)

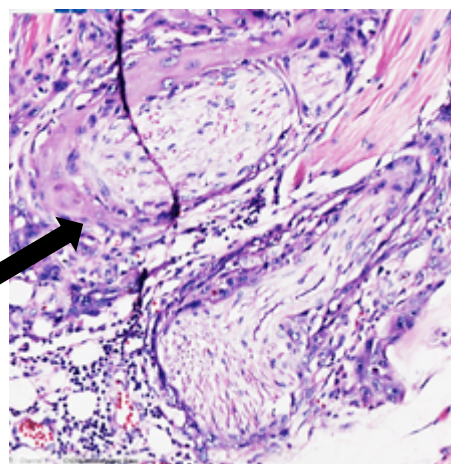


Figure. 2: Perineural invasion(H &E 40x)



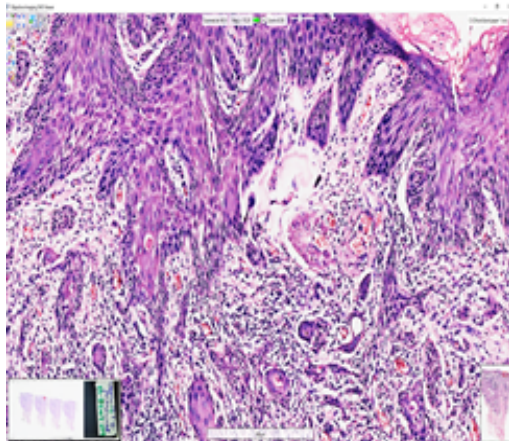


Figure 3: Worst pattern of invasion Type V (H & E 10x)

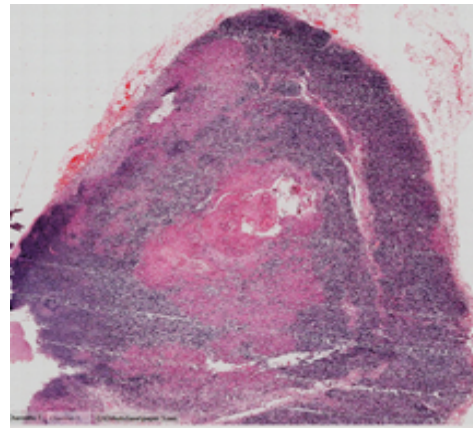


Figure 4: Lymph node metastasis (H&E scanner view)

### Discussion

In our study, we assessed the clinical and histopathological correlations and their prognostic capabilities in HNSCC

The ratio of affected male was higher than female (4.3:1) and most common affected site was buccal mucosa (42.5%) followed by lateral surface of tongue (10%), similar results were seen in study by Dasgupta S et al [6]

Among the clinical presentation seen in our study, most common was exophytic mass (58%). In a study by Pires et al [7] ulcers were the most common (62%) and mandibular alveolus was the common site in a study by Dasgupta S et al [6]

In our study grade 2 (61.25%) tumour were most common followed by grade 1 (37.5%) and least was grade 3 (1.25%). a study by Dasgupta S et al [6] reported grade 1 (64.04%) as the commonest grade, whereas in a study by Effiom OA et al [8] poorly differentiated tumour (grade 3) was most common.

Tumour grade, depth of invasion, worst pattern of invasion IV and V were associated with an aggressive behavior of tumour.

Our study revealed that the WPOI IV and V was strongly related to lymphovascular invasion (83.3%), perineural invasion (75%) and lymph node invasion (62.5%) and with p value <0.001 for lymphovascular and perineural invasion and p=0.013 for lymph node involvement.

Our findings are in accordance with results obtained by Brandwein et al [9] and Mishra et al [10] where they showed that aggressive pattern of invasion (WPOI IV and V) were significantly associated with poorer overall survival and positive lymph nodes, in comparison to non-aggressive one (WPOI I-III)

The aggressive behavior of WPOI IV and V pattern is due to biological mechanisms of malignancy, such as loss of contact inhibition, increased tumor cell

motility and secretion of proteolytic enzymes. [10,11]

Molecular studies on the pattern of invasion have shown that deep invasive tumour fronts have higher expression of Ki-67 and cyclin B1 markers with reduced E-cadherin expression. Thus, having a higher propensity for malignant cells to metastasize. [10,12]

### Conclusion

Our study provides insight on the connections between histological characteristics easily identifiable through standard histopathological assessment and their prognostic potential.

Histopathological features such as the size of the primary tumour, WPOI, DOI and status of surgically resected margin revealed significant correlations with aggressive tumor behaviour like lymphovascular invasion, perineural invasion and lymph node metastasis.

Thus all these histopathological characteristics which affect the prognosis must be considered in the evolution of staging system for HNSCC for accurate diagnosis and adjuvant treatment decisions.

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