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Original Research Article

Oral squamous cell carcinoma: Histological grading and co relationship with cervical metastasis, depth of invasion and perineural invasion

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ABSTRACT

Aim: The aim of the study is to ascertain whether there happens to be any relation between the histological grading (according to Broder's system) of oral squamous cell carcinoma cases and their regional metastasis, depth of invasion and perineural invasion.

Background: Squamous cell carcinoma is known to be the most common malignancy of the oral cavity. Staging and grading of OSCC are established as the main requirements for management, because they influence risk stratification and are one of the first steps towards personalized treatment. Histological grading was introduced for the first time by Broder's for squamous cell carcinomas of lip.

Materials and Methods: This is a retrospective study of 53 patients who were diagnosed as oral squamous cell carcinomas from April 2021 to January 2023. The specimen of the cases were sent to our Department of Pathology, Acharya Shri Chandra college of medical sciences and hospital, Jammu for histopathological examination after resection.

Result: Broder's grading does co relate to the metastasis, depth of invasion and perineural invasion.

Conclusion: There should be more studies at a larger level to ascertain the potential of Breslow grading.

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1. Introduction

Around, 95% of the cancers of the head and neck are known to be squamous cell carcinomas.¹

A WHO report in 1983 stated that, oral cancer is the most common cancer in southeast Asia. Most common traditional risk factors of oral cancers are tobacco and alcohol abuse.² It commonly affects men in the 6th to 8th decades of life and comparatively lesser cases occur in patients younger than 40 years.³ It has a higher incidence in males than females (M:F=1.5:1) mainly because more men as compared to women indulge in habits like tobacco and alcohol abuse.⁴ This carcinoma affects all areas of the oral cavity, but tongue,

floor of the mouth, and lower lip are the most common reported sites.³

The established pre requirements for management are staging and grading of oral squamous cell carcinoma, because they influence risk stratification and personalised treatment.

Broder's first introduced histological grading for squamous cell carcinomas of lip; it was based on differences in degree of differentiation between tumors.⁵ Broder's suggested a system in which a grade I lesion was highly differentiated (its cells were producing much keratin) while grade IV was poorly differentiated (the cells were highly anaplastic and showed almost no keratin formation). Broder's initiated quantitative grading in cancer. His classification is based on proportion of the neoplasm

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resembling normal squamous epithelium and has been used for squamous cell carcinoma for many years altogether.⁶

The metastasis of this carcinoma in cervical lymph nodes has shown to be a major influence on survival in oral cancer in many studies.⁷ It is an ominous prognostic factor in head and neck squamous cell carcinoma (HNSCC). Even if there is only one metastatic lymph node, it takes the patients to an advanced stage disease category and also changes the rate of survival of the patient.⁸

The American Joint Committee on Cancer (AJCC) staging system has taken into account numerous factors for nodal metastasis, including size, laterality, and number of malignant nodes. Recently another important factor has been added i.e the extranodal extension (ENE), also called extracapsular spread.⁹

Next parameter is the Depth of invasion (DOI) which is also called reconstructed tumor thickness and differs from clinical tumor thickness, specifically in exophytic and ulcerated lesions. DOI was originally called as distance from a theoretical reconstructed normal mucosal surface line to the deepest extent of growth of tumor.¹⁰

Many studies have included investigation on tumor thickness and depth of invasion as prognosis predictors.¹¹ However, in the literature, the depth of invasion and tumor thickness are often not very clear. According to the American Joint Committee on Cancer Classification (AJCC) 8th edition, DOI is measured from the level of the basement membrane of the closest adjacent normal mucosa. A vertical line is drawn from this plane to the deepest point of tumor invasion.¹² Therefore, depth of invasion is not the same as tumor thickness and neither of the two are interchangeable.¹³ Tumor thickness could be larger than DOI in exophytic tumors, and lower than DOI in an endophytic/ulcerated growth pattern. Also, tumor thickness is not shown to be a very good predictive factor.¹⁴

For a tumor entity explicitly characterised as neurotrophic, it is not surprising that perineural invasion is commonly observed in oral squamous cell carcinoma. If perineural invasion (PNI) is present, it is now widely accepted as an unfavourable prognostic factor.^{15,16}

Perineural invasion is a tropism of tumor cells for nerve bundles in the surrounding tissues. PNI is a type of metastatic tumor spread which is similar to but at the same time distinct from vascular or lymphatic invasion as it hinders the ability to establish local control of a malignancy because neoplastic cells can travel along nerve tracts far from the primary lesion and are often missed during surgery¹⁷ because of this these tumors have the ability to exhibit pain and persistent growth with a long clinical course and late onset of metastases, such a pattern other has been observed in neurotropic tumor such as prostate cancer, pancreatic cancer, melanoma and salivary gland malignancies such as adenoid cystic carcinoma and polymorphous low grade adenocarcinoma. Among all the

other parameters used, peri neural invasion is widely known as an indicator of aggressive behaviour.¹⁸ PNI is a well-known independent predictor of poor prognosis in carcinoma colon and rectum and salivary gland.¹⁹

2. Materials and Methods

The records of department of Pathology of Acharya Shree Chandra college of medical sciences and hospital were studied retrospectively from November 2020 to February 2023.

A total of 53 cases were found during the time period with age ranging from 27 to 83 years.

All the general information about the case including name, age, date of surgery, surgeon name were registered.

Record of histopathological report of all the 53 cases were studied.

Grading system

Broders system (descriptive system)

Tumors were graded as:

Well- differentiated (Grade 1) = <25% undifferentiated cells

Moderately- differentiated (Grade 2) = <50% undifferentiated cells

Poorly- differentiated (Grade 3) = <75% undifferentiated cells

Anaplastic or pleomorphic (Grade 4) = >75% undifferentiated cells

3. Results

A total of 53 cases were reviewed during the time period between April 2021 to Jan 2023.

All these cases were diagnosed according to the Broders classification.

Out of 53, there were 23 cases of well differentiated squamous cell carcinoma, 26 cases of moderately differentiated squamous cell carcinoma and 4 case of poorly differentiated squamous cell carcinoma.

First, we assessed the relationship between the histological grading and lymph node metastasis.

We found that, out of 23 cases of well differentiated squamous cell carcinoma, 9 had cervical lymph node metastasis; out of 26 moderately differentiated cancers, 14 were found positive for nodal metastasis and out of 4 poorly differentiated cancers 3 had cervical metastasis.

The tabular form of the above data is present below.

The chi square statistic is 2.2227. The p-value is 0.32911. [The result is not significant at $p < .05$]

Secondly, we assessed the relation between histological grading and depth of invasion.

We classified the depth of invasion into 3 categories:

1. Less than or equal to 5mm
2. Equal to 10mm or less than 10mm and more than 5mm
3. More than 10mm(6)

Table 1:

Grading	Lymph node metastasis	
	Positive	Negative
Well Differentiated (23)	9(11.28)[0.46]	14(11.72)[0.44]
Moderately Differentiated (26)	14(12.75) [0.12]	12 (13.25) [0.12]
Poorly Differentiated (04)	3 (1.96) [0.55]	1 (2.04) [0.53]
Column total	26	27

We found that out of that out of the 23 cases of well differentiated cancers, 6(26.1%) had a DOI of less than or equal to 5mm, 10(43.5%) had a DOI of equal to or less than 10mm and 7(30.4%) had a DOI of more than 10mm.

Out of the 26 cases of moderately differentiated oral cancers, 1(3.8%) had a DOI of less than or equal to 5mm, 9(34.6%) had a DOI of equal to or less than 10mm, and 16 (61.6%) had a DOI of more than 10mm.

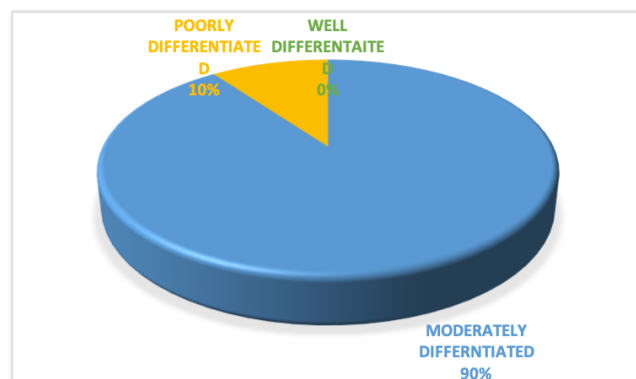
Out of the 4 poorly differentiated cancers, 1 had a DOI of less than or = 5mm; 1 had DOI of more than 5mm and less than or = 10mm, and 2 had a DOI of more than 10mm.

The tabular form of the above given data is present below:

The chi square statistic is 7.231. The p value is .124173. [The result is not significant at $p < .05$].

Lastly, we assessed the relationship between histological grading and perineural invasion.

We found that out of the 53 cases, 10(18.9%) had been diagnosed with perineural invasion. Moreover, we found that 9 cases were moderately differentiated squamous cell carcinomas and 1 case was of poorly differentiated carcinomas.

**Figure 1:**

4. Discussion

Oral cancer is a serious health problem which has caused a great number of mortality and morbidity through the years. In regions of the world where tobacco habits are practiced

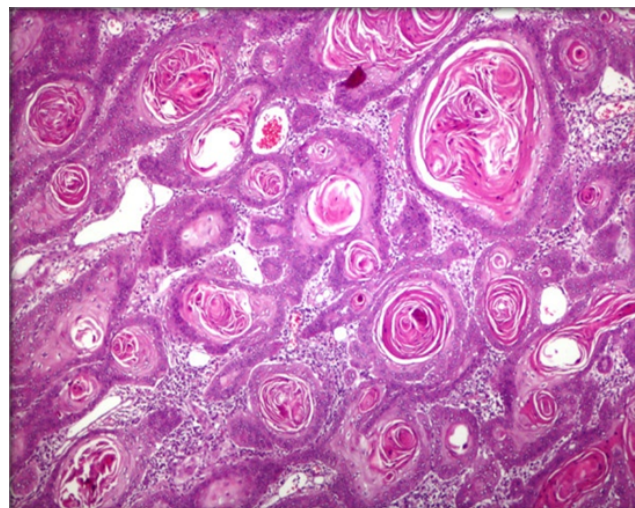
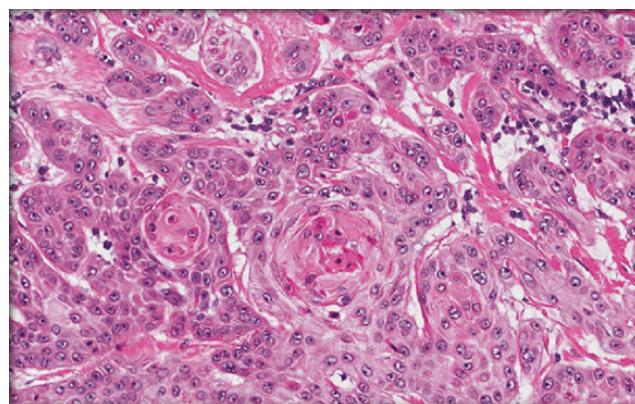
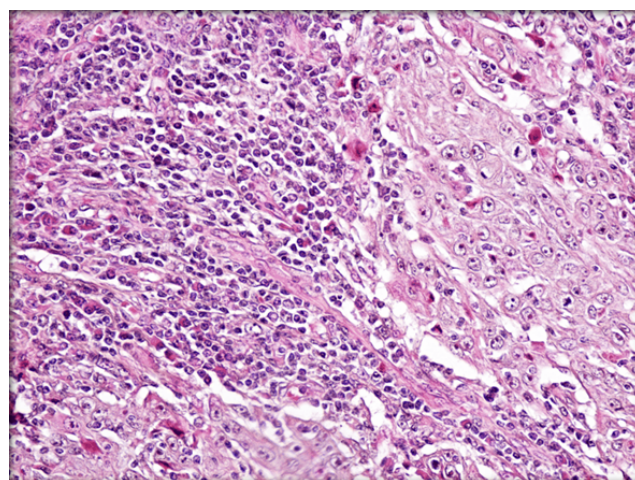
**Figure 2:** Well differentiated squamous cell carcinoma**Figure 3:** Moderately differentiated squamous cell carcinoma**Figure 4:** Poorly differentiated squamous cell carcinoma

Table 2:

Histological Grading	Less than 5mm OR =5mm	Equal to 10mm or less than 10mm and more than 5mm	More than 10mm
Well differentiated(23)	6(3.47) [1.84]	10 (8.68)[0.20]	7 (10.85)[1.37]
Moderately differentiated(26)	1(3.92) [2.18]	(9.81) [0.07]	16 (12.26)[1.14]
Poorly differentiated(01)	1(0.60) [0.26]	1(1.51) [0.17]	2(1.89) [0.01]

in the form of chewing or smoking, OSCC is a major oncological problem.²⁰

In the current times, the diagnosis and even the treatment are based on clinical and histo-pathological characteristics of OSCCC. Since many decades, histologic grading is being used in an attempt to predict the clinical behaviour of OSCC.²¹

In clinical practice, the treatment plan and prognosis of OSCC are mainly based on the tumor node metastasis (TNM) (primary tumor, regional lymph node metastasis, and distant metastasis) staging system. But this TNM system does not provide any information on the clinical behavior of the tumor and its biological characteristics.¹⁶

From the above results, we draw the inference that lymph node metastasis is more prevalent in a higher grade of oral squamous cell carcinomas.

Also, we get to know that higher grades of carcinomas invade more deeply as 16 moderately differentiated cancers invaded deeper than 1cm and only 9 out of 23 well differentiated cancers invaded more than 1cm.

Moreover, we see that perineural invasion is not at all present in well differentiated cancers in our study.

5. Conclusion

We conclude that breslow grading does relate to regional metastasis, DOI and PNI.

There should be more studies at a larger level to ascertain the potential of Breslow grading.

6. Source of Funding

None.

7. Conflict of Interest

None.

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