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Role of Cellular Dissociation Scoring as a Prognostic Factor in Squamous Cell Carcinoma

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ABSTRACT

Squamous cell carcinoma is the most common malignancy encountered in the head and neck region. Traditionally it has been graded into well, moderate and poorly differentiated based on the morphological features. Staging plays an important role in the prognosis and thereby survival. The lymph node status is the most important predictor. In recent years, extensive research is going on cellular dissociation grading (CDG) which is based on cell nest size and tumor budding. We have undertaken this study to evaluate cellular dissociation grading and correlate it with lymph node status so as to consider this CDG as an independent prognostic factor in Squamous cell carcinoma.

KEYWORDS: Cellular Dissociation Grade, Score, Squamous cell carcinoma

INTRODUCTION

The cellular dissociation grade is a novel histopathological grading system based on- (a) tumor size budding (tumor budding) and (b) cell nest size. This system has baffled the traditional grading systems which have been used for grading in organs such as lung, head & neck, cervix & esophagus. [1-5] The presence of lymph node metastasis is one of the most important predictors for survival. In the recent years, there is a need to identify additional criteria to avoid unnecessary lymphadenectomies especially in patients who do not benefit from lymph node excision as a part of the treatment. Several studies were done to evaluate tumor budding, a part of cellular dissociation grading as a prognostic factor in colorectal adenocarcinoma. [6-11] The aim of our present study was to evaluate the Cellular Dissociation Grading (CDG) in Squamous cell carcinoma in head & neck region.

Aim

To evaluate role of tumor budding as an individual prognostic factor in Squamous cell carcinoma.

Objectives

1. Calculate the Cellular Dissociation Grading (CDG) scoring based on tumor budding and cell nest size of the tumor.
2. Co relate Cellular Dissociation Grading (CDG) & grading of Squamous cell carcinoma.
3. Compare Cellular Dissociation Grading (CDG) scoring with Lymph node involvement.

MATERIALS & METHODS

Inclusion criteria

1. All the cases diagnosed as Squamous cell carcinoma during the study period.
2. Excision specimens are only included.
3. Cases having Lymph node status with follow up details.

Exclusion criteria

1. Cases diagnosed outside the limit of the study period.

2. Cases without relevant details and follow up.

3. Necrotised and hemorrhagic samples.

4. Small biopsies were not included.

Method

This retrospective study has been undertaken for a period of 3 years, from January 2021 to January 2024. All the cases as per the inclusion criteria were analysed with respect to clinical details including lymph node status. Consent was taken from the patients which was in the form of written consent. Ethical clearance was taken from the ethical committee of the institute after presenting the research study. The H&E slides were prepared. Tumor budding [Fig. 1] & Cell nest size was identified. Tumor bud is defined as single tumor cells or cluster of typically fewer than five cells that have detached from the main tumor mass; found at the invasive front of tumor. Cell nest is a collection of interconnected cells which can be tumor cells or other types of cells; it is rather a general term for any cluster of cells. Prognostic significance: Tumor bud represents an aggressive form of cancer and is associated with higher risk of nodal involvement, metastasis and poor survival rate, whereas the cell nest only when they are small or single cell clusters of pleomorphic cells; it is a prognostic marker of cancer. Based on these 2 parameters, Cellular Dissociation Grading (CDG) scoring was done in all the cases.

Histological Feature	Classification	Score & Grade
Score & Grade	No tumor budding	1
	1–5 tumor buds/HPF	2
	>5 tumor buds/HPE	3
Cell Nest Size (CNS)	>15 cells per nest	Score 1
	5–15 cells per nest	Score 2
	2–4 cells per nest	Score 3
	single cell invasion	Score 4
Cellular Dissociation Grade (CDG)	SumTB+CNS=2–3	Score 1
	SumTB+CNS=4–5	Score 2
	SumTB+CNS=6-7	Score 3

Table 1: Cellular dissociation grading [4-10]

Cellular Dissociation Grading (CDG) scoring: The high-power field with the highest budding activity was chosen for the evaluation.

Well-differentiated tumors had a sum of 2-3 [Fig. 2], moderately differentiated tumors had a sum of 4-5 [Fig. 3] and poorly differentiated tumors had a sum of 6-7 [Fig. 4].

Lymph nodes were resected as a part of the treatment modality in only 11 cases.

All the results were noted in Excel sheets for evaluation of p-value.

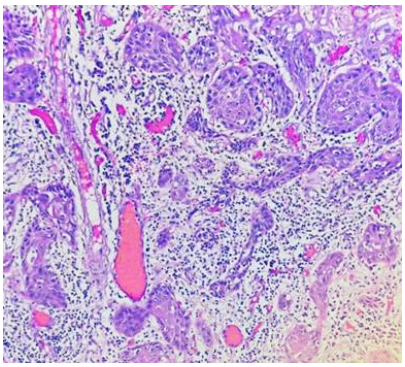

Fig. 1: Tumor buds (Hematoxylin & Eosin: 10X)

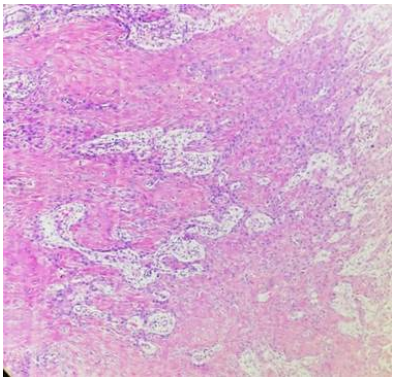

Fig. 2: Cellular Dissociation Grade: Score 1 (Hematoxylin & Eosin 40X)

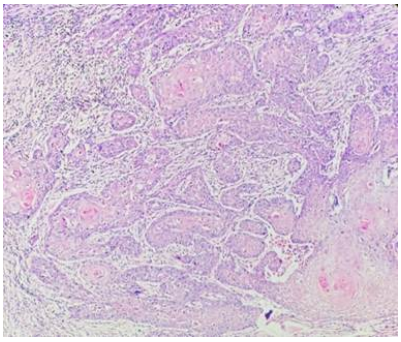

Fig. 3: Cellular Dissociation Grade: Score 2 (Hematoxylin & Eosin 40X)

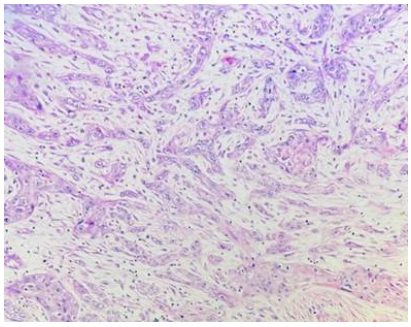

Fig. 4: Cellular Dissociation Grade: Score 3 (Hematoxylin & Eosin 40X)

RESULTS

A total of 32 cases were included in our study.

Age & Sex distribution: Out of 32 cases, 18 were males and remaining were females [Table. 2].

Most of the cases were in the elderly age group, above 60 years with the mean age group of 69.8years [Table. 3].

	Males	Females
No. of cases	18	14
% of cases	56.25%	43.75%

Table 2: Sex distribution

Age distribution	No. of cases	% of cases
< 40	01	3.125%
40–50	01	3.125%
50–60	13	40.625%
60–70	16	50%
70–80	02	6.25%

Table 3: Age distribution

Majority of the tumors were well differentiated ([Table. 4]).

Grading of SCC	No. of cases	% of cases
Well	18	56.25%
Moderate	08	25%
Poorly	06	18.75%

Table 4: Grading of tumors

According to grading of the tumor, the cases are divided into well differentiated, moderately differentiated and poorly differentiated. The Cellular dissociation grading is co related with the grading of the tumor; the well differentiated tumors have a less cellular dissociation score when compared to the poorly differentiated tumors [Table. 5].

S. No	Differentiation	CDG score 1	CDG score 2	CDG score 3
1	Well	18(56.25%)		
2	Moderate	04(12.5%)	04(12.5%)	
3	Poor		02(6.25%)	04(12.5%)

Table 5. Differentiation of tumor v/s Cellular Dissociation Grade score

The p value was significant as shown in [Table. 6].

	Differentiation	Cellular dissociation Grade score
Chi square test	<0.001-0.0021	0.001-0.0041
Univariate analysis	<0.001-0.006	0.001-0.0009

Table 6: p value comparing differentiation with cellular dissociation Grade score

During the Staging of the tumors, we have compared the cellular dissociation score with staging of the tumor [Table. 7]. Well differentiated tumors are usually Stage I, most of the moderately differentiated tumors were Stage II and almost all the poorly differentiated tumors were Stage III. The p value was 0.08; the p value was not significant.

S. No	Stage	Stage I	Stage II	Stage III
1	Well	16		
2	Moderate		2	6
3	Poor		1	5

Table 7: Staging of the tumor v/s Cellular Dissociation Grade score

All the cases were compared in respect to the Age, Grade and Cellular dissociation grading [Table. 8].

As seen in the table, well differentiated cases had a lesser cellular dissociation grade and belonged to age group less than 50-60 years whereas poorly differentiated tumors were of age group more than 60 with higher cellular dissociation score. The p value was 0.009 and was insignificant.

S. No	Age	No. of Cases	Grade	CDG Score Details
1	<40	1	Well	Score 1
2	40–50	1	Well	Score 1
3	50–60	12	Well – 8	Score 1
			Moderate – 4	2 cases – Score 1
				2 cases – Score 2
			Well – 7	Score 1
4	60–70	16	Moderate – 5	3 cases – Score 1
				2 cases – Score 2
			Poor – 4	2 cases – Score 2
				2 cases – Score 3
5	70–80	2	Poor	Score 3

Table 8: Age versus Grade of the tumor and Cellular Dissociation Grade score

Only 11 cases had undergone lymph node resection. These cases were scored according to the CDG as follows [Table. 9].

CDG	Nx	N1
Score 1	1(9%)	
Score 2	2(18%)	3(27.5%)
Score 3		5(45.5%)

Table 9: CDG scoring versus Lymph node status

The lymph node status were compared with the CDG scoring, Tumor budding & cell nest size. Statistical analysis was done and tabulated as follows [Table. 10].

Analysis Method	CDG	TB	CNS
Chi square test	<0.001-0.023	0.001-0.0047	0.004-0.019
Univariate analysis	<0.001-0.009	0.001-0.0011	0.006-0.022

Table 10: Comparison with lymph node status

P value was significant

DISCUSSION

The cellular dissociation grading which takes into consideration the tumor budding and cell nest size has shown to surpass the conventional grading system. [12] In our study we have taken these Two entities i.e. tumor budding and cell nest size were evaluated for the cellular dissociation score was compared with the differentiation or grading of the tumor.. The score is more in poorly differentiated squamous cell carcinoma, and it is less in well differentiated squamous cell carcinoma. These findings corelated with studies done by Derani *et al*. [12]. All the cases were then compared all the cases with the Staging of the tumor, though most of the well differentiated tumors were of Stage I and the poorly differentiated tumors were Stage III, the p value was not significant. The age of the patients, cellular dissociation score and finally the Staging were all compared. The poorly differentiated tumors which had a greater score belonged to age group above 68 years, but the p value was not significant. This p value was not significant probably due to smaller size of the study. Lymph nodes which were resected in the 11 cases were evaluated and compared to the CDG score. The chi square analysis was done, and the p value was found to be significant. Similar findings were also seen in the study done by Boxberg *et al*. [1], Jesinghaus *et al*. [4] and Derani *et al*. [12]. Staging strategies which may be noninvasive (clinical examination, imaging) or surgical (sentinel lymph node biopsy, staging lymphadenectomy), have a number of limitations like more number of false-negative findings and/or high morbidity rates [13]. In cases of tumor tissue after neoadjuvant chemotherapy, there is a prognostic role for cellular dissociation score as observed in various studies [4, 5]. In our study cellular dissociation score correlates with lymph node status as the p value was significant. Thus, lymph node status also can be taken as an independent prognostic factor apart from cellular dissociation grading.

CONCLUSION

In conclusion cellular dissociation grading had proved to be superior to the traditional grading system in predicting high risk features of the lesion. Cellular dissociation grading has been calculated by taking the cell nest size and tumor budding into consideration. All the well differentiated tumors have less score whereas poorly differentiated tumors have high score, thus this new scoring system can be taken as an independent prognostic factor in Squamous cell carcinoma.

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