

Correlation Between Current Histopathological Grading and Clinical Features of Mucoepidermoid Carcinoma of the Salivary Glands

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Abstract: Mucoepidermoid carcinoma (MEC) is a salivary malignancy with a widely diverse biologic behavior. Mucoepidermoid tumors are the one malignancy in which histologic grading and clinical behavior characteristics correlate. It is the most common among the different types of salivary gland cancer. Usually, these cancers are low-grade in nature but can realize into intermediate or high grade. The biological outcome of such cancer cases can be predicted using clinical and histological grading. The aim of the present study was to observe and evaluate the correlation between histopathological grading and clinical features of mucoepidermoid carcinoma of salivary glands, to determine whether an accurate diagnosis can be made based primarily on clinical findings. This observational descriptive cross-sectional multi-center study was conducted at the Department of Oral and Maxillofacial Surgery, Dhaka Dental College Hospital, Dhaka, Department of Otolaryngology & Head Neck Surgery, Dhaka Medical College Hospital, Dhaka, and Department of Otolaryngology-Head Neck Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The study duration was 1.5 years, from July 2011 to December 2012. A total of 20 patients attending the study centers with diagnosed case of mucoepidermoid carcinoma of salivary glands was selected for the study following inclusion and exclusion criteria. 40% of the participants were from the age group of 31-40 years, while another 30% were under the age of 21 years. 70% of the participants were female. Histological grading of the participants revealed 8 low-grade, 8 intermediate grade, and 4 high-grade MEC tumor cases. High-grade tumor MEC had an association with increasing age and male gender. The swelling was a common clinical feature among all the participants, whereas ulceration was observed in 75% of high-grade tumor patients. In mucoepidermoid carcinoma (MEC) of the salivary glands, it was suggested that the histopathological grade of MEC evaluated by Brandwein point-based histological grading schema significantly correlated with age, gender, and clinical features. These results suggest and emphasize that histological grading of MEC, as well as clinical features, should be considered when planning surgery for the MEC and the necessity of treatment outcome.

Keywords: Histological, Tumor, Carcinoma, MEC, Mucoepidermoid

1. Introduction

Mucoepidermoid carcinoma accounts for less than 10% of

all tumors of the salivary gland, it constitutes approximately 30% of all malignant tumors in the salivary gland. About half the cases occur in the major salivary glands, more than 80%

of these occur in the parotid, 8–13% occur in the submandibular gland, and 2–4% involve the sublingual gland. In the minor salivary glands, MEC most commonly arises on the palate, but a significant number may also be found in the retromolar area, the floor of the mouth, buccal mucosa, lip, and tongue [1]. Central osseous origin of this is exceedingly rare, representing only about 2%–4% of all MEC. It is the most common malignant salivary gland tumor to arise in children and adolescents under 20 years of age. The prevalence of mucoepidermoid carcinomas is noted to be highest in the third through fifth decades of life, and there is an equal gender representation has been noted. The annual incidence is 0.44 cases Per 100,000 persons [2]. In the major salivary glands, MEC usually presents as a solitary, firm, and painless lesion. Sublingual gland lesions may demonstrate pain in spite of their small size. Superficial intraoral neoplasms may exhibit a blue-red color and mimic a mucocele or vascular lesion. The mucosa overlying palatal tumors can be papillary. Cortical bone is sometimes superficially eroded. Similar to other malignant neoplasms, over 50% of patients with this carcinoma have had awareness of the tumor for less than 6 months. Two-thirds of individuals are asymptomatic. Some patients report rapid growth of the mass; others experience pain, bleeding, dysphagia, trismus, and facial paralysis. The clinical features of each can differ greatly and are important in the final determination of grading. Low-grade tumors are characteristically less than 3.0 cm in size and grow very slowly. Patients frequently become aware of their presence for about 3 to 6 years. Most tumors don't become ulcerated or only become ulcerated after many years, prompting the patient to seek treatment. The three most popular grading systems are the AFIP grading system, the modified Healey system, and the Brandwein system [3]. All categories assess a similar set of parameters, both cytomorphologic and architectural, and may also include perineural and angio-lymphatic invasion. Brandwein in their study, [1] proposed a grading schema with characteristic features' (cell component, cellular composition an intra-cystic component of <25%) and defining features' (necrosis, perineural spread, vascular invasion, bony invasion, mitoses). They believe that the defining features are those that dictate the grade of these tumors. Grade 1 tumors (low-grade) lack the defining features of Grade 3 (high-grade) tumors (necrosis, perineural spread, vascular invasion, bony invasion, >4 mitoses/10 HPF (X400), high-grade nuclear pleomorphism). Low-grade tumors have a score of 0; Intermediate grades have 2-3 points, and high grades have 4 or more points. However, the Brandwein system is generally easier to use and more reproducible, which would facilitate standardization and permit more accurate comparative analysis. Most of the studies on mucoepidermoid carcinoma of salivary glands are about the western population. Although MECs are not uncommon in this country, the actual data has yet not been established. The purpose of this study is to evaluate the correlation between histologic grading and clinical presentations of MEC, so it might shed some more

light on the topic and enrich our knowledge.

To evaluate the correlation between histopathological grading and clinical features of mucoepidermoid carcinoma of salivary glands.

2. Methods

This observational descriptive cross-sectional multi-center study was conducted at the Department of Oral and Maxillofacial Surgery, Dhaka Dental College Hospital, Dhaka, Department of Otolaryngology & Head Neck Surgery, Dhaka Medical College Hospital, Dhaka, and Department of Otolaryngology-Head Neck Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The study duration was 1.5 years, from July 2011 to December 2012. A total of 20 patients attending the study centers with diagnosed case of mucoepidermoid carcinoma of salivary glands was selected for the study following inclusion and exclusion criteria. General information including the patient's name, age, sex, and address was recorded in a performed questionnaire. Informed written consent was obtained from all the participants, and ethical approval was also obtained from the respective study hospitals. Clinical parameters including patients' age, gender, symptoms, tumor site, size, and duration were recorded. A histopathological examination was performed according to the protocol published by the Brandwein system [1]. This algorithm is recommended as the current standard because of its enhanced predictability and proven reproducibility with characteristic features. The grading schema assigned points to various histologic features, including the pattern of infiltration, vascular invasion, and bony invasion. Low-grade tumors have a score of 0; Intermediate grade, 2-3 points; and high grade, >4 points. Data was collected using a pre-made questionnaire and analyzed using SPSS v16 software. Descriptive statistics were generated to see the distribution of baseline characteristics of the patient. A two-sided $p < 0.05$ level of significance was selected for all analyses.

2.1. Inclusion Criteria

- 1) Patients histologically diagnosed with mucoepidermoid carcinoma of salivary gland neoplasm.
- 2) Patients who had given consent to participate in the study.

2.2. Exclusion Criteria

- 1) Have not given consent to be included in the study.
- 2) Lesion histological diagnosed as mucoepidermoid carcinoma of salivary gland neoplasm with suspicion.
- 3) Salivary gland swelling which are diagnosed with other neoplastic diseases and non-neoplastic lesion confirmed by histopathology.
- 4) Psychotic or handicraft patients having mucoepidermoid carcinoma of salivary gland neoplasm.
- 5) Exclude those affected with other chronic diseases etc.

3. Results

Table 1. Age distribution of the participants [N=20].

Age in group	Frequency	Percent
<21 years	6	30
21-30	3	15
31-40	8	40
41-50	2	10
51-60	1	5
Total	20	100

The table shows that 40% of the participants were from the age group of 31-40 years, while another 30% were under the age of 21 years. The mean age of the participants was 30.9 ± 11.42 years.

Table 2. Gender Distribution of the participants [N=20].

Gender	Frequency	Percent
Male	6	30
Female	14	70

Among the total 20 participants, female predominance was observed, as 70% of the participants were female and only 30% were male.

Table 3. Distribution of the participants by histological grading [N=20].

Histological Grading	Frequency	Percent
MEC low grade	8	40
MEC Intermediate grade	8	40
MEC high grade	4	20

According to the histological grading of the participants, 8 (40.0%) were diagnosed with MEC low grade, another 8 (40.0%) were diagnosed with MEC intermediate grade, and 4 were with MEC high grade.

Table 4. Distribution of the respondents by age in relation to histological grading [N=20].

Age in group	MEC low-grade n (%)	MEC intermediate grade n (%)	MEC high-grade n (%)	Total
<21 years	4 (20%)	2 (10%)	0	6 (30%)
21-30	1 (5%)	2 (10%)	0	3 (15%)
31-40	2 (10%)	4 (20%)	2 (10%)	8 (40%)
41-50	1 (5%)	0	1 (5%)	2 (10%)
51-60	0	0	1 (5%)	1 (5%)
Total	8 (40%)	8 (40%)	4 (20%)	100%

Observing the distribution of respondents by age and their histological grading, it was observed that all the MEC high-grade patients were over 30 years of age, while MEC low and intermediate-grade patients generally belonged to younger age groups.

Table 5. Distribution of the respondents by gender in relation to histological grading [N=20].

Sex	MEC Low grade n (%)	MEC Intermediate grade n (%)	MEC High grade n (%)	Total n (%)
Female	6 (42.9%)	7 (50.0%)	1 (7.1%)	14 (100.0%)
Male	2 (33.3%)	1 (16.7%)	3 (50.0%)	6 (100.0%)
Total	8 (40.0%)	8 (40.0%)	4 (20.0%)	20 (100%)

It was observed that MEC low and intermediate grades were more prevalent among the female population, whereas half the male population belonged to MEC high-grade group.

Table 6. Distribution of participants by the duration of symptoms (in months) in histological grading of MEC [N=20].

Grading	n	Mean	SD	Minimum	Maximum
MEC Low grade	8	17.25	7.47854	6	24
MEC Intermediate grade	8	23.375	13.98915	5	48
MEC High grade	4	21.25	33.84647	3	72

The table shows the mean duration of tumor symptoms among the patients of different tumor grades in months. It was observed that tumor symptoms were longer among intermediate grade in comparison to other varieties and shortest among low MEC grade patients. The overall mean duration was 20.5 ± 16.78 months.

Table 7. Distribution of participants by the clinical presentation of patients in relation to histological grading [N=20].

Clinical feature	Low-grade tumor		Intermediate grade		High-grade tumor	
	n	%	n	%	n	%
Swelling	8	100	7	87.5	4	100
Pain	0	0	1	12.5	2	50
Ulceration	0	0	0	0	3	75
Trismus	1	12.5	0	0	0	0
Discharge	0	0	1	12.5	0	0
Epistaxis	0	0	0	0	1	25
Total	8	100	8	100	4	100

Table 8. Distribution of participants by histological features (according to Brandwein's point based on defining histological features).

Parameter	Histological grading					
	Low-grade tumor		Intermediate grade		High-grade tumor	
	n	%	n	%	n	%
Intra-cystic component <25 %=2pts	0	0	0	0	4	100
Tumor invades in small nests and islands= 2pts	0	0	3	38	3	75
Pronounced nuclear atypia =2pts	0	0	3	38	3	75
Lymphatic and/or vascular invasion= 3pts	0	0	2	25	1	25
Bony invasion=3pts	0	0	0	0	0	0
>4 mitoses per 10 HPF=3pts	0	0	0	0	1	25
Perineural spread =3pts	0	0	1	12.5	1	25
Necrosis=3pts	0	0	0	0	2	50
Total Point						

Most of the low-grade tumor patients had swelling as the primary symptom, while Trismus was present in one patient as well. Some patients presented with multiple complications. Swelling and pain were also observed among the intermediate group patient, while all 100% of high-grade tumor patients had swelling, 50% had pain and 75% had ulceration. Ulceration was unique to high-grade tumor patients.

According to Brandwein's point-based histological defining features, each feature was given a specific point, and it was observed that the total of low-grade tumor patients' score was 0, for intermediate-grade patients it was 10, while for high-grade tumor patients it was 15. Low-grade tumors did not present any defining histological features, intermediate-grade tumors revealed no bony invasions and necrosis but high-grade tumors had all the defining features.

4. Discussion

In this study, 20 cases of mucoepidermoid carcinoma of salivary glands were clinically and histopathologically evaluated. This was conducted to find out the relation between clinical features and histopathological grading of mucoepidermoid carcinoma of salivary glands. All tumors were graded histopathologically based on the criteria Brandwein point-based histological grading schema, and the findings were as follows: low-grade (n=8), intermediate-grade (n=8), and high-grade tumors (n=4). The results obtained in this series are more or less in general agreement with similar reports in the literature [5, 6]. The greatest number of cases in the present series were equally distributed between the age group of <21 (30%) and 31-40years (30%). In this series out of 20 cases, 14 (70%) were female individuals and the remaining 6 (30%) were male. Female predominance observed in our study was similar to the

findings of a few other global studies [7, 8], but the difference was not as prominent among such studies. High-grade MEC was associated with patients older than 31 years, while younger-aged populations had low-grade or intermediate-grade MEC. This was similar to a large-scale study in 2014 [9]. Association of high grade of MEC tumor was also observed among the male population. Most of the study subjects who were affected by high-grade tumors complained about swelling, pain, ulceration, and epistaxis. However, trismus was only reported in low-grade tumors in the submandibular gland. Discharge was only associated with intermediate-grade tumors. In this study all grading of mucoepidermoid carcinoma of salivary glands, none of the patients have any facial nerve paralysis. The present study demonstrated that the average point value in low-grade tumors was 0 without any defining features, and the average point in high-grade tumors was >4, associated with defining features including lymphatic involvement, bony invasion, necrosis, etc. One clear deficiency in all systems, particularly point-based systems, is the difficulty in application. Grading under these systems is a cumbersome and time-consuming activity, and many of the criteria are not at all well-defined. Based on personal experience, if asked, most histopathologists tend not to use a formal system because of the time commitment and lack of 'user-friendliness.' Recently, reviews of the pathology literature have established the consensus that the Brandwein grading scheme is the best classification system available given its reproducibility and predictability [10-12]. In this present study, we observed that some low-grade tumors placed in the intermediate grade were associated with their defining features by the Brandwein grading system but those were seen and reported by the AFIP system as low-grade tumors. Cytological and histological diagnosis of low MEC remains challenging due to overlapping cytomorphologic features seen in other salivary

gland lesions. However, in the hands of experienced histopathologists ensuring proper sampling and specimen handling, the diagnosis of MECs is possible [13, 14]. The findings of the current study showed that a meticulous, uniform, reproducible, histopathologic grading systems are of great importance for better management of mucoepidermoid carcinoma of salivary glands in our country.

Limitations of the Study: The study was conducted with a small sample size. So, the results may not represent the whole community.

5. Conclusion

The study showed an apparent correlation between histologic grading and clinical findings of mucoepidermoid carcinoma of salivary glands. These results suggest that histological grade of malignancy as well as clinical features, should be considered when accurate and early diagnosis, treatment plan with prediction of prognosis of the diseases.

Conflict of Interest

The authors declare that they have no competing interests.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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