Study on Correlation between Brandwein Points Based Histological Grading and Clinical Features of Mucoepidermoid Carcinoma of Salivary Glands

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Abstract

Background: Mucoepidermoid Carcinoma (MEC) is the one malignancy in which histologic grading correlate with clinical behavior. The findings of the current study revealed that meticulous, uniform histopathologic grading is of importance of MEC of salivary glands. The aim of our study is to evaluate correlation between histopatholological grading with clinical features of mucoepidermoid carcinoma of salivary glands.

Materials and methods: This cross sectional study was conducted in patient attending tertiary level hospital in Dhaka, Bangladesh. A total 20 patients of histopathological grading of the mucoepidermoid carcinoma of salivary glands were undertaken using the currently established Brandwein point based histological grading systemand also evaluated the clinical features of the patients according to age sex and location. The data obtained were recorded and statistically analyzed.

Results: Twenty patients with mucoepidermoid carcinoma of salivary glands clinically and histopathologically evaluated. All tumors were graded histopathologically based on the criteria Brandweinpoint based histological grading system that among the 20 respondents 8 (40.0%) were diagnosed as MEC low grade, intermediate MEC 8 (40.0%), 4 (20.0%) were found as MEC high grade. Low grade tumors were not present any defining histlgical feature, intermedtate grade tumors revealed no bony invasion and necrosis but high grade tumors got all defining features.

Conclusion: Histological grading of MEC mucoepidermoid carcinoma of salivary glands which is apparently correlate with clinical findings found in our study.

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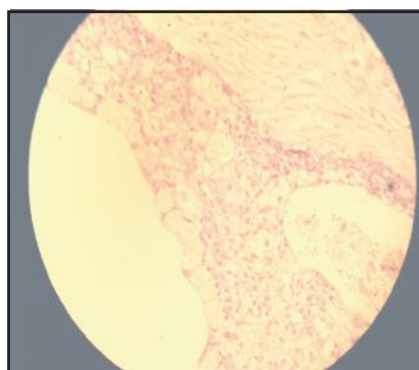
Image 1 Photomicrograph of of mucoepidermoid carcinoma, low-grade demonstrating the well-formed gland, macro cysts (H&E, x40)
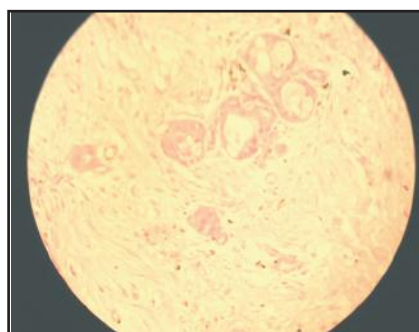

Image 2 Photomicrograph of of mucoepidermoid carcinoma, intermediate grade showing tumor invades in small tumor nests and islands (H&E, x40)
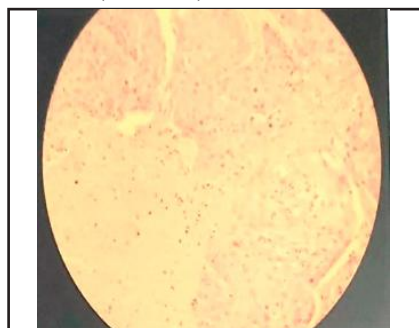

Image 3 Photomicrograph of mucoepidermoid carcinoma, high grade with no cystic spaces and a highly infiltrative growth pattern, showing anaplasia or pronounced nuclear atypia and area of necrosis (H&E, x 40)

Photograph 1 Intermediate grade mucoepidermoid carcinoma of parotid gland measuring about 3x 2cm, regular & cystic in nature

Photograph 2 Low grade mucoepidermoid carcinoma of parotid gland measuring about 3x 2.5cm, regular & firm in nature
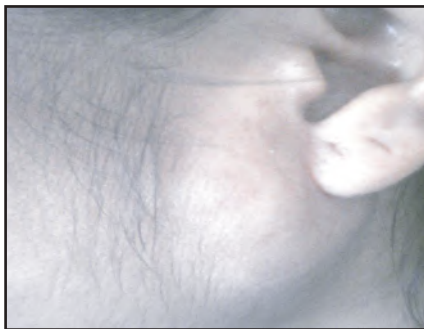
Photograph 3 Low grade mucoepidermoid carcinoma of parotid gland measuring about 3x 2.5cm, regular & firm in nature

Photograph 4 Photograph showing high grade mucoepidermoid carcinoma of palate, an irregular ulcerated growth in anterior palatal area measuring about 6x 4c

Introduction

Mucoepidermoid carcinoma accounts for less than 10% of all tumors of the salivary gland; it constitutes approximately 30% of all malignant tumors the salivary gland.About half the cases occur in the major salivary glands, more than 80% of these occur in the parotid, 8–13% occurs in the submandibular gland and 2–4% involves 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, floor of the mouth, buccal mucosa, lip, and tongue.[1,2] Central osseous origin of this exceeding rare, central osseous origin of this exceeding rare, representing only about 2%-4% of all MEC.[3] It is the most common malignant salivary gland tumor to arise in children and adolescents <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.[4] The clinical features of each differ and are important in the final determination of grading. Low grade tumors are characteristically less than 3.0 cm and grow very slowly. Many tumors will appear bluish because their well–differentiated character creates mucin-filled spaces that they appear blue through the mucosal cover. Most will not invade bone until late in their course. Intermediate and high grade mucoepidermoid carcinomas are faster growing, more diffuse, and ulcerate early. Many are obviously destructive to underlying bone and some are painful. They will present as solid mass with a normal color of the overlying epithelium or with an ulcerated surface.[5] Facial paralysis is also present.

Histologically, MEC is comprised of 3 different cell types: mucinous cells, intermediate cells and epidermoid cells.

Traditionally, MECs were histologically classified into low-, intermediate-, and high-grade based on the relative proportion of cell types. The MEC are usually graded as low grade/well differentiated (Tumor exhibiting greater than 50% of mucous elements) intermediate grade (10–50% of mucous elements and high grade (Less than 10% of mucous elements).[6,7] The three most popular grading systems are: The AFIP grading system, modified Healey system and the Brandwein

system. All categories assess a similar set of parameters, both cytomorphologic and architectural and may also include perineural and angio-lymphatic invasion. Brandwein et al 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).[1] 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 grade, 2-3 points; and high grade,4 0r more point.

However, the Brandwein system was easier to use and more reproducible, which would facilitate standardization and permit more accurate comparative analysis. The aim of our study is to evaluate correlation between histopatholological grading with clinical features of mucoepidermoid carcinoma of salivary glands.

Materials and methods

This descriptive observational cross-sectional study was carried out in 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 and Dhaka. During the period of from July 2011 to December 2012 patients who attended the Indoor of the department. The samples were collected by convenient sampling. Patients attending with diagnosed case of mucoepidermoid carcinoma of salivary glands irrespective of age and sex were selected for the study. After getting consent general information including patient's name, age, sex, and address was recorded in a preformed questionnaire. Clinical parameters investigated included patients age, gender, symptoms, tumors site, size and duration. Histopathological examination has performed according to protocol published by Brandwein system, with characteristic features' (Cell component, cellular composition an intra-cystic component of <25%) and defining features' (Necrosis, perineural spread, vascular invasion,

bony invasion, mitoses). 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, high grade nuclear pleomorphism). Their grading schema assigned points to various histologic features, including 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. Stained with H & E slide and reported. All relevant data were noted and recorded on pre tested data sheet. Data sheet included all of the variables regarding to the study. Data were analysed by using of SPSS16 software. Data will be presented in tabular and graphical form Demographic and baseline characteristics were compared with the use of chi-square test for categorical variables and analysis of variance acceptance test for continuous variables. One way ANOVA was used for multiple groups comparisons. Descriptive statistics were generated to see the distribution of baseline characteristics of the patient. Qualitative variables were expressed as mean and standard deviation.A two-sided $p<0.05$ level of significance was selected for all analysis.

Permission for the study was taken from the concerned departments and appropriate authorities.

An informed written consent will be taken for every patient explaining the nature and objectives of the study.

Results

All the cases were evaluated according to protocol published by Brandwein point based histological grading schema.

The findings obtained from data analysis are presented here. During the study period 20 patients were diagnosed to have mucoepidermoid carcinoma and included in the study. Baseline demographic, clinical characteristics and histopathological grading of these patients are summarized below.

Table I Distribution of the respondents by Age

Age in group	Frequency	Percent (%)
<21 years	6	30.0
21-30	3	15.0
31-40	8	40.0
41-50	2	10.0
51-60	1	5.0
Total	20	100

Table I shows among the study subjects maximum from the age group of 31-40 years with mean age 30.9 ± 11.42, Min-11years and Max-55 years.
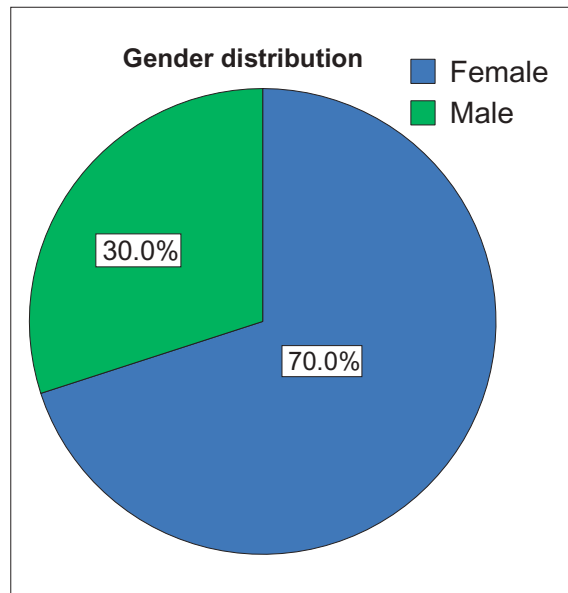

Figure 1 Gender distributions of the subject

Figgure 1 Pie diagram shows among the study subjects female is predominant with 14 female (70%) and 6 male (30%).
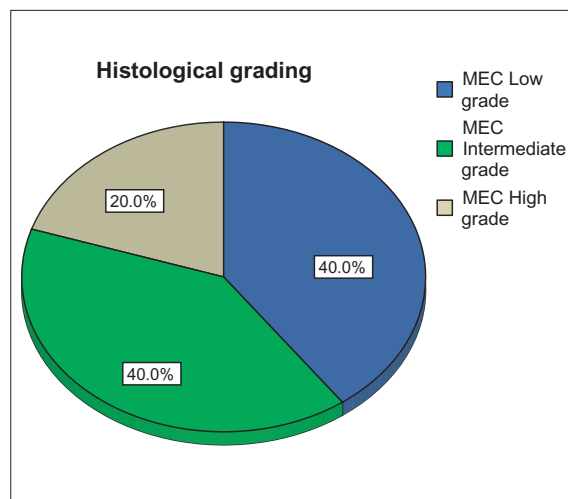

Figure 2 Frequency of histological grading

Figure 2 pie diagram shows that among the 20 respondents 8 (40.0%) were diagnosed as MEC low grade, intermediate MEC 8 (40.0%), 4 (20.0%) were found as MEC high grade.

Table II Clinical presentation of patients in relation to histological grading

Clinical feature	Low grade tumor		Intermediate grade		High grade tumor	
	n	%	n	%	n	%
Swelling	8	42.1	7	36.8	4	21.1
Pain	0	.0	1	33.3	2	67.7
Ulceration	0	.0	0	33.3	3	100.0
Facial nerve paralysis	0	.0	0	.0	.0	.0
Trismus	01	100.0	0	0	0	0
Discharge	0	6.7	1	100.0	0	0
Epistaxis	0	6.7	0	0	1	100.0

Table II shows the nature of complaints of the study patients. 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. Discharge were only associated with intermediate grade tumors.

Table III Histological features in relation to defining histological features (According to Brandwein point based grading system)

Parameter	Low grade tumor n	%	Histological grading Intermediate grade Tumor n	%	High grade tumor n	%
Intra-cystic component <25 %=2 pts	0	.0	0	.0	4	100.0
Tumor invades in small nests and islands = 2 pts	0	.0	3	38.0	3	75.0
Pronounced nuclear atypia = 2 pts	0	.0	3	38.0	3	75.0
Lymphatic and/or vascular invasion = 3 pts	0	.0	2	25.0	1	25.0
Bony invasion = 3 pts	0	.0	0	0.0	0	.0
>4 mitoses per 10 HPF = 3 pts	0	.0		.0	1	25.0
Perineural spread = 3 pts	0	.0	1	12.50	1	25.0
Necrosis = 3 pts	0	.0	0	.0	2	50.0

Table III analyses the presence of defining histological feature of three types MEC. Low grade tumors were not present any defining histolgical feature, intermedtate grade tumors revealed no bony invasion and necrosis but high grade tumors got all defining features.

Discussion

In these study 20 cases of mucoepidermoid carcinoma of salivary glands clinically and histopathologically evaluated. This was conducted to find out corelation between clinical features and histopathological grading of mucoepidermoid carcinoma of salivary glands. All tumors were graded by histopathologically based on the criteria Brandwein point based histological grading system. In this study low-grade (n=8), intermediate-grade (n=8) and high grade tumors (n=4) were found.

The findings in the present study were observed that all of the cases of MEC intermediate and high grade of salivary glands presented with a swelling. All of parotid tumors, palatal and submandibular gland except maxilla tumors presented with swelling. Pain and ulceration is second most presentation.Most of the study subjects who were affected by high grade tumors complained about swelling, pain, ulceration and epistaxis. No facial nerve paralysis was found.

In this present study identified that average point value in low grade tumors 0 without any defining features, and average points in high grade tumors >4 associated with defining features included lymphatic involvement, bony invasion, necrosis etc. Intermediate grade shows prominent intermediate cell population, periglandular lymph nodal infiltration got points scores 3 consistent point based Brandwein grading system. In this study one of the high grade tumors in submandibular gland, a focal area of necrosis and hyalinization were seen by histopathologically.

One clear deficiency in all systems, particularly the point based schemes, the difficulty in application. Grading under these systems is aninconvenient and time consuming activity, and many of the criteria are not at all well-defined. In fact, 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.[8,9] In this present study we observed that some low grade tumors placed in intermediate grade associated with their defining features by the Brandwein grading system but those was seen and reported by 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.[10] So we need good number of well experienced and knowledgeable histopathologist in Bangladesh for interpretation and correct diagnosis of MEC.

The findings of the current study showed that a meticulous, uniform, reproducible, histopathologic grading system are great importance for better management of mucoepidermoid carcinoma of salivary glands in our country. In this present series it was found that point based Brandwein grading system to be a good guide to diagnosis mucoepidermoid carcinoma of salivary glands which is apparently correlate with clinical findings of mucoepidermoid carcinoma of salivary glands. Large multi-institutional and broad spectrum prospective study of mucoepidermoid carcinoma of salivary glands has taken in to this study a new horizon and dimension.

Limitation

The present study suffers the following limitation:
● This is a small scale hospital based study in a low resourceful which may not be representative of the whole population
● Small scale, small sample size
● Limited duration study
● Short the length of follow-up.

Conclusion

An apparent correlation was found 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.

Recommendation

● For better management a more detail and longer duration of study with a large population is needed. Large scale community based study is needed for better yields.
● Appropriate sampling and methods of investigation needed involving comprehensive and homogenous data.

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