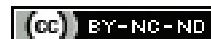


Epidemiology of Mucoepidermoid Carcinoma of Minor Salivary Glands: A Single-Institution Experience in Mumbai, Maharashtra over 20 Years

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ABSTRACT

Introduction: Encountering a soft tissue swelling in the oral cavity during routine dental practice is infrequent yet practical. Salivary gland tumours of the oral mucosa are associated with minor salivary glands, although they are uncommon and can be considered as a differential diagnosis. Mucoepidermoid Carcinoma (MEC) constitutes a significant percentage of salivary gland tumours of minor salivary glands and exhibits varied biological behaviour.

Aim: The aim of the present study was to investigate the clinical and histological characteristics of MEC of the minor salivary glands to comprehend the epidemiological pattern of these tumours and compare the findings with those of other studies.

Materials and Methods: For this cross-sectional study, data on salivary gland tumours were accessed from the Department of Oral Pathology and Microbiology, Government Dental College and Hospital, Mumbai, archives spanning from 2003 to 2022 (a 20-year period). Out of the 22 reported cases of salivary gland tumours, 12 cases were identified as MEC. Clinical details and slides of these MEC cases were obtained from the departmental

archives and graded according to Brandwein MS grading. The patients' clinical features were described through descriptive analysis using SPSS software.

Results: Based on gender distribution, there were 8 (66.66%) females and 4 (33.33%) males. The age distribution of the patients revealed that the maximum number of patients (n=4, 33.33%) belonged to the 4th decade of life. The site involvement, in ascending order, included the palate (n=10; 83.83%), alveolus (n=1), and upper anterior gingiva (n=1). Regarding laterality, 7 (58.33%) cases were on the right-side, and 5 (41.66%) were on the left-side of the palate.

Conclusion: The study found that females in their 4th decade were commonly affected, with the palate being the most commonly affected site. MEC is one of the common differential diagnosis to consider, and its aggressiveness and treatment planning are related to histological grading. Therefore, epidemiological studies from different parts of the globe are needed to provide a better understanding of the lesion's biological behaviour, common sites, gender, and age predilection.

Keywords: Head and neck pathology, Minor salivary gland tumours, Paediatric

INTRODUCTION

The MEC is the largest group among all other SGN of the minor salivary glands. It is one of the most frequently encountered malignancies of the salivary glands, with varying potential for aggressive behaviour in both paediatric and adult populations [1]. The current 5th edition of the classification of salivary gland tumours categorises MEC as a malignant neoplasm [2].

According to studies, MEC may account for up to 45% of all Minor Salivary Gland Tumours (MiSGT) [3,4]. Globally, the prevalence was found to be 16.5%, with a site predilection in the palate [5]. It exhibits a wide range of biological behaviours connected to the tumour's histological grade. The histological diagnosis of MEC is based on the discovery of four intermixed tumour components: 1) Mucus cells; 2) Intermediary cells; 3) Clear cells; and 4) Epidermoid cells [6]. The approach that divides lesion subtypes into low, moderate, and high-grades is the most commonly used among the various histological grading systems for MEC [7,8]. In this system, "High-grade" refers to a solid growth pattern, a higher mitotic rate, tumour necrosis, and neural invasion, all of which have been linked to a poor prognosis in MEC patients.

MEC of the minor salivary glands clinically manifests as a firm to rubbery intraoral swelling, mimicking various other tumours [9]. Although, various epidemiological studies have been conducted to

study salivary gland tumours [10-19], literature on MEC of minor salivary glands is sparse.

To better understand the epidemiological pattern of MEC and compare our results to those of other epidemiological studies, the current study was designed to examine the clinical and histological characteristics of MEC of the minor salivary glands.

MATERIALS AND METHODS

The cross-sectional study was conducted between November 2022 and January 2023 at the Department of Oral Pathology and Microbiology, Government Dental College and Hospital, Mumbai. Since the data was obtained retrospectively without any patient interventions, ethical approval from the Institutional Ethical Board was not obtained.

Clinical records of salivary gland tumours reported from 2003 to 2022 were accessed from the archives of the department, and the obtained clinical and radiographic data were tabulated in an Excel sheet. A total of 22 diagnosed cases of salivary gland tumours, including pleomorphic adenoma, MEC, and adenoid cystic carcinoma, were reported. Among them, 12 cases of MEC were included in this study. Slides of the cases included in the study were obtained from the departmental archives and graded histopathologically following the criteria proposed by Brandwein MS et al. This grading system assigns a tumour grade from low (Grade-I) to high (Grade-III) grades [8].

Three investigators were involved in data collection, and three investigators were involved in histological grading to verify inter-observer variability. Each investigator graded the slides twice with one-week intervals to substantiate intra-observer variability. The final histopathological grade was determined based on the grade with the highest frequency among the grades obtained from the three investigators.

STATISTICAL ANALYSIS

The data was tabulated in an Excel sheet. Using SPSS, descriptive statistics (mean, range, and frequency) were employed to summarise the clinical and demographic characteristics of the patients. This included percentage and frequency for categorical variables, as well as mean, range, and frequency for continuous variables.

RESULTS

Out of the 22 reported cases of Salivary gland neoplasms, 12 (54.54%) were MEC. Among the 14 malignant salivary gland tumours reported during the time period {MEC n=12, Adenoid Cystic Carcinoma (AdCC) n=2}, the relative frequency of MEC was 85.71%. Based on the gender distribution of MEC, there were 8 (66.66%) females and 4 (33.33%) males [Table/Fig-1].

Tumour	Pleomorphic adenoma	Mucoepidermoid Carcinoma (MEC)	Adenoid cystic carcinoma
Gender			
Female	4	8	1
Male	4	4	1
F:M	1:1	2:1	1:1

[Table/Fig-1]: Distribution of minor salivary gland neoplasms (according to gender).

The age distribution of patients affected with MEC revealed that the maximum number of patients (n=4, 33.33%) belonged to the 4th decade of life. The palate was the most commonly involved site (n=10; 83.83%). Other involved sites included the alveolus and upper anterior gingiva, with one case each (n=1). Regarding laterality, 7 (58.33%) cases were on the right-side, and 5 (41.66%) were on the left-side [Table/Fig-2].

Tumour	Pleomorphic adenoma	Mucoepidermoid Carcinoma (MEC)	Adenoid cystic carcinoma
Site			
Palate	7	10	1
Maxilla			1
Gingiva		1	
Lip	1		
Alveolus		1	

[Table/Fig-2]: Site distribution of minor salivary gland neoplasms.

Age (years)	Gender	Anatomic location	Size	Clinical diagnosis	Radiological radiographic finding	Histopathological diagnosis	Grading
50	Female	Left hard palate	2x1 cm	MEC	No abnormality detected	MEC	Low-grade
18	Female	Right-side of palate in relation to 15 to 17	3x2 cm	Pleomorphic Adenoma	No abnormality detected	MEC	High-grade
45	Female	Palatal mucosa in the region of 15 to 17	2x3 cm	Pleomorphic Adenoma	No abnormality detected	MEC	Low-grade
35	Female	Palatal region in relation to 16,17	1x1 cm	Minor salivary gland tumour of the hard palate	Mixed radiolucent radiopaque lesion w.r.t. 16,17	MEC	Low-grade
22	Female	Right-side of posterior palate	5x3 cm	Cystic lesion of maxilla	No abnormality detected	MEC	High-grade
48	Female	Right posterior palate in relation to 15 to 18	1.5x1.5 cm	Pleomorphic adenoma	No abnormality detected	MEC	Intermediate-grade
36	Female	Upper left anterior gingiva in relation to 23,24	5x3 cm	Benign odontogenic tumour	Mixed radiolucency radiopacity with respect to 23,24 region.	MEC	Low-grade
60	Male	Lower left mandible in relation to 41 to 35	2x1 cm	Carcinoma of the alveolus	No abnormality detected	MEC	Intermediate-grade

Out of these 12 cases, eight cases (66.66%) revealed no radiographic changes on OPG, while the other cases reported variations ranging from a mixed radiolucent radiopaque appearance to diffuse radiolucency [Table/Fig-3].

After the histopathological examination was carried out, it was revealed that 7 (58.33%) cases belonged to low-grade MEC, 3 (25%) were intermediate-grade, and 2 (16.66%) were high-grade MEC [Table/Fig-4]. The findings of all the cases have been tabulated in [Table/Fig-3].

DISCUSSION

The MEC is the most frequent malignant salivary gland tumour, accounting for about 5% of all salivary gland tumours. The World Health Organisation defines MEC as 'a malignant glandular epithelial neoplasm characterised by mucous, intermediate, and epidermoid cells, with columnar, clear cell, and oncocytic features' [20].

In the current study, the majority of the salivary gland tumours were intraoral and histopathologically diagnosed as MEC. This finding contrasts with a study conducted by Bobati SS et al., at a Pathology Department of a tertiary health center in Bagalkot, Karnataka, India, where the majority of the lesions in the major salivary glands were encountered, and only three out of 59 cases were MEC [10]. This difference could be due to patients with intraoral lesions typically reporting to a dental hospital, compared to cases of extraoral lesions in the head and neck area where patients may report to an Ear, Nose, and Throat (ENT) specialist. However, in a dental institutional study conducted at Loni, Maharashtra, India, Kalburge V et al., observed that MEC was the most common malignant salivary gland tumour (58.53%), followed by adenoid cystic carcinoma (33.33%) [11]. These findings align with those of Triantafyllidou K et al., who reported 16 cases of MEC over a 15-year period in a study conducted in Greece [12].

The variations in histology, clinical presentation, and behaviour result in varied prognoses for these tumours as well. According to the literature, MEC has a slight female preponderance [5], which is consistent with the findings of the present study. The male-to-female ratio in the current study was 1:2. In contrast, a male predominance was reported in Greece (1.5:1) by Rapidis AD et al., in Turkey by Kizil Y et al., and in Pakistan by Zaman S et al., (1.4:1) [13-15], which differs from the current study's findings (1:2).

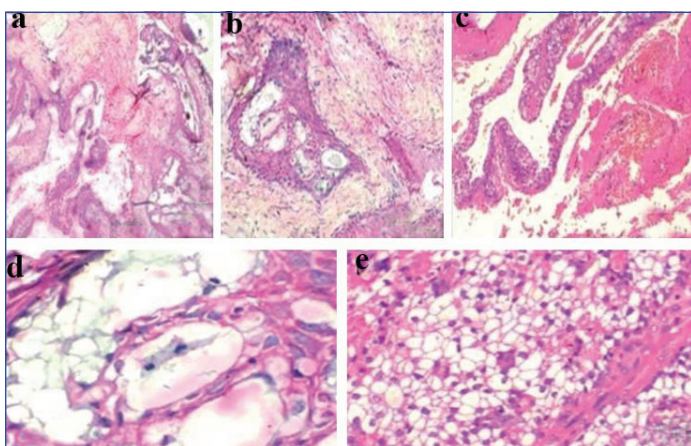
Regarding the age distribution of the patients in the present study, a comparatively maximum number of patients (n=4, 33.33%) belonged to the fourth decade of life. This aligns with the literature, where the most common age group affected was found to be the fourth to sixth decades [20]. Similar observations were made by Buchner A et al., and Kakarala K et al., [16,17].

In terms of the site of these tumours in the current study, the hard palate (83.83%) was the most common location for MEC, which is consistent with findings described in many studies in the literature [18,19].

27	Female	Palate	5x5 cm	Pleomorphic Adenoma	No abnormality detected	MEC	Intermediate-grade
48	Male	Left-side of palate	5 cm	Adenoma, Ossifying fibroma	Hazyness of left maxillary sinus	MEC	Low-grade
40	Male	Palate	2 cm	Pleomorphic adenoma	No abnormality detected	MEC	Low-grade
65	Male	Palate extending from 13-18	3x1.5 cm	Minor salivary gland tumour Squamous cell carcinoma	Diffuse radiolucency tending from right maxillary canine till right maxillary molar	MEC	Low-grade

[Table/Fig-3]: Summary of Clinicopathological characteristics of 12 patients diagnosed as Mucoepidermoid Carcinoma (MEC).

MEC: Mucoepidermoid Carcinoma



[Table/Fig-4]: Histopathological features of MEC: (a) H&E stained section (4x) shows epithelial islands with cystic spaces with fibrous connective tissue stroma; (b) H&E stained section (10x) shows islands consisting of squamous cells with cystic spaces and mucous cells; (c) H&E stained section (10x) shows cystic cavities; (d) H&E stained section (40x) shows minimal pleomorphism, hyperchromatism and mitotic figures (e) H&E stained section (40x) shows presence of numerous clear cells.

Since cases of MEC have been reported following radiation therapy for thyroid cancer or leukaemia, it is possible that prior ionising radiation exposure played a role in tumour development [21]. A three-tier grading system is being used to categorise tumours into low, intermediate, and high-grade. However, the description of “intermediate cells” varies across the literature, making them challenging to define. According to a review study [6], intermediate cells are “non-descript” cells with morphologies that do not correspond to developed or recognised phenotypes, such as mucous or squamoid cells.

In the present study, 58.33% of the cases belonged to the low-grade MEC category. Brandwein MS et al., conducted a clinicopathological analysis of 80 MEC patients and developed a grading scheme based on distinguishing markers, including necrosis, perineural dissemination, vascular invasion, bone invasion, and mitoses. They concluded that these distinguishing characteristics determine the grade of these malignancies [8].

The most frequently encountered diagnostic issue in these cases is determining the acceptable level of keratinisation for MEC. The only key differentiation between SCC and MEC is the presence of intermediate and mucous cells [22]. This distinction is crucial because the prognosis and treatment options differ. Adults with low-grade MECs have a better prognosis than those with SCCs. However, those with high-grade tumours have worse survival chances than SCC patients. Therefore, it is recommended to apply mucicarmine stain to all cases except obvious SCC arising from the surface mucosa. In almost all our cases of MEC, mucicarmine stain and PAS stain were done to rule out the presence of eosinophilic mucin material. MEC typically does not have anaplastic nuclear characteristics and is not connected to carcinoma in situ of the overlying surface epithelium [23].

Advancements in research have also focused on genomic alterations and immunohistochemical markers in MEC. According to Tonon G et al., the fusion of exons 1 and 2 of CRTC1 on chromosome 19p13 and MAML2 on chromosome 11q21 (a member of the mastermind-like gene family) impairs the NOTCH signaling pathway [24].

Limitation(s)

The current single-institution study involves only a small number of cases (12 cases). Therefore, multiple institutional-level and demographic studies should be conducted to better understand the clinicopathological aspects of MEC of minor salivary glands. Such studies can assist clinicians and dental practitioners in comprehending the biological behaviour and planning treatment effectively.

CONCLUSION(S)

The MEC is one of the most frequently encountered malignancies of the minor salivary glands. These neoplasms are more common in women in the 4th decade of life, with the palate being the most common site. A more conservative approach can be used for low-grade MEC compared to high-grade MEC, especially in young adults. This approach could avoid disfigurement for a lifetime. Hence, grading of MEC plays a vital role in reporting a case. Although MEC is uncommon intraorally, considering it as a differential diagnosis when encountering a firm swelling is advised.

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