Minor salivary gland Mucoepidermoid Carcinoma in the Jaws: A Case Series and Review of Literature

Abstract: Background: Salivary gland tumors represent 1% of head and neck tumors, with Pleomorphic adenoma the first highest rate of occurrence among all the salivary gland tumors followed by the Mucoepidermoid carcinoma (MEC), a malignant epithelial tumor. The study is a Descriptive, Retrospective and Multicenter analysis of a series of 15 patients above 23 years to below 63 years who were treated for salivary gland MEC in the Department of oral and maxillofacial pathology, oral surgery and oral medicine. Vishnu Dental College, Bhimavaram from 2002 to 2021. Method: Of the 15 cases of MEC, 1 male patient of age 35 was excluded, which was diagnosed as a High grade MEC since proper data could not be attained from the archival files and when communicated for the details he died in 2014. In the study H & E, PAS, Diastase and IHC markers like pan cytokeratin were used to know the nature of the lesion. Aim of the study: All the relevant clinical, radiological and histopathological information regarding the diagnosed cases of MEC were retrieved from the archival files and co-related for Clinicopathological findings. Conclusion: Clinical, radiological and pathological correlation is necessary for preoperative diagnosis of the high grade aggressive MEC. MEC is not only restricted to the children and adolescent age group but can affect any age group. Intraosseous minor salivary gland MEC are more prevalent in the maxillary and mandibular posterior region. While histology is playing a role of gold standard, the IHC is further aiding in the diagnosis of MEC.

Keywords: Mucoepidermoid carcinoma (MEC).

INTRODUCTION:
Salivary gland tumors represent 1% of head and neck tumors, among epithelial tumors of the salivary glands, MEC and adenoid cystic carcinoma are the most frequent histologic types in adults. MEC is usually associated with salivary glands and comprises 5–10% of all salivary gland tumors. MEC has been defined as “a malignant glandular epithelial neoplasm characterized by mucous, intermediate and epidermoid cells, with columnar, clear cell and oncocytoid features (Text book of surgical pathology of the Head and Neck 3rd Edition).” In 1945, Stewart, Foote and Becker first used the term mucoepidermoid tumor and described its mucous-secreting and epidermal cellular elements thus establishing it as a distinct pathologic entity with a case series of 45. The 1st edition of the WHO Histological classification of salivary gland tumors, published in 1972, retained the term mucoepidermoid tumor while the 2nd edition in 2005 of the WHO classification adapted the term Mucoepidermoid carcinoma.

MEC can arise from terminal part of the excretory duct as stated by Pleur-it-potent bicellular hypothesis theory, exposure to ionizing radiations for therapeutic purposes, from developmental disorder like adenoid hyperplasia of mucous glands, ectopic salivary gland tissue in the periparotid lymph nodes and while the histogenesis of the central MEC remains controversial, but one highly possible theory is that this malignancy arises from the lining epithelium of odontogenic cyst.

CASES PRESENTATION
There are around 31 salivary gland neoplasms in the archival files of the Department of oral pathology, Vishnu Dental College, Bhimavaram out of which only 14 cases are MECs. Out of the 14 MEC cases included in the study 8 were females and 6 were males and 7 occurred in the posterior maxilla while 7 in the posterior mandible. 5 were High grade, 6 were low grade and 3 were intermediate grade among the fourteen MECs. The patients are in age range of 23 to 63 and the mean age and the median age are 40.2 and 37 years respectively.
A search of the English language Medical and Dental literature was performed for well documented minor salivary gland MEC cases in the adolescent age group. The search was carried out in Medline, and PubMed for MEC and salivary gland carcinoma occurring in all the age group. The search was last updated in July 2016. Once the studies were identified, individual articles and their references were checked for additional studies.

<table>
<thead>
<tr>
<th>Si.No.</th>
<th>Age</th>
<th>Sex</th>
<th>Type of mucoepidermoid carcinoma</th>
<th>Area /site of lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>26</td>
<td>F</td>
<td>Low grade</td>
<td>Left max post.</td>
</tr>
<tr>
<td>2.</td>
<td>26</td>
<td>F</td>
<td>Intermediate grade</td>
<td>Right maxillary palatal region of 14, 15, 16 &amp; 17.</td>
</tr>
<tr>
<td>3.</td>
<td>23</td>
<td>M</td>
<td>Low grade Clear cell variant</td>
<td>Left maxillary post palatal region</td>
</tr>
<tr>
<td>4.</td>
<td>36</td>
<td>F</td>
<td>Intermediate grade</td>
<td>Swelling in the right posterior palate</td>
</tr>
<tr>
<td>5.</td>
<td>58</td>
<td>M</td>
<td>High grade</td>
<td>Right lower back tooth region</td>
</tr>
<tr>
<td>6.</td>
<td>45</td>
<td>M</td>
<td>High grade</td>
<td>Left post. Part of palate</td>
</tr>
<tr>
<td>7.</td>
<td>24</td>
<td>F</td>
<td>Low grade</td>
<td>Right max. post palatal region</td>
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<tr>
<td>8.</td>
<td>65</td>
<td>F</td>
<td>Low grade</td>
<td>Right posterior mandibular region i.r.t. 46, 47, 48</td>
</tr>
<tr>
<td>9.</td>
<td>53</td>
<td>M</td>
<td>High grade with clear cell changes</td>
<td>Right posterior mandibular region</td>
</tr>
<tr>
<td>10.</td>
<td>25</td>
<td>F</td>
<td>High grade with clear cell changes</td>
<td>Right posterior mandibular region</td>
</tr>
<tr>
<td>11.</td>
<td>60</td>
<td>M</td>
<td>Low grade</td>
<td>Lower Left retro molar region</td>
</tr>
<tr>
<td>12.</td>
<td>45</td>
<td>F</td>
<td>High grade</td>
<td>Lower Right buccal mucosa and alveolar ridge</td>
</tr>
<tr>
<td>13.</td>
<td>37</td>
<td>F</td>
<td>Low grade</td>
<td>Right maxillary posterior region</td>
</tr>
<tr>
<td>14.</td>
<td>63</td>
<td>M</td>
<td>Intermediate grade</td>
<td>Lower anterior mandibular alveolar ridge and vestibule</td>
</tr>
</tbody>
</table>

Site of occurrence

- MAXILLARY
- MANDIBULAR
DISCUSSION:

The histologic grade of the MEC usually reflects the clinical manifestations of the tumor. Intra orally, low-grade MECs tend to be asymptomatic enlargements appearing as fluctuant light blue or purplish sub mucosal lumps, resembling the reactive salivary gland mucocele (mucous retention phenomenon) and other benign tumors of the salivary gland. The reason they have similar clinical appearance is that low grade MECs and mucoceles possess mucous cyst formation and mucous pseudo cyst formation, respectively. While the high grade MECs are symptomatic with three defined patterns of invasion like borders with partial encapsulation or good circumscription, broad pushing borders with limited invasion and infiltrative growth with permeation into surrounding tissue. The high grade MECs should be clinically differentiated from the squamous cell carcinoma and other malignant tumors.

It is most likely that the treating dentist would take an intra-oral radiograph or an orthopantomograph or both at the time of the initial clinical presentation for better understanding the tumor and co relate clinically as well as histologically. However, the treating oral surgeon would need a computed tomography scan to establish the extent of the lesion prior to the surgical exploration. In the case series, all of the MECs are intraosseous, which are studied using one or more of the radiological diagnostic aids like IOPAs, Oclusal radiographs, PNS view and OPGs. Prognosis of the MEC on the basis of the imaging modalities has not been investigated and to date the only prognostic indicator is the histological grading of the lesion. Microscopically, the grading of the MEC is based on the three factors, the amount of cystic formation, degree of cytological atypia and relative number of mucous, epidermoid and intermediate cells. Histological grading of the tumor is done using the stains like Hematoxylin and Eosin (H & E), special stains like Periodic Acid Schiff (PAS), Alcian blue, Mucicarmine and Diastase, while IHC markers like epithelial membrane antigen, carcinoembryonic antigen, calponin, Pan cytokeratin, α-SMA (smooth muscle actin), Vimentin and p63 will further aid in the grading of the tumor.

In the study H&E, PAS, Diastase stains and IHC marker like Pan cytokeratin are used and here are the histological pictures under 4x, 10x & 40x respectively of low, intermediate and high grade MEC from left to right. As originally stated the term mucoepidermoid emphasizes the presence of the mucous and epidermoid cells, but the diagnosis can be established even in the absence of the epidermoid cells. The recognition of this tumor involves identification of mucous, epidermoid, intermediate, columnar or clear cells each proliferating alone or in many different combinations. The IHC marker Pan Cytokeratin stained study slide shows an island of tumor cells where it is clearly evident that the cell membrane of the tumor cells takes the IHC marker pan cytokeratin and the cystic space can be seen clearly. Sams et al., comparison of p63 expression among 31 cases of acinic cell carcinoma and 24 cases of MEC have proved p63 is a useful differentiating marker, as MECs were strongly positive and Acinic cell carcinomas were negative for p63 (Zhu, S. et al., 2015; & Sams, R. N., & Gnepp, D. R. 2013). While p63 even helps in differentiating Oncocytic MECs from oncocytoma and oncocytic carcinoma by its staining pattern. In oncocytic MEGs more than 50% of cells throughout the tumor nests were positive for p63, while only scant peripheral cells of the tumor nests in oncocytoma and oncocytic carcinoma were positive for p63 (Zhu, S. et al., 2015; & Weinreb, I. et al., 2009).

The clear cell variant of MEC should be demarcated from the other various salivary gland tumors composed predominantly of clear cells, such as sebaceous carcinoma, clear cell adenocarcinoma (NOS), epithelial-myoeipithelial carcinoma, oncocytoa, acinic cell carcinoma and metastatic renal cell carcinoma. In
In the study, two cases of MECs were seen with predominant clear cell changes. Only MECs display both epidermoid and mucous cell differentiation.

**LOW GRADE MUCOEPIDERMOID CARCINOMA**

**INTERMEDIATE GRADE MUCOEPIDERMOID CARCINOMA**

**HIGH GRADE MUCOEPIDERMOID CARCINOMA**

IHC of Pan cytokeratin in High grade MEC
CONCLUSION:
MEC is not only restricted to the children and adolescent age group but can affect any age group. More prevalent in the maxillary and mandibular posterior region. The classification and terminology of salivary gland lesions are constantly evolving with the use of newer techniques and better understanding of the pathologic processes involved. Histology is currently considered the gold standard for the accurate diagnosis while immunohistochemistry is further playing a role in the diagnosis of the MEC. Clinical, radiologic and pathologic correlation is necessary for preoperative diagnosis of the high grade aggressive MEC that frequently present with neck node metastasis. Identification of consistent genetic translocations that can be easily detected by FISH (Fluorescent in situ Hybridization) can augment our diagnostic and prognostic armamentarium for MEC and adenoid cystic carcinoma. It is essential that surgeons, pathologists, oncologists and all those involved in the diagnosis and management of patients with salivary gland lesions are aware of these developments when determining the optimal treatment approach.

REFERENCES


