Calcifications may be a frequent finding in mucoepidermoid carcinomas of the salivary glands: a clinicopathologic study

Wilfredo Alejandro González-Arriagada, DDS, a,b Alan Roger Santos-Silva, DDS, PhD, a Fabio Augusto Ito, DDS, PhD, c Pablo Agustin Vargas, DDS, PhD, a and Marcio Ajudarte Lopes, DDS, PhD, a Piracicaba and Londrina, Brazil; Valparaíso, Chile STATE UNIVERSITY OF CAMPINAS, UNIVERSIDAD DE VALPARAÍSO, AND STATE UNIVERSITY OF LONDRINA

Calcifications in mucoepidermoid carcinoma (MEC) of the salivary glands are considered to be exceptionally rare and are often associated with high-grade tumors. This study reviewed 30 cases of MECs to access the frequency of calcifications and the clinical profile of the patients and histopathologic aspects of the tumors. In total, 6 cases of calcifications (20%) were identified. Five patients were women and 1 was a man, patients’ ages ranged from 22 to 69 years old, and calcifications were found in conventional and clear cell–type MECs. Areas of calcification showed positivity for periodic acid–Schiff and mucicarmine, supporting the hypothesis that they originate from the precipitation of mucous secretion. The presence of calcifications in MECs was independent of the histologic grade of the tumors and the histopathologic variants. Calcifications in salivary MECs may not be as rare as previously mentioned in the literature and may be not associated with high-grade tumors. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:482-485)

Mucoepidermoid carcinoma (MEC) is the most common malignant salivary gland tumor. In major salivary glands, MEC mainly affects the parotid gland and when it occurs in the minor salivary glands, the palate is frequently involved. MECs are commonly diagnosed between the third and sixth decades of life, with a slight predilection for women.

From a microscopic point of view, MECs are composed of 3 main cellular types: mucous cells, intermediary cells, and epidermoid cells. The histologic grade is mainly based on the amount of the cystic component and the presence of mucous cells, being classified as low-, intermediate-, or high-grade tumors. Other features, such as neural invasion, necrosis, mitotic rate, and anaplasia, are also considered. The prognosis is frequently correlated with the histologic grade of the tumor. There are several histologic variants of MEC described in the literature, including clear cells, sclerosing, oncocytic, sebaceous, and spindle cell. Conventional MEC is the most frequent type, being followed by the clear cell subtype.

Calcifications in MEC have been considered to be uncommon, and there are scarce reports available in the literature, most of them detected in clear-cell tumors (Table I). The lack of data contributes to suggestions that calcifications in MECs would be associated with high-grade tumors and more aggressive outcomes. Therefore, the present study aims to review a series of patients diagnosed with MEC of the salivary glands to identify the presence of calcifications as well as to perform a review of the pertinent literature.

PATIENTS AND METHODS

A retrospective study was designed to investigate the presence of calcifications in MECs of the salivary glands. This study was approved by the Ethics Committee for Human Studies, Piracicaba Dental School, University of Campinas.

Patients and clinical features

A retrospective review was performed for the files of 2 oral pathology centers at University of Campinas (Piracicaba Dental School) and State University of Londrina (Department of Pathology). Demographic data (age and gender) and site of the tumors were collected from the patients’ charts. All patients who had MEC of the salivary gland were identified, and tumor tissue specimens were retrieved.
Histopathologic features

Selected specimens were retrieved and 5-μm-thick sections were cut from their paraffin blocks, stained with hematoxylin and eosin, and reexamined under light microscopy for diagnostic confirmation. Each specimen was then histologically graded according to World Health Organization guidelines.10 Cases were further stained with the histochemical techniques of periodic acid–Schiff (PAS) and Mayer mucicarmine.

RESULTS

Thirty cases of MEC were identified: 21 from minor salivary glands and 9 from major salivary glands (8 from parotid gland and 1 from submandibular gland). Nineteen patients (63.3%) were women, 10 (33.3%) were men, and 1 (3.3%) was unknown. The patients’ ages ranged from 5 to 80 years (mean age 44.07 years). According to the histologic grading, 19 (63.3%) were diagnosed as low grade, 4 (13.33%) as intermediate grade, and 7 (23.33%) as high grade. The majority of the cases evaluated (25) were conventional type, 3 cases were clear cell type, and 2 were oncocytic cell type. Four cases (66.6%) were diagnosed as low-grade lesion, 1 case (16.6%) was an intermediate-grade tumor, and 1 case (16.6%) a high-grade MEC.

All MEC cases showed positive staining reactions for PAS and mucicarmine in mucous cells and mucin plugs. Calcifications showed variable size, number, and irregular and concentric laminations in their structure (Table II). They were observed inside duct structures as well as within nests of tumor cells, which were circumscribed with epidermoid, mucous or intermediate cells (Figs. 1 and 2). Intraluminal areas of calcification were also observed in ducts formed by mucous and intermediate cells (Fig. 3) and in fibrous tissue surrounding solid areas of MEC of the parotid gland (Fig. 4). All calcifications were PAS and mucicarmine positives (Fig. 5).

DISCUSSION

There have been only 5 cases of MEC of the salivary glands with calcifications reported in the English-language literature. The first report was a recurrent conventional-type MEC affecting a 64-year-old woman.16 The other 4 cases reported were observed in clear-cell MECs.17-19

Interestingly, in the present study most of the tumors with calcifications were conventional type (5 cases) and only 1 case a clear-cell MEC. It is relevant to mention that all of the previous tumors reported in the literature affected minor salivary glands. In the present series, most of the cases with calcification also were observed in the minor salivary glands. However, 1 case was in the parotid gland, probably the first report of calcification in MEC in this location.17-19

Table I. Previously reported cases of calcifications in mucoepidermoid carcinomas of the salivary glands

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Histologic grade</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Histologic type</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siar, Ng, and Loh, 198716</td>
<td>n/d</td>
<td>64</td>
<td>F</td>
<td>Conventional</td>
<td>Palate</td>
</tr>
<tr>
<td>Yoon et al., 200517</td>
<td>Low</td>
<td>48</td>
<td>F</td>
<td>Clear cell</td>
<td>Palate</td>
</tr>
<tr>
<td>Do Prado et al., 200718</td>
<td>Intermediate</td>
<td>39</td>
<td>F</td>
<td>Clear cell</td>
<td>Floor of mouth</td>
</tr>
<tr>
<td>Yang and Chen, 201019</td>
<td>n/d</td>
<td>29</td>
<td>M</td>
<td>Clear cell</td>
<td>Palate</td>
</tr>
<tr>
<td>Yang and Chen, 201019</td>
<td>n/d</td>
<td>35</td>
<td>M</td>
<td>Clear cell</td>
<td>Palate</td>
</tr>
</tbody>
</table>

n/d: Not determined; F: Female; M: Male.

Table II. Clinicopathologic features of mucoepidermoid carcinomas with calcifications

<table>
<thead>
<tr>
<th>Case</th>
<th>Histologic grade (Barnes et al., 2005)10</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Histologic type</th>
<th>Site</th>
<th>No. of calcifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Low</td>
<td>50</td>
<td>F</td>
<td>Clear cell</td>
<td>Buccal mucosa</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Low</td>
<td>n/d</td>
<td>F</td>
<td>Conventional</td>
<td>Palate</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>Intermediate</td>
<td>22</td>
<td>M</td>
<td>Conventional</td>
<td>Retromolar area</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>Low</td>
<td>60</td>
<td>F</td>
<td>Conventional</td>
<td>Palate</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>Low</td>
<td>26</td>
<td>F</td>
<td>Conventional</td>
<td>Palate</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>High</td>
<td>69</td>
<td>F</td>
<td>Conventional</td>
<td>Parotid</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>

Abbreviations as in Table I.
Some authors have suggested that the presence of calcifications in salivary gland tumors is associated with high-grade malignant tumors. On the other hand, the present results showed that calcifications in MEC may occur independently of the tumor grade.

The histologic findings of the calcifications found in this series showed irregular and concentric lamellar structures, which is in accordance with the results of other authors. Although the nature of these calcifications in MECs is still open to debate, there is a strong suggestion that they could develop as a dystrophic calcification affecting mucin secreted by malignant cells. Yoon et al. proposed 4 mechanisms to explain this process of tumor calcification: a result of hypercalcemia, a component of the tumor, dystrophic calcifications of necrotic areas, and calcifications of the material secreted by the tumor cells. Do Prado et al. found positivity for PAS staining and lack of reaction for mucicarmine staining in MEC calcifications. Conversely, all of the cases described in the present study were positive for PAS and mucicarmine staining.

Remarkably, 5 cases of calcification affecting MECs were found in minor salivary gland tumors. This observation may suggest that calcifications are more likely to develop in tumors affecting mucous salivary glands, reinforcing the theory that calcifications may originate from the precipitation of salivary gland mucous secretion. Differences between the mucus pro-
duced by major and minor salivary glands could be another reason that explains why calcifications are more likely to develop in minor salivary gland tumors.

However, there is not enough evidence in the literature to support the theory that the mucous produced in the MEC differs between tumors occurring in conjunction with major and those with minor salivary glands.

In summary, a significant number of calcifications were detected in a relatively small number of MECs of the salivary glands that were diagnosed in a short period of time. Thus, it is possible that calcifications in MEC are not as rare as previously mentioned and could be often misidentified during the oral pathology routine or not reported because of their apparent limited relevance for diagnosis. Apparently, the presence of calcifications in MECs is not related to the histopathologic grade of differentiation and consequently not associated with poor outcomes.

REFERENCES


Reprint requests:
Professor Marcio A. Lopes
Oral Diagnosis Department
Semiology Area
Piracicaba Dental School
State University of Campinas
Avenida Limeira, 901
Piracicaba, SP
CEP 13414-903
Brazil
malopes@fop.unicamp.br