Clinicopathologic study of odontogenic keratocysts in Singapore and Malaysia

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Abstract: This was a retrospective study of odontogenic keratocysts in people from the Singapore-Malaysian region. The purpose of this study was to present the clinicopathologic features of odontogenic keratocysts in the Oriental population and to compare these data with those from other reported studies. Biopsy records from 1981 to 1992 of 61 cases of odontogenic keratocysts from patients in Malaysia and Singapore showed that 42.6% of patients were female and 57.4% of patients were male. Among patients with cysts, 75.4% were Chinese, 6.6% were Malays, 9.8% were Indians and 8.2% were other ethnic groups. The mean age of these patients was 26.98 ± 15.38 years with a peak incidence occurring in the second to fourth decades. The location of the lesions was more often in the mandible (65.5%) than the maxilla (31.0%). There was a marked predilection for lesions to occur in the posterior mandible. Histologically, 90.2% of the cysts were lined with a parakeratinised stratified squamous epithelium while only 3.3% of the cysts were lined with orthokeratinised stratified squamous epithelium. Mixed parakeratinised and orthokeratinised epithelial linings were observed in 4 cases (6.5%). The cyst linings were mainly uninflamed (95.1%). Inflammation of the cyst wall was found in 42 cases (68.8%). Twelve (19.7%) cases contained keratin in the lumen. A satellite cyst was observed in only 6 cases (9.8%). In conclusion, most clinical and histological features seen in this study were similar to those found for Caucasians. The only clinical feature that was different was the peak age incidence, that ranged from the second to fourth decades, with an absence of a second peak. Odontogenic keratocysts presenting at the site of the dentigerous cysts were observed in 7 cases (11.5%). (J. Oral Sci. 42, 9-14, 2000)

Key words: cyst; odontogenic keratocyst; clinical; histology; Orientals.

Introduction

The odontogenic keratocyst (OKC) is a cyst arising in the tooth-bearing areas of the jaws, or posterior to the mandibular third molar, and is characterised by a thin fibrous capsule and a lining of keratinised stratified squamous epithelium usually about five to eight cells in thickness and generally without rete ridges (1). It represents about 10-12% of all developmental odontogenic cysts (1). It is an unusual odontogenic cyst because of its unique clinical behaviour and high recurrence rate. The diagnosis of an OKC is made based on its specific histopathologic features.

A number of good articles have been written about the clinicopathologic features of odontogenic keratocysts (2-26). However, the data for these studies were obtained from predominantly Caucasian populations. The purpose of this paper was to present the clinicopathologic features of OKCs in the Oriental population, specifically from the multiethnic populations in Singapore and Malaysia; and to compare these data with data from other reported studies.

Materials and Methods

The materials for this study were obtained from specimens submitted to the Histopathology Laboratory, Dental School, University of Singapore (1981-1991) and the Oral Pathology Laboratory, Dental Faculty, University
of Malaya (1982-1992). There were altogether 61 specimens, 23 from Malaysia and 38 from Singapore. To be included in the study, clinical and histological criteria were applied in order for a given specimen to be designated as an OKC. The specific criteria for this type of lesion was that it had to be within the jaw bone and it had to be a cyst that had a thin fibrous capsule and a lining of keratinised stratified squamous epithelium, usually about five to eight layers of thickness and generally without rete ridges (Fig. 1)(1).

Data on the subjects providing the specimens, such as age, sex, ethnic group, as well as lesion location data were obtained from the information on the biopsy forms submitted to the laboratories. Radiographs were reviewed whenever necessary. Haematoxylin and eosin staining were performed. The prepared slides were evaluated for the type of lining epithelium as well as presence of inflammatory cells.

Results

A total of 61 specimens were reviewed. The age of the patients in this study ranged from nine to eighty-seven years. The mean age with standard deviation (± SD) was 26.98 ± 15.38. The median age was 21 years. Almost 84% of the cases had been diagnosed in people between 11 to 40 years of age. This translates to a peak prevalence that ranged from the second to fourth decades.

Male subjects in this study made up of 57.4% of all patients (Fig. 2). The male-to-female ratio was 1.35. The majority of the patients were Chinese (75.4%).

The location of the lesions in this study were more often in the mandible (65.5%) than the maxilla (31.0%) (Table 1). The location of the lesions in the mandible were more often in the posterior mandible (27 cases).

About twenty-six percent (26.2%) of the OKCs reviewed showed an association with impacted teeth (Table 2). Seven cases (11.5%) had a dentigerous-like radiographical appearance. Three (4.9%) periapical OKCs were also observed.

Parakeratinisation was found in 90.2% of the cases reviewed (Table 3). Two cases (3.3%) showed only orthokeratinisation with both occurring in male Chinese patients. One case occurred in the posterior mandible.

Table 1 The anatomical location of odontogenic keratocysts in Singaporeans and Malaysians

<table>
<thead>
<tr>
<th>Location</th>
<th>Number (N=58)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior maxilla only</td>
<td>5</td>
<td>8.6</td>
</tr>
<tr>
<td>Posterior maxilla only</td>
<td>9</td>
<td>15.6</td>
</tr>
<tr>
<td>Anterior and posterior maxilla</td>
<td>4</td>
<td>6.9</td>
</tr>
<tr>
<td>Anterior mandible only</td>
<td>4</td>
<td>6.9</td>
</tr>
<tr>
<td>Posterior mandible only</td>
<td>27</td>
<td>46.6</td>
</tr>
<tr>
<td>Anterior and posterior mandible</td>
<td>7</td>
<td>12.0</td>
</tr>
<tr>
<td>Other location/multiple locations</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>58</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Missing information</strong></td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 The relationship to the odontogenic keratocyst to the teeth in Singaporeans and Malaysians

<table>
<thead>
<tr>
<th>Relationship to Teeth</th>
<th>Number (N=61)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relationship to impacted wisdom tooth</td>
<td>13</td>
<td>21.3</td>
</tr>
<tr>
<td>Relationship to other impacted teeth</td>
<td>3</td>
<td>4.9</td>
</tr>
<tr>
<td>Relationship to apex of tooth</td>
<td>3</td>
<td>4.9</td>
</tr>
<tr>
<td>Dentigerous-like cyst</td>
<td>7</td>
<td>11.5</td>
</tr>
</tbody>
</table>
year old patient) while the other occurred in the maxilla (28 year old patient), mimicking a dentigerous cyst. The remaining cysts (6.5%) consisted of mixed parakeratinised and orthokeratinised variants.

Satellite cysts were evident in only 6 cases (9.8%) (Table 3). Only 4.9% of the OKCs presented with island of epithelial cells. The cyst linings were mainly uninflamed (95.1%). There were differing thicknesses of the uninflamed linings epithelium with the majority (77.0%) having only a thin lining. A mixed thick and thin lining occurred in 14.8% of the cases and only 3.3% had a thick lining. The uninflamed epithelial linings were corrugated in 63.9% of the cases. Stellate-like inflamed epithelium was observed in 9.8% of the cases. Twelve (19.7%) cases had keratin in the lumen. There were two primary cysts (3.3%) that did not have typical features of keratocysts.

Inflammation of the cyst wall was found in 42 cases (68.8%) (Table 3). There were increases in the thickness of epithelium adjacent to parts of the inflamed cyst wall (Fig. 3) leading to branching rete ridges. Branching epithelial rete ridges were observed in 21.4% of the inflamed cyst walls in this study. Nineteen cases had keratin in the inflamed cyst wall.

Discussion

Clinical data

Odontogenic keratocysts have been well studied (2-26). These studies indicate that OKCs make up 3.0 to 17.4% of all jaw cysts, however, these data are largely based on a predominantly Caucasian population. There is little data on the Oriental population, specifically the population from the Southeast Asian region. Only several studies have been conducted on OKCs in the Malaysian population and none on the Singapore population (26-30). Studies on the Malaysian population have indicated that OKCs make up of about 3.1 to 17% of all cystic lesions (26-30). The OKCs may be found in patients ranging from infancy to old age. The age range in this study (9 to 87 years) was similar to the age ranges reported by Brannon (2), Ahflors et al. (10), Kakarantza and Nicolatou (11), Haring and Van Dis (12) and Regezi et al. (31). Almost 84% of the cases in the present study had been diagnosed in people between 11 to 40 years of age, i.e. had a peak prevalence that ranged from the second to fourth decades. In contrast, Vedtofte and Praetorius reported a peak incidence of only the second decade (15). This finding is also contrary to the peak prevalence of the fifth and sixth decades reported by Kakarantza and Nicolatous (11). A second lower peak incidence at the fifth decade has been reported in some studies (13,15,24). However, no second peak was observed in the current study.

The mean age of the 61 patients was 26.9 years which is in agreement with two studies done in Malaysia (28,30) but is younger than the 32 years 9 months reported by Brannon (2), the 32.1 years reported by Browne (32), the 36 years reported by Regezi et al. (31) and is markedly younger than the 40.0 years reported by Haring and Van Dis (12).

There were slightly more men than women in these studies (1,2,5,7,13). Male subjects in the current study made

### Table 3 The histopathological features of cyst lining epithelium, cyst wall and lumen of odontogenic keratocysts in Singaporeans and Malaysians

<table>
<thead>
<tr>
<th>Type of stratified squamous epithelium (SSE) lining</th>
<th>Number (N=61)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parakeratinised SSE only</td>
<td>55</td>
<td>90.2</td>
</tr>
<tr>
<td>Orthokeratinised SSE only</td>
<td>2</td>
<td>3.3</td>
</tr>
<tr>
<td>Mixed parakeratinised and orthokeratinised SSE</td>
<td>4</td>
<td>6.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other epithelial (SSE) lining features</th>
<th>Number (N=61)</th>
<th>Percentage (%)</th>
</tr>
</thead>
</table>
a) Inflamed                              | 3             | 4.9            |
b) Uninflamed                            | 58            | 95.1           |
i) Thick lining only                     | 2             | 3.3            |
ii) Thin lining only                     | 47            | 77.0           |
iii) Thick and thin lining               | 9             | 14.8           |
(iv) Corrugated surface                  | 39            | 63.9           |

<table>
<thead>
<tr>
<th>Cyst wall and lumen features</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation of cyst wall</td>
<td>42/61</td>
<td>68.8</td>
</tr>
<tr>
<td>Branching epithelial rete ridges within inflamed cyst wall</td>
<td>9/42</td>
<td>21.4</td>
</tr>
<tr>
<td>Keratin in lumen</td>
<td>12/61</td>
<td>19.7</td>
</tr>
</tbody>
</table>

Fig. 3 Inflamed cyst wall showing an increase in thickness of the epithelial cyst lining and formation of rete ridges in an inflamed OKC. Haematoxylin and eosin stain; Original magnification × 50.
up 57.4% of all patients. The male-to-female ratio in the current study of 1.35:1 is in total agreement with that reported by Brannon (2), and is in close agreement with the 1.3:1 ratio reported by Haring and Van Dis (12), and the 1.4:1 ratio reported by Arafat (14). The results of the current study supports the finding that the OKC has a propensity to occur more frequently in males than in females.

As for ethnic group distribution, the majority of the patients in the current study were Chinese (75.4%); which is not surprising as the sample population was from Malaysia and Singapore, Singapore being predominantly Chinese and about 32.2% of Malaysians are Chinese as well (Malaysian census, 1991). A preponderance of Chinese was also reported by Siar et al. (27). Other researchers have also suggested the possibility of a racial predilection. Rachannis and Shear (13) and Brannon (2) reported a considerably higher incidence of OKCs in Caucasians than blacks.

Odontogenic keratocysts tend to involve the mandible more frequently than the maxilla. Studies by Brannon (2), Crowley et al. (7), Haring and Van Dis (12), Vedtofte and Praetorius (15), Hjørting-Hansen (20), Regezi et al. (31) and Browne (32) showed that the mandible was involved in 60 to 83% of cases, with a marked predilection (about 73% of the mandibular lesions) for these cysts to be on the posterior body and ascending ramus of the mandible. The location of the lesion in the current study was more often in the mandible (65.5%) than the maxilla (31.0%), which concurs with the Western studies. The location of the lesion in the mandible was more often in the posterior mandible (69.2%), a finding that is also consistent with the Western studies (2,4,19,20,32).

In 26.2% of the cases, the OKCs were seen in association with impacted teeth. This percentage is remarkably close to the 26.6% reported by Brannon (2) as well as the 25% reported by Toller (17). In contrast, Forsell (33) and Zachariades et al. (25) reported an association with impacted teeth in 41% and 56.2% of the cases, respectively. It is also not uncommon to find OKCs that are located at the apex of the teeth (34,35). In the present study, three (4.9%) pericoronal OKCs were observed. This percentage is higher than that observed by Stockdale and Chandler on 1108 biopsies (0.1%)(36).

Approximately 40% of the OKCs were associated with an unerupted tooth (10,12,32). Radiographically, an OKC may be observed in the pseudodentigerous position. This may occur because the cyst envelops the adjacent unerupted tooth or because the tooth may have erupted into the cavity of the keratocyst. These lesions may be misdiagnosed as dentigerous cysts with keratinising linings (1). Forsell reported this relationship in 41% of a series of 135 cases (33). Altini and Cohen used the term 'follicular primordial cyst' to describe an OKC that develops a dentigerous relationship with an erupting tooth, where the tooth erupts into a pre-existing keratocyst in the same way a tooth erupts into the oral cavity (37-38). In this study, 7 cases (11.5%) of OKCs were dentigerous-like. As there is a danger of misdiagnosing keratocysts in a dentigerous cyst location, it is important that the final diagnosis be done using histopathological methods in addition to radiographic and clinical examinations.

**Histopathological Features**

Most studies have found an incidence of parakeratinisation between 83.2 - 98.3% in OKCs (3,4,7,10-12). However, although most authors agree that part of the lining may be orthokeratinised in a small number of cysts, the presence of orthokeratinisation alone is uncommon(4). Parakeratinisation was found in 90.2% of our cases. This is comparable with the Western findings. Four cases (6.5%) showed mixed parakeratinisation and orthokeratinisation. This falls within the range reported in the Caucasians (1.6% to 7.1%)(3,7). Two cases (3.3%) showed only orthokeratinisation; this also falls within the documented range for Caucasians (0 to 12.2%)(7,12).

An important feature of the fibrous capsule is the presence of rests of odontogenic epithelium and satellite cysts. Most studies suggest an incidence of satellite cysts of between 7 and 33.3% (3,4,14,10,11). In this study, satellite cysts were evident in only 6 cases (9.8%) but this figure is still within the reported percentages. Epithelial rests were observed in 13.5% to 60.0% of OKCs (3,10,12,33). Only 4.9% of OKCs presented with island of epithelial cells in this study. This is obviously lower than those reported for the Caucasian samples.

The cyst linings were mainly uninflamed (95.1%). There were differing thicknesses for the uninflamed lining epithelium; as expected the majority (77.0%) had only a thin lining. Almost fifteen percent (14.8%) had a mixed thick and thin lining, and only 3.3% had a thick lining. About sixty-four percent (63.9%) of the uninflamed epithelial lining were corrugated.

Reports on the presence or absence of inflammation in the connective tissue wall of the OKCs remain conflicting. Some studies report that little or no inflammation was observed in the OKCs analysed (4,17,18). Others reported that a high percentage of OKCs (72.4% to 98.0%) were present with a predominantly chronic inflammatory cell infiltration and that this was often in a generalised pattern of distribution (3,11,12,14) Our findings are consistent with the latter findings. In our study, inflammation of the
cyst wall was found in 42 cases (68.8%). This is in agreement with the findings of Browne in which approximately a third of the fibrous capsule was entirely free from inflammatory cell infiltrate. In approximately 50% of the remaining cases, there were isolated foci of inflammation while the remainder exhibited a more diffuse inflammation (4).

The presence of rete ridges has been described as very rare (1,25). Haring and Van Dis observed their presence in less than half of their samples (12). Ong and Siar observed the presence of rete ridges in 39.4% of their samples (28). Branching rete ridges were observed in 21.4% of the inflamed cyst walls in this study.

Twelve cases (19.7%) demonstrated keratin in the lumen. This rate is lower than that observed by Brannon who found that in 30.8% of OKCs, the lumen was full of keratin (3). Ong and Siar, in their study of OKCs in Malaysia, suggested that the lower percentage observed was due to the fact that many of these cysts were removed piecemeal and an intact lumen was therefore not available for their study (28). This may also be the reason for the low percentage of keratin in the OKC lumen in the current study.

The orthokeratinised variant is a clinically less aggressive lesion, occurs predominantly in males and is often found in the second to fifth decades of life (9). It is more prevalent in the posterior mandible. Only two cases of orthokeratinised OKCs were noted in this study. Both occurred in males, with their age being 38 and 28 years. One case occurred in the posterior mandible while the other at the maxilla, mimicking a dentigerous cyst. This is similar to Wright's observation that orthokeratinised OKCs were more often found in a dentigerous cyst in relation to impacted teeth (9). Crowley et al. noted that the location of the orthokeratinised and parakeratinised OKCs was similar, with both occurring more frequently in the mandible. The only significant difference was that the orthokeratinised OKCs occurred more often in the midline than parakeratinised OKCs (7). As there were only two cases of orthokeratinized OKCs observed, there is no statistical value presented.

In conclusion, most clinical features seen in this study are similar to that for the Caucasian populations, such as the age range of the people with OKCs, the predilection for OKCs in males and the predilection for OKCs in the mandible, especially the posterior mandible. The only obvious difference was the peak age of incidence, that ranged from the second to fourth decades with an absence of a second incidence peak. Eleven and a half percent of the OKCs had a clinical presentation similar to dentigerous cysts. As there is a danger of misdiagnosing keratocysts in a dentigerous cyst location, it is important that the final diagnosis be done using histopathological methods in addition to radiographic and clinical examinations.

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