Calcifying Odontogenic Cyst
Case Reports, Variations, and Tumorous Potential

by
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Introduction

Calcifying odontogenic cyst (C.O.C.) was first classified and so named in 1962 by GORLIN et al.[1]. An attempt at classification was later made by PINDBORG et al[2], WHO[3], LUCAS[4] and BASKER[5] who considered it a nonneoplastic cystic lesion but nonetheless classed it under the category of benign odontogenic tumors.

There are a number of reports available in which the disease was regarded as neoplastic in nature. Some of the features presented make its definition as a merely cystic lesion unwarrantable, e.g., epithelial induction and growth with clinical features such as root resorption[6], bone destruction[7] and recurrence[8,9]. These features have led some investigators to define the disease as a neoplastic lesion to be qualified by descriptive terms such as “Cystic calcifying odontogenic tumor”[7], “Dentinogenic ghost cell tumor”[10], “Calcifying ghost cell tumor”[11] and so on. Thus, there is no agreement as to the definition and nomenclature of the disease.

Many reports refer to melanin pigmentation associated with C.O.C.[6,8,13, 14,15]. It is debatable as to whether odontogenic epithelium can produce melanin. LAWSON[16], however, observed melanocyte in the dental germ of a normal human fetus, a finding of interest in view of melanin pigmentation in odontogenic cyst.

Clinical features of the disease so far reported also vary, including those documented by SHEAR[12] and FREEDMAN[7] in a series of 70 cases of C.O.C. and those found in world literature.

In short, there is diversity of variation in the clinical and histopathological features of the C.O.C. so far reported. In the 6 C.O.C. cases, diagnosed according to the criteria of GORLIN et al.[1], light microscopic studies were made of the lesions to compare the results with those of the 94 reported foreign cases (37 reports) and the 56 cases (46 reports) identified in Japan.

Case Report

Case 1 A 13-year-old boy was seen complaining of a swelling extending from the right mandibular incisor region to the mandibular angle. His face looked asymmetrical with the right cheek swollen. A hen’s egg size induration was palpable in the mouth and the oral mucosa was dark red in color. Cutting the specimen revealed that the cyst contained tooth-like structures.
Case 2 A 33-year-old man was seen with swelling of the mouth as his chief complaint. No spontaneous pain was present. On X-ray examination impacted teeth were disclosed within a cystic radiolucent area.

Case 3 A 25-year-old man had a small hen’s egg size swelling extending from the left mandibular first molar to the ascending branch. No changes were detectable in the oral mucosa but fluctuation was palpable.

Case 4 A 9-year-old girl was seen with a mild bulging of the chin with labiobuccal swelling of the gingiva of the left mandibular first to the right second deciduous molar with fluctuation in part of the involved region. X-ray examination revealed a sharply demarcated unicystic lesion extending to the lower margin of the mandible which was interspersed with small calcareous deposits. At the lower margin of the mandible there were 7 impacted teeth with undeveloped roots. A cystectomy was performed to remove the lesion.

Case 5 A 19-year-old man was seen with a painless swelling of the right cheek that had developed about 10 months before. In the mouth the left maxillary canine was missing with swelling of the labial gingiva of the left maxillary central incisor to the second premolar with fluctuation in some of the involved regions. X-ray examination revealed a relatively well-defined radiolucent area extending from the sockets of the involved teeth to the bottom of the maxillary sinus along with a radiopaque region indicative of an impacted left maxillary canine with adjacent calcified material. After extraction of the impacted teeth a cystectomy was performed in such a manner as to imitate a radical operation on the maxillary sinus.
Case 6  A 35-year-old woman was seen complaining of bulging in the region of the right maxillary incisors which had grown gradually over the previous year. No spontaneous pain was present. There was diffuse swelling around the lower ala of the nostrills and the mucosa was normal in color. A hemispheric growth as large as a thumb’s head was present in the region of the right maxillary central and lateral incisors. A parchment-like sound was audible and fluctuation palpable. X-ray examination disclosed root resorption of the left maxillary canine. (Fig. 1)

**Histopathological Findings**

Serial sections stained with hematoxylin-eosin, Masson-Fontana and van Gieson were analyzed. Melanin was identified by Masson’s method (lugol). The 6 cases can be classified into 4 different types:

**Type 1**  
(Case 2,3,5)  
Simple and unicystic lesion morphology showed a thin epithelium covering consisting of 2 or 3 layers. The inner cavity wall was lined with cuboid and squamous epithelium in a palisado arrangement. Small amounts of stellate reticulum and ghost cells were present in some portions of the lesions (Fig. 2). No dental hard tissue or dentinoid existed in the areas which were in contact with the epithelium or connective tissue. Melanin pigment was not present.

**Type 2**  
(Case 4)  
This type was almost solid with scanty cystic spaces. The solid tissue showed odontoids[11] as in a compound odontoma (Fig. 3).
Fig. 3  Low-power view of an intracapsular odontoid in the form of compound odontoma.

Fig. 4  Medium-power view of tooth-like structures in a cyst
Fig. 5  High-power view of melanocyte-like cell seen abutting the basal cell layer

Fig. 6  Medium-power view of melanophores present in the connective tissue
Fig. 7  Low-power view of a large amount of ghost cells in a cyst

Fig. 8  High-power view of the basal cell layer. A process of polarization of nuclei
Epithelial buds of basal cells and islands of odontogenic epithelium were present in the connective tissue of the cystic wall. A large amount of odontoid was seen adjacent to the odontogenic epithelium and connective tissue (Fig. 4). Numerous ghost cells with melanin pigment in the islands of luminal proliferation were seen. Melanocyte-like cells (Fig. 5), which were seen abutting the basal cells, were also present in the form of melanophores in the connective tissue (Fig. 6).

Type 3
(Case 6)

This is the type in which ghost cells occupied most of the cystic space (Fig. 7). Calcification in varying degrees was seen. Calcerous deposits in the form of dentinoids occurred in the areas adjacent to the epithelium. Large amounts of melanin pigment were present in the ghost cells and also in some portions of the matrix surrounding the sites of calcification.

Type 4
(Case 1)

Most of the epithelium underwent ameloblastome island formation and the basal cell layer a process of polarization (Fig. 8). Cyst developed within some of the individual islands. Ghost cells were seen in large numbers with the islands. Odontoids were scattered in some areas adjacent to the epithelium. Melanin pigment was sporadically present in the stellate reticulum.

Literature Review

A comparative study was made of our series of 6 cases along with the 94 cases in 37 foreign reports and 56 cases in 46 reports made public in Japan. Table 1 shows the age distribution of C.O.C. The youngest patient was 9 years of age in Japan and 6 years of age in the foreign reports. The distribution peaked at 10–19 years of age in both the Japanese and foreign reports, as shown in Table 1. The mean age of the patients was 27 in Japan compared to 36 in the foreign reports. Table 2 shows the sex of the patients, the location of the cyst and the presence or absence of complicating odontomas or impacted teeth. No significant differences existed in the age distribution between the sexes. In our series the maxilla was found to be more often affected with a ratio of 7 to 3 in Japan. But the mandibular region in the foreign

<table>
<thead>
<tr>
<th>Age at discovery</th>
<th>Abroad</th>
<th>Japan</th>
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<tbody>
<tr>
<td>0–9</td>
<td>3(3%)</td>
<td>2(4%)</td>
</tr>
<tr>
<td>10–19</td>
<td>25(27%)</td>
<td>26(50%)</td>
</tr>
<tr>
<td>20–29</td>
<td>15(17%)</td>
<td>9(17%)</td>
</tr>
<tr>
<td>30–39</td>
<td>10(11%)</td>
<td>5(9%)</td>
</tr>
<tr>
<td>40–49</td>
<td>8(9%)</td>
<td>3(6%)</td>
</tr>
<tr>
<td>50–59</td>
<td>11(12%)</td>
<td>3(6%)</td>
</tr>
<tr>
<td>60–69</td>
<td>12(13%)</td>
<td>1(2%)</td>
</tr>
<tr>
<td>70–79</td>
<td>6(7%)</td>
<td>3(3%)</td>
</tr>
<tr>
<td>80–89</td>
<td>1(1%)</td>
<td>0(0%)</td>
</tr>
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Age distribution was not identified or could not be determined in 10 cases.
reports showed 6 to 4. In Japan 33% of the teeth were impacted compared with 6% in the foreign reports.

**Discussion**

FREEDMAN et al.[7] and SHEAR[12] were each able to collect 70 cases of C.O.C. Our present study covered a total of 60 cases and 46 reports found in Japan and 94 cases and 37 reports from abroad. Some of the data thus obtained are outlined below. The ages of our subjects were from 9–71 years in Japan with teenagers constituting the peak age group. The peak incidence of patients in the same age group was also reported by FREEDMAN et al[7], whereas SHEAR[12] pointed out another peak of age distribution at 60–69 years.

Some investigators including FEJERSKOV et al.[11], EDA[17] and Lucas[4] found that the disease occurred more frequently in the maxillary than the mandibular region, whereas FREEDMAN et al.[7], ALTINI et al.[18] and BASKER[5] reported the disease to be of comparable incidence in both these regions. In our series the maxilla was found to be more often affected with a ratio of 7 to 3 in Japan. But, the mandibular region in the foreign reports was 6 to 4.

The disease was also frequently complicated by the impaction of a tooth, the incidence being 20% according to FEJERSKOV et al.[11] and 33% in Japan compared to 6% in the foreign reports in our series. There were no significant differences in clinical findings between our present series and a series of 111 cases of adenomatoid odontogenic tumor reported by GIANsANTi[19] et al., suggesting the difficulty of making a clinical diagnosis of C.O.C. in these cases.

Type 1 or the simple unicystic type is almost structurally similar to other cysts of odontogenic nature and is distinct from other types, i.e., Type 2 the odontoma producing type, Type 3 the ghost cell dominant type and Type 4 the ameloblastoma producing type. Assuming that the tumor represents a growth of monoclonal cells, then Type 2, 3 and 4 are clearly dissimilar to other odontogenic cyst in that they all present features suggestive of a neoplastic potential. In 6 of our cases having a definite diagnosis of C.O.C., 4 distinct histopathological types could be identified.

ABRAMS et al.[6] considered that a C.O.C. complicated by an odontoma resulted from the processes of differentiation and degeneration of the odontogenic epithelium. EDA[17], SARK[13] postulated that epithelium and connective tissue might induce one another to differentiate into dental hard tissue. The formation of ameloblastoma proliferations makes it highly likely that the tumor is derived from odontogenic
epithelium. The so-called ghost cells are reported to be a result of an abnormal type of keratinization with an affinity for calcification[20]. It appears in association with craniopharyngioma, calcifying epithelioma of malherbe[21], ameloblastic fibro-odontoma[22] or complex-compound odontoma[23,24,25]. Ghost cells in C.O.C. are believed to be of an odontogenic epithelial origin. Their development is ascribed to an abnormal process of differentiation because of a lack of evidence to the contrary.

Duckworth et al.[26] observed melanocytes in odontogenic epithelium and Lawson et al.[16] confirmed the presence of melanocytes in the dental germ of normal fetuses. The embryologic fact that both melanocytes and dental germs are generated at 5–6 weeks of embryonic life makes it very likely that the former erratically gains entrance to the latter. However, there are no available reports so far concerning the presence of melanin pigment in odontogenic cysts (so-called dentigerous cysts) as in some of our experiments. Melanin pigment is often seen in the presence of a tumor. In pigmented squamous cell carcinoma[27] and some basal cell carcinoma, there is a growth of basal cells in conjunction with a proliferation of melanocytes. In our present series a number of pigment blockade melanocyte-like cells were seen adjacent to the odontogenic epithelium. This suggests that melanocytes undergo activation and proliferation in response to an increasingly high degree of differentiation of the odontogenic epithelium. Melanin pigment was observed in all the neoplastic type cases in the present series, although this is not the case in some previous reports. The explanation is that melanocytes are not present in all dental germs.

It is of great interest to note that the presence of melanin pigment is a feature common to odontoma-producing or ghost cell dominant types and ameloblastic proliferation marked by a high degree of differentiation and neoplastic nature. Such melanin pigment is absent in other types of odontogenic cyst, suggesting that a clinical distinction should also be made between C.O.C. and other cystic diseases.

Conclusion

Six new cases of C.O.C. were subjected to light microscopic investigation. These cases fell into 4 different histologic categories: 1) the simple unicystic type, 2) the odontome-producing type, 3) the ghost cell-dominant type and 4) the ameloblastoma-producing type. The latter 3 types of C.O.C. were associated with the presence of melanin pigment in the cyst when it was highly differentiated.

An effort was made to gather as many cases as possible from the series documented both in Japan and abroad, in which a diagnosis of C.O.C. was established or appeared to be justifiable.

Note: While this paper was in press, Soames et al. observed a pigmented new variant of calcifying odontogenic cyst similar to ours. (Soames, J. V. et al.: Oral Surg 53: 395–400, 1982)

References