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Calcifying epithelial odontogenic tumor: An updated analysis of 339 cases reported in the literature

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ABSTRACT

Purpose: The aim of this study was to integrate the available data published on calcifying epithelial odontogenic tumors (CEOT) into a comprehensive analysis of its clinical and radiologic features.
Materials and methods: An electronic search was undertaken in May 2016. Eligibility criteria were publications having enough clinical, radiological and/or histological information to confirm definite diagnosis.
Results: A total of 362 lesions were found, 339 with enough information were analyzed. Variants clear cells (n = 33) and Langerhans cells (n = 10) were rarely described in the literature, as well as lesions with malignant transformation (n = 8). Central lesions (n = 264) were more prevalent than their peripheral counterparts (n = 24). A higher prevalence characterized the mandible, posterior region, and third and fourth decades. About 40% of the peripheral lesions showed signs of underlying bone erosion, and about half of the central ones showed signs of cortical bone perforation. Recurrence was found in all lesions (12.6%), peripheral lesions (18.8%), central lesions (11.6%), clear cell (10.7%), Langerhans cell (0%), and those with malignant transformation (42.9%). Excision or curettage was associated with the highest recurrence rate. None of the variables showed a statistically significant influence on the recurrence rate.
Conclusions: The possible locally aggressive behavior of the lesions recommends a less conservative management than simple curettage. The clear cell variant shows similar demographic data and biological behavior compared to the non-variant lesions, suggesting that the presence of clear cells does not have an important clinical significance.

1. Introduction

The calcifying epithelial odontogenic tumor (CEOT), also called the Pindborg tumor, is an epithelial odontogenic neoplasm first reported by Thoma and Goldman (1946) some 70 years ago. CEOT is predominantly an intraosseous (central) neoplasm, but it also occurs as a rare, less aggressive peripheral (extraosseous) tumor (Afrogheh et al., 2014). Two variants of CEOT have been described in the literature: the clear cell CEOT and the Langerhans cell CEOT, first reported in 1967 by Abrams and Howell (1967) and in 1990 by Asano et al. (1990), respectively.

Cases of CEOT are not so often reported in the literature. Epidemiological study of such rare lesions is of great importance because it provides information that can improve the diagnostic accuracy and will allow pathologists and surgeons to make informed decisions and refine the treatment plan to optimize the clinical outcome. The aim of the present study was to integrate the available data published in the literature on CEOT into an updated comprehensive analysis of its clinical and radiologic features, as well as the frequency of recurrence.

2. Materials and methods

This study followed the PRISMA Statement guidelines (Moher et al., 2009). A review protocol does not exist.

2.1. Search strategies

An electronic search without time restrictions was undertaken in May 2016 in the following databases: PubMed/Medline, Web of Science, and Science Direct. The following terms were used in the

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search strategies: (calcifying epithelial odontogenic tumor) OR (Pindborg tumor).

Google Scholar was also checked. A manual search of related journals, including *Acta Oto-Laryngologica*, *Annals of Otology Rhinology and Laryngology*, *British Journal of Oral and Maxillofacial Surgery*, *Cancer*, *Head & Neck*, *Head and Neck Pathology*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Dental Research*, *Journal of Craniofacial Surgery*, *Journal of Cranio-Maxillofacial Surgery*, *Journal of Laryngology and Otology*, *Journal of Maxillofacial and Oral Surgery*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Oral Pathology and Medicine*, *Laryngoscope*, *Oral Diseases*, *Oral Oncology*, *Oral Surgery Oral Medicine Oral Pathology Oral Radiology*, *Otolaryngology – Head and Neck Surgery*, and *Quintessence International*, was performed. The reference list of the identified studies and the relevant reviews on the subject were also scanned for possible additional studies. Publications with lesions identified by other authors as being CEOT, even not having the terms "calcifying epithelial odontogenic tumor" or "Pindborg tumor" in the title of the article, were also re-evaluated by an author of the present study.

2.2. Inclusion and exclusion criteria

Eligibility criteria included publications written in any of the official European languages reporting cases of CEOTs. The studies needed to have enough clinical, radiological and histological information to confirm a definite diagnosis of CEOT. The definitions and criteria of the World Health Classification of Tumors–Head and Neck Tumors book (WHO, 2005), were used to diagnose a lesion as CEOT. Although we have used the WHO criteria of 2005 for CEOT diagnosis, reports of studies that did not perform specific staining for amyloid deposition were not excluded. Randomized and controlled clinical trials, cohort studies, case–control studies, cross-sectional studies, case series, and case reports were included. Exclusion criteria were immunohistochemical studies, histomorphometric studies, radiological studies, genetic expression studies, histopathological studies, cytological studies, cell proliferation/apoptosis studies, in vitro studies, and review papers, unless any of these publication categories reported any cases with enough clinical, radiological and histological information.

2.3. Study selection

The titles and abstracts of all reports identified through the electronic searches were read independently by the authors. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained. Disagreements were solved by discussion between the authors. The clinical and radiological aspects, as well as the histological description of the lesions reported by the publications, were thoroughly assessed by one of the authors of the present study, who is an expert in oral pathology (R.S.G.), to confirm the diagnosis of CEOT.

2.4. Data extraction

The review authors independently extracted data using specially designed data extraction forms. The data extraction forms were piloted on several papers; these were modified as required before use. Any disagreements were solved by discussion. For each of the identified studies included, the following data were then extracted on a standard form, when available: year of publication, number of patients, patient sex, age and race, follow-up period, duration of the lesion previously to treatment, lesion location in relation to the jaws (maxilla/mandible), specific location and extension of the lesion, recurrence, recurrence period, lesion size, histological features, presence of erosion of the subjacent cortical bone (for peripheral lesions), cortical bone perforation, locularity (unilocular/multilocular), presence of radiopacities in the radiological examinations, association of the lesion with a tooth (the tooth could either be erupted with the entire root(s) encompassed by the lesion or unerupted encompassing the entire tooth), and tooth displacement and tooth root resorption due to lesion growth. The lesion size was determined according to the largest diameter. Although focal areas that resemble CEOTs may be found in some adenomatoid odontogenic tumor (AOT), as these tumors behave like AOT, they were not considered for this study. Contact with authors for possible missing data was performed.

2.5. Data analyses

The mean, standard deviation (SD), and percentages were presented as descriptive statistics. The Kolmogorov–Smirnov test was performed to evaluate the normal distribution of the variables, and the Levene test was used to evaluate homoscedasticity. The performed tests for two independent groups were the Student *t*-test or Mann–Whitney test, depending on the normality. The Pearson chi-squared or Fisher exact test was used for categorical variables, depending on the expected count of events in a 2×2 contingency table. The probability of recurrence was calculated for seven variables, in odds ratios (95% confidence intervals). The variables were (a) locularity, (b) presence of radiopacities in the radiological examinations, (c) association of the lesion with a tooth, (d) perforation of cortical bone, (e) lesion location (maxilla/mandible), and (f) tooth displacement and (g) root resorption due to lesion growth. The degree of statistical significance was considered as $p < 0.05$. All data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS) version 23 software (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Literature search

The study selection process is summarized in Fig. 1. The search strategy in the databases resulted in 1417 papers. Search in Google Scholar resulted in 29 eligible papers not found in the three main databases. A total of 486 articles were cited in more than one database (duplicates). The reviewers independently screened the abstracts for those articles related to the study. Of the resulting 960 studies, 617 were excluded for not being related to the topic. Additional hand-searching of journals and of the reference lists of selected studies yielded 7 additional papers. The full-text reports of the remaining 350 articles led to the exclusion of 105 because they did not meet the inclusion criteria. Thus, a total of 245 publications were included in the review.

3.2. Description of the studies and analyses

A total of 245 publications (see Supplementary Appendix) were included in the present review, with 362 CEOTs. Two publications deserve some consideration. The first one is Buchner et al. (2006), which listed 45 cases of peripheral odontogenic tumors, of which 6 were CEOTs (5 central, 1 peripheral). However, the authors did not provide details about these 6 lesions. The second publication is Azevedo et al. (2013), listing 19 CEOTs (17 central, 2 peripheral), but with only a few details about the lesions, and still not separately by each case. The 2 peripheral lesions of this publication were the ones described in detail by Abrahão et al. (2009), and these entered the present analysis, but not the 17 central CEOTs. Thus, of the total of