Odontogenic Keratocyst: A Literature Review

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Summary

Odontogenic Keratocyst is a lesion located in the maxilla and mandible, being highlighted by its destructive, aggressive properties and high potential for recurrence. Its prevalence is established between 10 and 12% of odontogenic cysts, reaching more males. Microscopically, it presents a thin cystic layer, with squamous epithelial limiting stratified and flat epithelium-conjunctiva junction. Radiographically, they present well-defined edges, sclerotic edges, and may have tooth involvement included. The differential diagnosis occurs through microscopic study of the biopsy and by puncture of the fluid contained inside the lesion. They can be easily confused with ameloblastoma, dental cysts, ameloblastic fibroma, calcifying odontogenic cyst, lateral periodontal cyst, traumatic bone cyst, denomatoid odontogenic tumor, giant cell central lesion, and cyst of the palatine duct, since it does not present pathognomonic characteristics. The main treatments proposed are marsupialization, decompression, enucleation with adjuvant therapies and surgical resection with safety margins.

Keywords: Odontogenic Keratocyst; Diagnosis; It's a treatment

Introduction

Odontogenic cysts are usually benign lesions with a high probability of occurrence in the gnathic bones, coated with epithelium derived from the tissues that give rise to the teeth and are observed in dental practice by radiographic examinations of Routine. Thus, for its diagnosis it is necessary to associate clinical examination, complementary imaging exams together with histopathological [1].

In addition, it is worth mentioning that among the odontogenic cysts, those with the highest predominance in the population are: root cyst, dentiger and keratocistodontogenic [2].

Keratocyst odontogenic (CO) presents a slow and continuous growth, manifesting in most cases in the posterior region of the mandible. Depending on their size, patients may experience pain and increased volume in the region. In view of this, it differs by being an aggressive, expansive and recurrent lesion [3].

Among the predisposing factors for the development of CO, Gorlin-Goltz syndrome (GGS) is associated. As a result of the alteration of pro-oncogenes or tumor suppressor genes, SGG accompanies a set of manifestations, the most common being the presence of numerous basal cell carcinomas and odontogenic keratocysts in the jaws, associated with palmoplantar hyperkeratosis, skeletal anomalies, ectopic intracranial calcifications and facial dysmorphia [4].

Epidemiological studies have shown that this odontogenic lesion affects more males in the second and third decades of life. When multiple cases of odontogenic keratocysts occur or are developed sequentially, the association with Gorlin syndrome should be investigated [5,6].

Thus, this literature review study aims to describe the diagnosis, treatment and prognosis of odontogenic keratocyst.

Literature Review

Odontogenic keratocyst is characterized by a cystic lesion and may be associated with the remnants of the dental lamina or extensions of the cells of the basal layer of the oral squamous epithelium [7,8]. This cystic lesion needs close attention, as it presents a high recurrence rate, aggressiveness, differentiated histopathological aspects and present genetic alterations [9,10]. In view of the genetic alterations, there is a modification of the patched gene (PTCH) which is a tumor suppressor gene located on chromosome 9q22.3-q311, 2, 4, 5. PTCH performs the function of a component of the Hedgehog signaling pathway. Hedgehog genes encode signaling molecules that play a key role in embryonic standardization, conservation of hemostasis in old tissues, tissue repair, and carcinogenesis. In addition, it is possible that other defects within the Hedgehog signaling pathway may be responsible for some of the syndrome’s defects, and these would naturally be affected by epithelial proliferation. However, there is expression of different mutations within the same gene and/or effects of modified genes and environmental factors. Therefore,
spectrum of differentiated clinical and genetic anomalies can be analyzed in patients and their affected relatives [11].

Initially, the CO is mostly asymptomatic, being detected through radiographic examinations, tomographies and biopsies for analysis. In more advanced states, it may develop signs and symptoms such as increased volume, pain, paresthesia, changes in tooth positioning, and trismus [5,6].

In its radiographic aspect, this cystic lesion may be uni or multilocular showing radiolucent, well-defined characteristic, sclerotic edges, and may have tooth involvement included [5,12].

Histologically, it is characterized by a cystic cavity coated with parakeratinized stratified pavement epithelium, presenting cell layers with corrugated edges. The basal layer cells are found with hyperchromatic nuclei and are arranged pale. Its capsule is formed by fibrous connective tissue, and may develop small cysts-children [5,6,12] When infection involves, and the common histological conformations are modified, with the replacement of the epithelial lining by hyperplastic. Rarely, CO may undergo dysplastic variations or malignant evolution to squamous cell carcinoma [5,6,7].

In the literature, there are several treatment options for odontogenic keratocyst. They are: marsupialization, enucleation, decompression, to decrease the pressure inside the cystic cavity; enucleation followed by adjuvant therapies (Carnoy solution, peripheral osteotomy, cryotherapy or electrocautery); and surgical resection, being a recommended method in view of recurrence rates, always prioritizing a safety margin and performing a bone graft for large lesions [5].

Prognosis is established through histopathological characteristics, and the para keratinized epithelium is considered with a higher degree of sombreadity, due to its greater tendency to relapse. However, histopathological aspects presenting orthosanated epithelium are less likely to relapse. The potential for recurrence usually develops in the first and second postoperative year, and will depend on the origin of the lesion and its surgical intervention [13].

Methodology

To achieve the objective of this study, a literature search was conducted, based on publications of scientific articles from journals of virtual database sites, such as: Scientific Electronic Library Online (SciELO), Virtual Health Library (VHL) Brazil, Latin American and Caribbean Literature on Health Sciences (LILACS) and Medical Publications (PUBMED). The descriptors used were: odontogenic cyst, keratocystodontogenic, odontogenic keratocyst and cystic lesion.

The eligibility criteria for the selection of studies were: to be original studies, which address the theme highlighted, in the languages Portuguese, English and Spanish, with a summary available in the databases for evaluation, and studies published in journals, journals specialized or indexed in these databases until 2019.

Exclusion criteria will be: articles in any languages other than English, Spanish or Portuguese; studies that were presented in duplicate between the bases, whose theme did not contemplate the objective proposed in this study, or that are not available in the digital environment.

Data collection occurred from October to December 2019, followed by a thorough evaluation of the studies found, which included an exploratory, selective, analytical and interpretative reading. When 119 articles with this theme were found and after the application of the criteria 28 articles were selected.

Discussion

According to the authors, and numerous discussions about the origin and characteristics of odontogenic keratocysts (CO), such as its high recurrence rate, and its association with the presence of genetic alterations, such as mutations in the PTCH gene, although such evidence was not sufficient for the treated lesion to be considered a tumor, therefore, in the current WHO classification in 2017 at the 28th Congress of the European Society of Pathology, [14] THE is again described as a cystic odontogenic lesion. This thesis was supported due to the analysis that other cysts, such as dental cysts, also present alterations in the PTCH1 gene, such as loss of heterozygosity [15] added to this, a study that also revealed regression of these lesions after decompression [16]. Due to this, in the new WHO classification, the possibility of CO being a neoplastic lesion has not been ruled out, however, current evidence is few to consider it as a tumor. Because of this, disarmed attention, since in addition to having high recurrent power due to its friable capsule and the presence of satellite cysts, it has a clinical characteristic of growth quite interesting that would be the preferential growth in the medullary bone, a fact that makes its diagnosis very late, discovered only in routine radiographic examinations [17].

Keratocyst expands in an axifpae form, and presents mural growth in the anteroposterior sense, with tissue proliferation to the interior of the spongy bone. It can then reach considerable size before bone expansion becomes clinically apparent. In addition, it tends to appeal, leading to the statement that it is aggressive and has an inherent growth potential [18].

Hardly, small odontogenic keratocysts are diagnosed, because they are usually asymptomatic, that is, they are discovered only during the course of a radiographic examination. Large odontogenic keratocysts may be associated with pain, edema, or drainage. However, extremely large cysts are not sporadic to be asymptomatic. Multiple odontogenic keratocysts may be present and such patients should be evaluated for other manifestations of basal cell nevoid carcinoma syndrome (Gorlin) [19].
Over the years some authors have considered the hypothesis of CO representing a neoplastic condition [9,10,20]. This hypothesis is based on the facts of the high expression of proliferative markers and bcl-2 protein, the loss of heterozygosity or methylation of tumor suppressor genes, in addition to mutation in homologous tumor suppressor gene 1 to the patched Drosophila gene (PTCH1) [10,15,20]. Consequently, in 2005 the WHO (World Health Organization) classified it as a tumor called a “keratocystic odontogenic tumor”, due to its aggressive biological behavior, which resembles aspects of a neoplasm.

There are different forms of treatment for CO such as: marsupialization, decompression, enucleation with adjuvant therapies (Carnoy solution, peripheral osteotomy, cryotherapy or electrocautery); and surgical resection with safety margins [5].

In moreover, there is a survey and therapeutic tests aimed at more conservative interventions, especially in individuals with multiple, recurrent or wide lesions, intervening in elements of the hh [10].

Thus, studies were conducted to minimize cystic injury, such as an experiment by Ally et al. [21] with the use of the Hh pathway inhibitor (Vismodegib), orally (150mg/day for 18 months), where he observed that the drug reduced the diameter of the lesions.

Goldberg et al. [22] cited the almost total resolution of three keratocysts in a patient who had Gorlin Syndrome, who in turn received the Hh pathway inhibitor as a possible treatment, GDC-0449. Conducted an in vitro study of human primary CO cells in conjunction with smo antagonist, which paralyzed cell development, in addition to the negative balance of the Hh signaling pathway. However, further studies on the subject are needed in order to achieve an ideal therapeutic modality.

Conclusion

Although the pathological clinical aspects of CO are well established in the literature, the importance of a correct diagnosis is essential to establish the appropriate treatment plan. Being marsupialization or decompression, the most used due to its high success rate in relation to the most aggressive treatments, since they promote a lower morbidity and preserve important structures, such as dental units and nerves.After reviewing the literature, it was possible to conclude that the odontogenic lesion has a cystic nature, due to comparative analysis with other cysts, as well as dentiger cysts, they also present alterations in the PTCH1 gene and loss of heterozygosity.

References

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