

ODONTOGENIC KERATOCYSTS: A 22-YEAR EPIDEMIOLOGICAL STUDY AND CASE REPORT

Queratocisto odontogênico: um estudo epidemiológico de 22 anos e relato de caso

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ABSTRACT

Odontogenic Keratocyst (OKC) is a cyst that presents local aggression and a high recurrence; thus, a better understanding of its clinical characteristics and treatment options is required. The aim of this study is to report a case and describe the epidemiology and characteristics of OKCs diagnosed at a referral service for patients with oral lesions. Patients with histopathological diagnosis of OKC were included in the sample over 22 years. The study highlights the demographic and clinical-radiological characteristics, as well as the treatment options. In addition, a case of an extensive OKC in the mandible is reported. 3064 medical records were analyzed and 16 cases of OKC (0.52%) were found, with two recurrences (12.5%). The mean age of the patients was 33.19 years,

being the third decade of life more affected (31.25%), with equal prevalence for both sexes. The mandible was more affected (68.75%), mainly its body. The differential diagnosis included the dentigerous cyst (11.54%) and the ameloblastoma (11.54%). The most frequent treatment was the curettage enucleation (50%). In the reported case, enucleation associated with cryotherapy was performed, followed by rehabilitation with xenogen graft and osseointegrated implant. OKC presents a wide spectrum of differential diagnoses due to its non-specific clinical-radiographic characteristics. The case reported shows that treatments such as enucleation may be efficient when accompanied by adjuvant techniques.

Keywords: Epidemiology. Diagnosis. Odontogenic cysts.

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RESUMO

O Queratocisto Odontogênico (QO) é um cisto que apresenta agressividade local e alta taxa de recorrência, necessitando de um profundo entendimento acerca das características clínicas e opções de tratamento. O objetivo deste estudo é apresentar um caso clínico e descrever a epidemiologia e as características de QOs diagnosticados em um serviço regional de referência a pacientes com lesões bucais. Pacientes com diagnóstico histopatológico de QO foram incluídos na amostra ao longo de 22 anos. O estudo destaca as características demográficas, clínico-radiológicas e tratamento, além de relatar um caso clínico de um extenso QO em mandíbula. Dos 3064 prontuários avaliados retrospectivamente, foram encontrados 16 casos de QO (0,52%), com duas recidivas (12,5%). A média de idade dos pacientes foi de 33,19 anos, com maior frequência na 3ª década de vida (31,25%) e com mesma prevalência para ambos os sexos. A mandíbula foi mais acometida (68,75%), principalmente o corpo. O diagnóstico diferencial incluiu o cisto dentígero (11,54%) e o ameloblastoma (11,54%). A escolha terapêutica mais frequente foi a enucleação seguida de curetagem (50%). No caso relatado, a enucleação associada à crioterapia foi o tratamento de escolha, seguido de reabilitação com enxerto xenógeno e implante osseointegrado. O QO apresenta um amplo espectro de diagnósticos diferenciais devido às suas características clínico-radiográficas inespecíficas. O caso clínico relatado reforça que tratamentos como a enucleação podem ser eficientes quando acompanhados de técnicas adjuvantes.

Palavras-chave: Epidemiologia. Diagnóstico. Cistos odontogênicos.

INTRODUCTION

Odontogenic keratocyst (OKC) was classified by the World Health Organization (WHO) as an odontogenic tumor in 2005, being admitted as a keratocystic odontogenic tumor (KCOT) due to its aggressive behavior and its potential for recurrence¹. In 2017, the WHO reclassified it as a cyst².

The OKC is an odontogenic cyst, with locally invasive and infiltrative growth, with a recurrence rate of 62%^{3,5}, depending on the type of treatment, which makes this lesion quite unique^{3,6}. The lesion is among the most prevalent pathologies in the epidemiological studies of maxillary bone lesions^{7,9}, with indexes varying from 19.50%¹⁰ to 74.20%⁹. Epidemiological studies are essential, since they allow for a more accurate establishment of the occurrence of OKC in different populations, which helps in establishing a diagnostic hypothesis and planning a biopsy based on clinical and radiographic characteristics¹¹. In addition, knowledge of the clinical-pathological characteristics recorded in various populations can help identify possible causes associated with these lesions¹.

The aim of this study is to report a case and describe the epidemiology and characteristics of OKC in a regional reference service in Brazil and compare the findings with other studies available in international databases.

MATERIAL AND METHODS

After ethical approval (CAAE # 50017015.6.0000.0104), this retrospective and observational study was developed according to Helsinki Declaration. Data from medical records of patients referred to the Service of Oral Diagnosis of the Maringa State University (LEBU/UEM) from 1995 to 2017 were collected. Diagnoses were adapted to the 2017 WHO classification, and only confirmed cases of OKC by histopathological examination were included. The following demographic data were collected: age, sex, race, lesion location, clinical signs and symptomatology, image findings, differential diagnosis, treatment modality, and follow-up. The descriptive statistics of the data were performed using Software R version 3.3.1.

RESULTS

Among a total of 3,064 records of the 22 years examined in this study, 16 cases (0.52%) of OKC were identified, with two recurrences (12.5%). The mean age of the patients was 33.19 years, with a wide range varying from 13–54 years. The most often affected patients were in the third decade of life (31.25%). Thirteen (86.67%) patients were leukodermas, and the prevalence of CCA was the same for both sexes. Recurrences were observed after an average period of 2.5 years. Both in women, in the right mandibular body and in the third and fifth decades of life. In one patient, the first treatment was not recorded and in the other case the excisional biopsy was performed. After recurrence, enucleation and decompression were performed, respectively.

In the physical examination, seven patients (43.75%) had mild asymmetry, six patients (37.5%) had no clinical signs, and three medical records did not contain this information. Regarding the symptomatology, nine (56.25%) patients presented with pain and seven (43.75%) were asymptomatic.

The mandible was the most commonly affected area, with 11 (68.75%) cases. The most commonly affected regions were the right mandibular body, the ramus, and the angle of the left mandible and the right maxilla, as described in Table 1.

Table 1: Distribution of the anatomical location of the OKCs.

Region	Frequency	%
Right posterior maxilla region	3	18.75
Left posterior maxilla region	1	6.25
Anterior maxilla region	1	6.25
Right mandibular ramus	1	6.25
Right mandibular body	4	25
Left mandibular body	1	6.25
Right mandibular ramus and angle	1	6.25
Left mandibular ramus and angle	3	18.75
Left mandibular ramus, body and angle	1	6.25
Total	16	100

Regarding the radiographic findings, all patients had radiolucent lesions with a radiopaque halo, of which two (13.33%) were not well delimited.

In relation to the differential diagnosis, the OKC hypothesis was raised in 11 cases (42.31%). In three patients (11.54%), dentigerous cyst was considered, since the third molar was impacted, and in three patients (11.54%) ameloblastoma was included in the diagnostic hypotheses. Other lesions have been suggested, such as nasopalatine duct cyst, residual cyst, simple bone cyst, aneurysmal bone cyst, central giant cell granuloma, ameloblastic fibroma, odontogenic myxoma, cicatricial fibrosis, and bone sequestration.

Eight patients (50%) were treated with enucleation followed by curettage, four (25%) by marsupialization followed by enucleation and curettage, two (12.5%) by marsupialization, and two (12.5%) by decompression. Surgical treatment of recurrence was classified in the same treatment group as primary lesions. No case was associated with Gorlin-Goltz Syndrome. The follow-up time was up to nine years after treatment.

CASE REPORT

A 41-year-old man, leukoderma and asymptomatic was referred with a panoramic radiography for implant planning that revealed a well-delimited multilocular radiolucent lesion of approximately 6cm, with a radiopaque halo and located in the posterior region and right mandibular ramus, apically and distally to the right third molar (Figure 1).



Figure 1: Initial panoramic radiograph shows an extensive, multilocular radiolucent lesion with scalloped borders, delimited by a radiopaque halo in the posterior region and the mandibular ramus, extending towards the right-side coronoid process.

Physical examination revealed no swelling, and the right third molar exhibited pulp vitality. Cone-beam computed tomography (CBCT) showed a scalloped multilocular hypodense area with evident septa and no signs of bone cortical perforation. Axial reconstructions revealed a slight expansion of the cortices in the posterior region and a more pronounced expansion of the lingual cortical bone in the ascending ramus, close to the coronoid process. No external root resorption of tooth 48 was detected, and the mandibular canal was displaced inferiorly (Figure 2).

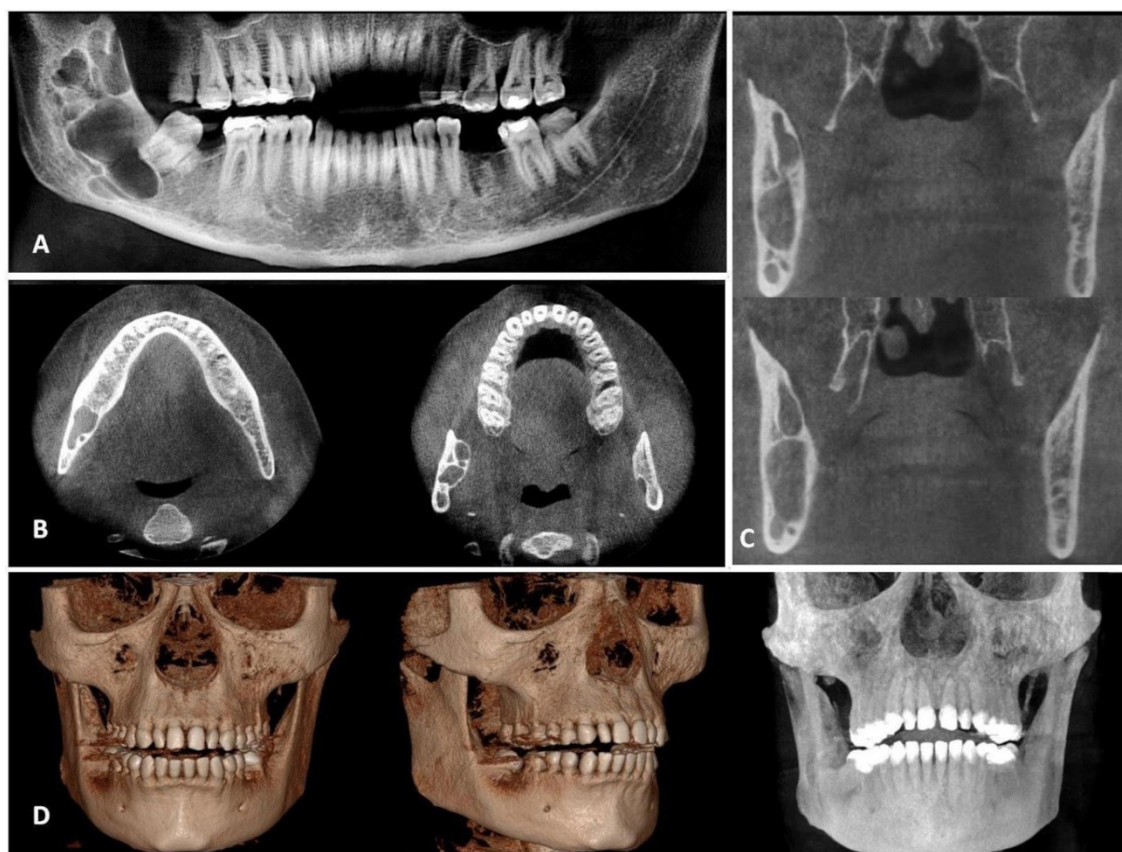


Figure 2: (A) Panoramic coronal section; (B) coronal reconstructions; (C) three-dimensional images; and (D) showing a scalloped multilocular hypodense area with evident septa showing signs of discrete cortical expansion without perforation.

The presumptive diagnoses were of OKC, solid ameloblastoma, ameloblastic fibroma, and odontogenic myxoma. After incisional biopsy, the histopathological examination showed a thin fibrous capsule and parakeratinized surface epithelium and a basal layer showing palisaded and hyperchromatic cells. An excessive degree of epithelial lining folds was also visible as well as a flat epithelial-conjunctive junction, confirming the diagnosis of OKC (Figure 3).

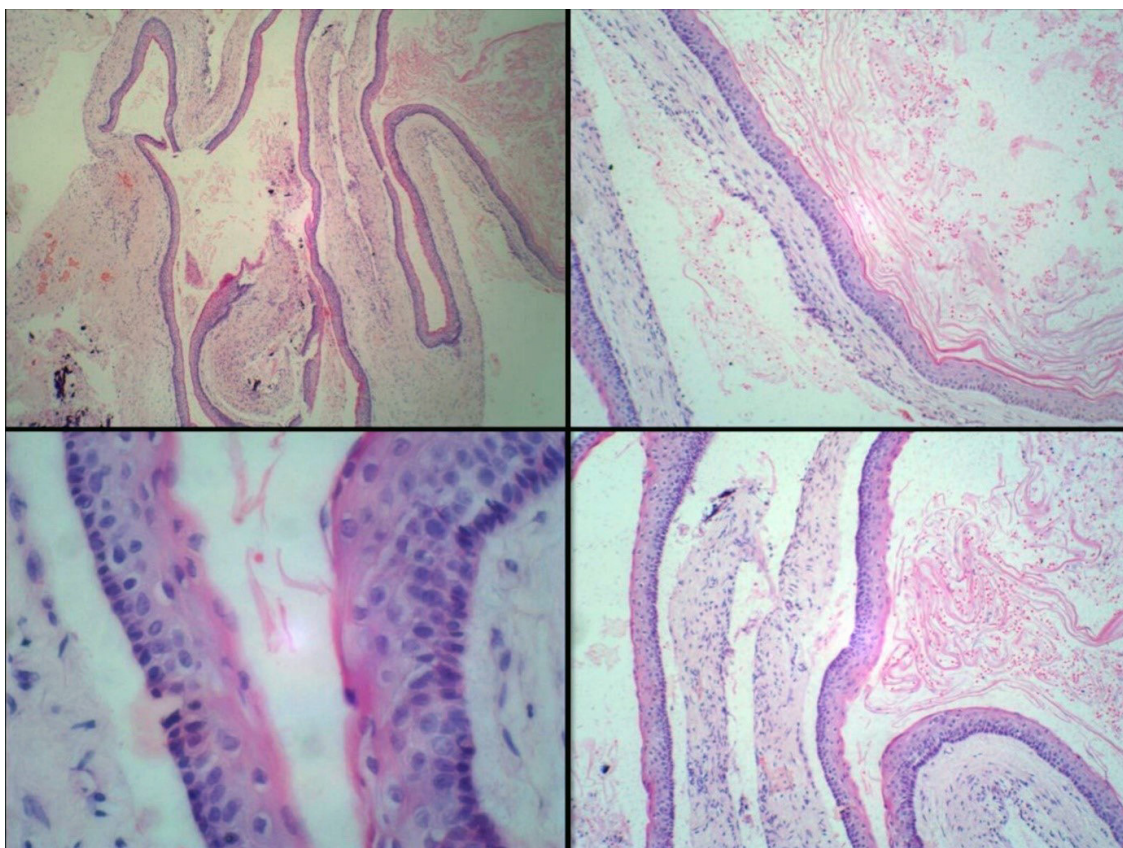


Figure 3: Thin fibrous capsule and parakeratinized surface epithelium and a basal layer showing palisaded and hyperchromatic cells. An excessive degree of epithelial lining folds was also visible as well as a flat epithelial-conjunctive junction (hematoxylin and eosin).

Enucleation followed by cryotherapy with liquid nitrogen spray (two 30-second intervals and lavage with saline solution) under general anesthesia was performed. The cavity was filled with freeze-dried bovine bone graft with osteoconductive properties (Bio-Oss®, Geistlich Biomaterials, Switzerland) and bovine bone cortical resorbable membrane (GenDerm Baumer®, Mogi Mirim, São Paulo, Brazil), to provide a natural osteoprotective biological barrier, allowing for bone remodeling. During surgery, the right third molar was also extracted.

After 10 months, the osseointegrated implant was installed at the surgical site and 45 days later the patient was released for prosthesis preparation. (Figure 4A). At two-year follow-up, panoramic radiography showed bone not completely remodeled although the implant was osseointegrated and functional, with no signs of recurrence (Figure 4B).

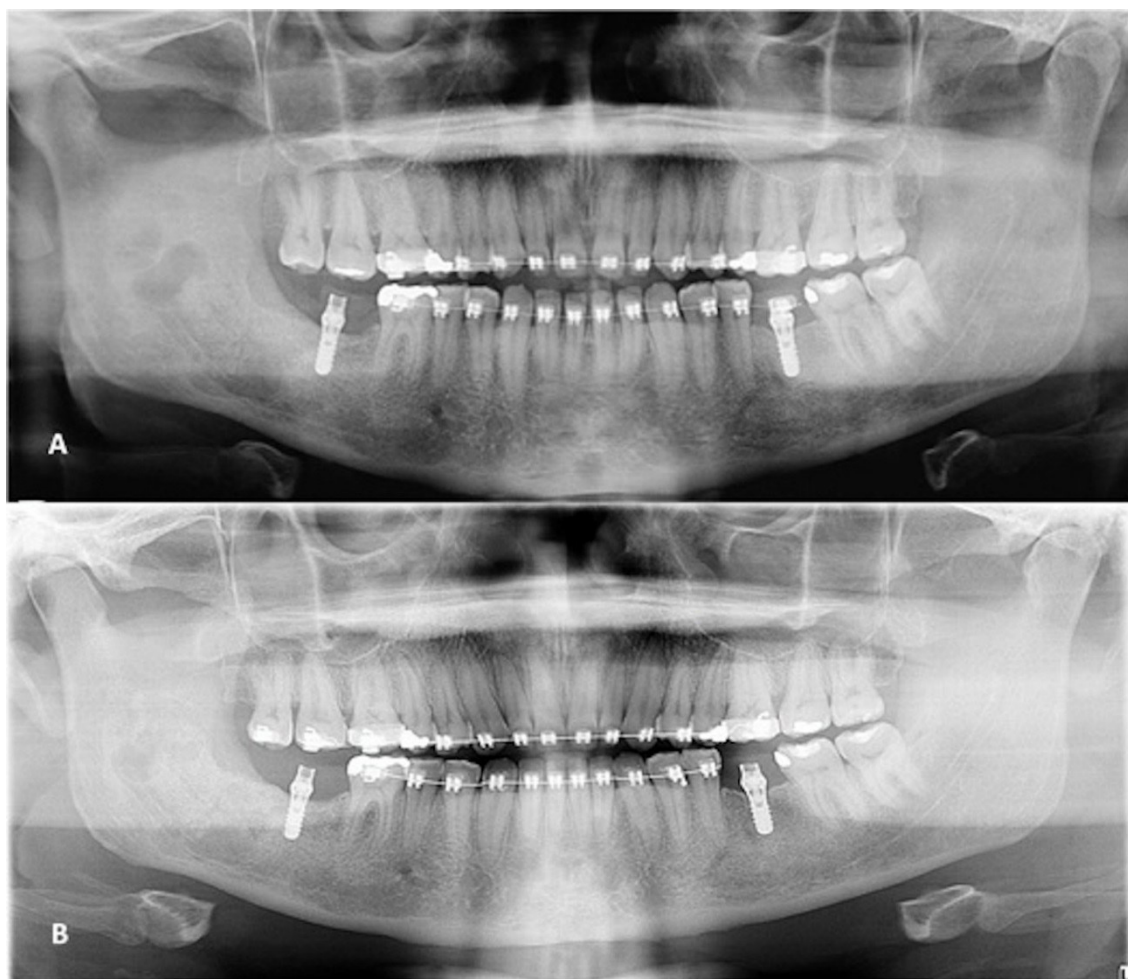


Figure 4: (A) 10-month follow-up panoramic radiograph showing the implant, with no signs of recurrence. (B) 2-year follow-up panoramic radiograph.

DISCUSSION

Epidemiological studies on odontogenic cysts and tumors are widely reported in the scientific literature, with emphasis on more destructive lesions such as OKC^{7,9,11}. In the present study, the prevalence of OKC was 0.52% when all patients were considered. When only cysts were considered, OKC represented 5.7% of the sample. If considered as a tumor, OKC represented 4.5% of cases (46.87%)¹². The literature indicates a variation in the prevalence of OKCs in different geographic regions. The prevalence of OKC was 19.5% in Egypt¹⁰ and 74.2% in Australia⁹ when odontogenic tumors and odontogenic and non-odontogenic lesions were considered. In Brazil, the prevalence of OKC also varied among different investigations. In Rio de Janeiro, the OKC had prevalence of 32.3%⁷ among odontogenic tumors and in Minas Gerais, the OKC represented 7.2%¹³ of the sample of odontogenic cysts. Certainly, differences in OKC classification made the results discrepant between different studies and populations.

None patient showed association between OKCs and Gorlin-Goltz Syndrome in this study. Some authors reported Gorlin-Goltz syndromic patients with OKC ranging from 1 to 28¹⁴; in other study in Indian patients this association was of 3:6¹⁵, while a retrospective study with 33 patients reported an association of 1 to 6¹⁶.

In the present study, the mean age of the patients was 33.19 years, similarly to the findings of Siriwardena et al.⁸ (31.3 years), Tawfik and Zyada¹⁰ (30.5 years), Osterne et al.¹¹ (31.9 years) and Mun et al.¹⁷ (36.8 years). The cases were distributed between 13 and 54 years old, with a higher prevalence in the third decade of life, corroborating other studies^{18,19}. Regarding the sex, no difference was observed between, contrary to other studies, in which there was a greater involvement of the male sex^{4,5,7,10,20,21}.

Regarding the symptomatology, 43.75% of the patients were asymptomatic and, in all other cases (56.25%), local pain and discomfort were the main complaints, corroborating other studies that reported that 50 to 67% of the OKCs are symptomatic at the time of diagnosis^{22,23}. As in other studies^{4,5,17,20}, swelling was found in 43.75% of cases.

The mandible was more affected (68.75%) with a ratio of 2.2: 1 in relation to the maxilla. This result is similar to previous studies^{4,5,11,20,21}. Mandibular OKCs occur mainly in the body and angle^{4,8,10,11,20}, as seen in the present study. All mandibular lesions occurred in the body, angle and mandibular ramus region.

Radiographically, OKC presents as an uni or multilocular radiolucent image, with a rounded or oval shape, circumscribed by a radiopaque halo^{4,22}. The literature shows the radiolucency as the main radiographic finding⁵. However, this pattern is observed in several other lesions. A list of pathologies is mentioned in the literature as differential diagnosis, such as solid and unicystic ameloblastoma, dentigerous cyst, ameloblastic fibroma, simple bone cyst, odontogenic myxoma, central giant cell lesion and many other benign odontogenic neoplasms, odontogenic cysts and intraosseous lesions^{4,24,25}. In the present study, nasopalatine duct, lateral periodontal and inflammatory periapical cysts were also considered.

The clinical history associated with the imaging characteristics may limit the scope of differential diagnosis²². In the reported case, CBCT was used to aid diagnosis and treatment plan. This imaging exam allows you to evaluate the region of interest on different planes without overlapping and with high definition. This modality has been spreading in Dentistry field. However, its use should not be indiscriminate as it provides high doses of radiation when compared to radiographs.

Magnetic resonance imaging (MRI) can reliably discriminate the OKC²⁶. In 2015, Probst et al.²⁶ sought features that distinguished OKCs from other odontogenic cysts in contrast MRI scans. The authors concluded that the signal strength of the lesion walls appears to be a characteristic that differentiates odontogenic cysts from OKC in MR images²⁶. The walls of the cysts appear regularly with a high signal intensity homogeneously, while the OKCs show low signal intensity homogeneously or heterogeneously after contrast enhancement²⁶. The authors argue that this imaging modality should be considered for the evaluation of cystic lesions and may have a significant impact on subsequent diagnosis and treatment²⁶. Another advantage is the absence of ionizing radiation²⁶. However, the lesion does not show clinical or imaging pathognomonic signs. The OKC has a unique and distinct histopathological profile. Thus, the gold standard that establishes the diagnosis is histopathological examination^{3,26}.

Treatment options for OKC are yet controversial and there is no consensus on the most effective surgical technique^{4,20}. Although more conservative treatments are less traumatic, they increase the recurrence rates, while more radical techniques may cause major bone defects and mutilations. In any case, the main objective should be the eradication of the lesion, minimal complications and prevention of recurrence^{3,4,20}. Ebenezer and Ramalingam²⁷ emphasize that the treatment modality should be decided taking into account the aggressiveness of the lesion, its size and the age of the patient. Among the treatment options are enucleation, marsupialization and decompression^{6,27}, which may be associated with adjuvant therapies such as mechanical curettage, chemical curettage with Carnoy's solution or cryotherapy. Marsupialization and decompression may be followed by enucleation with or without curettage.

The aggressive character, the high rate of recurrence and its tendency to infiltrate and invade adjacent tissues make the OKC a singular lesion.^{18,20,27} Recurrence rates can reach 62%, depending on the area and established therapy^{3,17}. It is necessary a long-term follow-up, cause many OKCs can recur within 5 to 10 years²⁸. Pogrel²⁹ recommends a follow-up every 6 months for 2 years, every year for 5 years and every 2 years for 10 years²⁹. The follow-up time described here was up to nine years, in which two cases of recurrence were observed (12.5%). This recurrence was lower than Sánchez-Burgos *et al.*⁵ (25%) and higher the null recurrence found by Ebenezer and Ramalingam (2014)²⁷.

The reported case presents a mandibular OKC diagnosed in a man, in the 4th decade of life. Enucleation associated with cryotherapy with liquid nitrogen and extraction of the tooth 48 was performed. For reconstruction, filling with lyophilized bovine bone and resorbable membrane of bovine bone cortex were used, followed by rehabilitation with osseointegrated implant, with quite satisfactory results regarding function and absence of signs of recurrence in two years of follow-up. In addition to providing a more predictable and efficient bone repair, bovine bone particles become an integral part of the newly formed bone structure and conserve their volume over the long term^{30,31}. Despite the treatment was conservative, even though the lesion was quite extensive, the association with cryotherapy and the extraction of the involved tooth reduced the possibilities of recurrence, besides allowing the immediate reconstruction of the bone defect. Therefore, the importance of adjuvant therapies in the treatment of OKCs is highlighted.

CONCLUSION

The prevalence of OKC vary among studies due to the alterations in its classification (cyst *versus* tumor). The lesion presents a broad spectrum of differential diagnosis due to its non-specific clinical and radiographic characteristics, with no sex preference, between the 3rd and 4th decades of life, and the most common involvement of the body, angle and mandibular ramus. The case reported reinforces that conservative treatments such as enucleation can be efficient when accompanied by adjuvant techniques, such as cryotherapy. Despite the great bone defects, patients can be rehabilitated through bone grafts and osseointegrated implants.

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