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Case Report

Odontogenic Keratocyst in Pediatric Patients: Case Report and Literature Review

Juan Mancilla Uribe[1]*, Diego Garcia Nova[2], Loreto Castellon Zirpel[3], Carlos Fuenzalida Kakarieka[4], German Laissle Casas del valle[4], Carlos Bahamondes Asencio[4] and Carla P. Cittadini[2]

[1] *DDS, Universidad Andrés Bello, Santiago, Chile.*

[2] *DDS, Oral & Maxillofacial Surgery resident, Universidad Mayor, Santiago, Chile.*

[3] *Head of Oral and Maxillofacial Surgery Unit Hospital Luis Calvo Mackenna, Santiago, Chile.*

[4] *DDS, Oral and Maxillofacial Surgery surgeon, Hospital Exequiel Gonzalez Cortes, Santiago, Chile.*

***Corresponding Author**: Juan Mancilla Uribe, DDS, Universidad Andrés Bello, Santiago, Chile.*

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Abstract

Odontogenic Keratocysts (OKC) are bone lesions that represent 10% of cystic lesions of the jaws. They are commonly reported as radiographic findings since they are usually asymptomatic given the anteroposterior development through the bone marrow, although they can generate large increases in volume with displacement of surrounding structures and perforation of the bone cortices. These lesions are closely associated with Nevus Basal Cell Syndrome (NBCS) also known as Gorlin Syndrome (GS) or Gorlin-Goitz (GZ), where the 75 to 89% of these patients exhibit OKC lesions. This report presents the treatment of a case present in the mandible of a pediatric patient associated to NBCS and bibliographic review The purpose of this paper is to present recommendations on the current management of this pathology based on the available literature.

***Keywords:** Odontogenic Keratocyst; Gorlin-Goitz Syndrome; Head and Neck Pathology; Pediatrics*

Introduction

Odontogenic keratocysts (OKC) were first described by Philipsen in 1956; these are benign intraosseous lesions of odontogenic origin that represent approximately 10% of jaw cysts. They are characterized by aggressive behavior with a high recurrence rate. Histologically, OKC arise from the dental lamina and are constituted by a cystic space containing desquamated keratin, lined by a uniform parakeratinized squamous epithelium of five to ten cell layers, with a distinct basal layer of columnar or cubic palisade cells, whose nuclei They tend to be oriented vertically. The interface with adjacent connective tissue is normally flat with potential for budding of the basal layer and formation of small satellites. Mitotic activity is greater than that of other cysts of odontogenic origin.[1]

It is more common in men than in women and the mandible is significantly the most affected structure, with the angle and ramus region being the site with the highest prevalence. The Odontogenic Keratocyst has a wide age distribution that ranges from the first to the ninth decades of life, but it is mostly observed in the second and third decades.

Characteristically, OKC grows rapidly within the medullary bone in an anteroposterior direction, so that the increase in volume becomes clinically evident late. Therefore, patients generally do not have symptoms until the lesion reaches a considerable size. Other features of the OKC include; pain (generally when infected), discharge of cystic contents and pathological fracture, which is why cases of this condition are usually discovered incidentally in routine radiographic examinations.[2]

Radiographically, OKC appear as a well-defined radiolucent, unilocular or multilocular lesion delimited by corticalized margins. Unilocular lesions are the most prevalent, while the multilocular variant is observed in approximately 30% of cases. On panoramic radiography, mandibular unilocular OKCs may present complete and incomplete septa within the lesions; This finding is more common in large OKCs, it can also present with displacement of the roots of adjacent teeth, but root resorption is not common. Approximately 30% of OKCs are associated with at least one unerupted tooth, more commonly the third molars. This association occurs particularly in young patients.[1]

The radiographic presentation of OKC (unilocular or multilocular radiolucent lesion) is often similar to that of other odontogenic lesions, so it is necessary to make a differential diagnosis with other entities such as dentigerous cyst, calcifying odontogenic cyst, calcifying epithelial odontogenic tumor and ameloblastoma. cystic.[2]

OKC maintains its cyst status in the 2017 and 2022 classifications. The most frequent genetic modification associated with pathogenesis occurs in the PTCH1 gene (Hedgehog (Hh) signaling pathway) and has been identified in up to 93% of cases. the cases.[3]

The presence of multiple OKCs, which also occur at different times during patients' lives, is typically associated with basal cell nevus syndrome (NBCS), an autosomal dominant multisystem disease. In these patients, the average age of diagnosis is twenty-five years.[1]

NBCS, also known as Gorlin syndrome (GS), Gorlin-Goltz (GG) or nevoid basal cell carcinoma syndrome (NBCCS), is an autosomal dominant genodermatosis with complete penetrance and variable expression caused by mutations in the signaling pathway. of Hedgehog (Hh). With heterozygous mutations in the patched 1 gene (PTCH1) in most cases and less frequently in the suppressor of the fused gene (SUFU) or in the patched 2 gene (PTCH2).[4]

It is characterized by the development of multiple odontogenic keratocysts, frequently seen in young patients under 20 years of age, and basal cell carcinomas (BCC), usually seen in middle-aged patients.[5]

Approximately 5% of patients with GS develop medulloblastoma. About 60% of individuals have macrocephaly, frontal ridges, coarse facial features, and facial milia.

Additionally, most patients have skeletal abnormalities, such as bifid ribs and wedge-shaped vertebrae. Cardiac fibroma is observed in approximately 2% of patients and ovarian fibroma in approximately 20% of patients, OKC of the jaw, hyperkeratosis of the palms and soles (palmar and/or plantar fossae), ectopic calcification, especially in the brainstem or intracranial falx in more than 90% of patients by the age of 20 years. Macrocephaly with frontal elevation, cleft lip or palate, and ocular abnormalities are also seen in some patients. Intellectual disability is found in up to 5% of patients.[5]

Material and Method

The literature review was performed using the search for “Odontogenic – Keratocyst” in the PubMed database. Systematic reviews from 2018 to 2022 related to odontogenic keratocysts and Gorlin-Goitz syndrome were included.

Case Report

8-year-old female patient, who attended the Maxillofacial Surgery service of the Exequiel Gonzales Cortes Hospital in May 2019 due to an asymptomatic increase in left mandibular volume of 6 months. (Fig. 1) Clinically, she presents an increase. of volume in the region of the body and left mandibular ramus, with a firm consistency on palpation. The intraoral examination revealed first-phase mixed dentition, an increase in volume in the left mandibular vestibule from tooth 7.3 to the mandibular angle, and no displacement or symptoms were observed in the teeth. Patient comes with panoramic radiography where two radiopaque lesions are observed, the first located between the distal of tooth 3.2 and the mesial of tooth 3.6 generating displacements of teeth 3.3, 3.4, 3.5 towards the mandibular basilar edge, the second lesion is observed from distal of piece 3.6 to the midline of the mandibular ramus, moving piece 3.7 towards the mandibular basilar edge. There are no signs of hidralysis in the pieces adjacent to the lesion. Both lesions are well-defined and rounded in morphology approximately 3 cm long each. A CT scan was requested for evaluation in which bulging of the lingual and buccal tables was observed with perforation of both in both lesions. (Fig.2)

In the central ward under general anesthesia, an initial biopsy of the lesion is taken, together with the installation of drains with cannulas in both lesions to perform decompression with the aim of reducing the size of the lesion, for which periodic controls are carried out and give instructions for irrigation with diluted chlorhexidine to parents.

Through anatomopathological study in conjunction with the clinical examination, the lesions are confirmed as odontogenic keratocysts.

The patient was referred to genetic medicine for confirmation of Gorlin syndrome, which was positive as he presented two major criteria, calcification of the falx cerebri and mandibular keratocyst, and a minor criterion, macrocephaly.

After four months of treatment, a control CT scan was requested, where a decrease of approximately 50% in the size of the lesion was observed. (Fig.3)

In August 2020, a decrease in the left mandibular lesions with bone neoformation was observed in the control Computed Tomography, but a new lesion was observed in the right mandibular body which was subjected to exceresis. The patient continued under control without recurrence. In July 2021 control, it was decided to perform exceresis of left mandibular lesions along with extraction of teeth 3.7, 3.8 and washing with Carnoy solution, a surgery that was performed in November 2021.

After this, control is carried out at a week, two weeks, a month, three months and six months, remaining in control every six months until now, where a favorable evolution is observed without recurrences, eruption of pieces 3.4-3.5 and complete bone neoformation. (Fig.4)

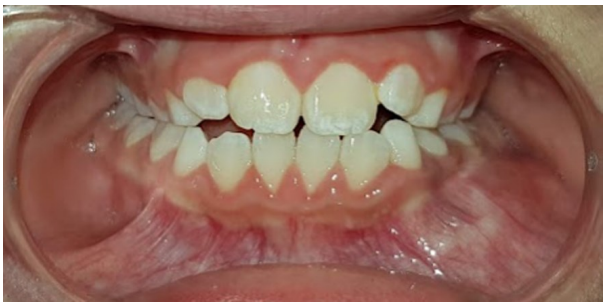

Figure 1. *increased left mandibular volume, occupied vestibule, without displacement of teeth.*

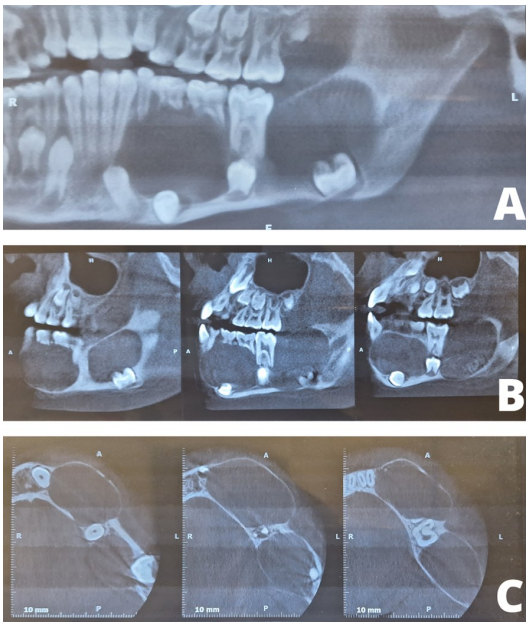

Figure 2. *Two lesions approximately 3 cm wide are observed in the ramus and mandibular angle (A). Sagittal section of the mandibular lesions, the displacement of the teeth towards the basilar edge is observed (B). Axial sections of mandibular lesions, the bulging of the tables is observed (C).*

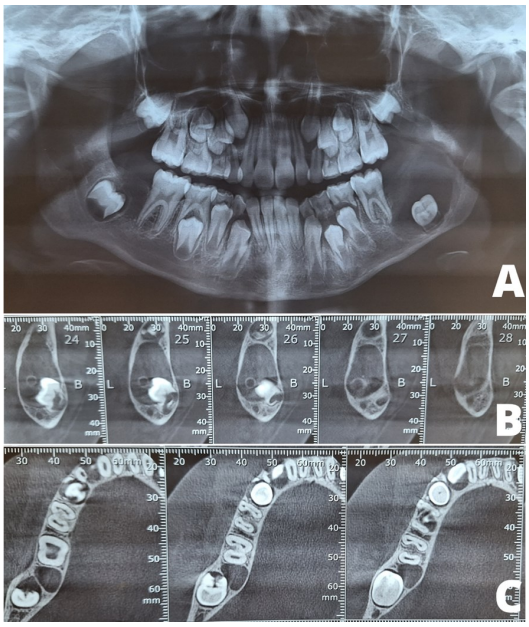

Figure 3. *Control panoramic radiograph four months after treatment, new bone formation and new lesion are observed in the right mandibular body (A). Coronal sections of the lesion of the left mandibular body, in situ drainage with bone neoformation is observed (B). Axial sections of the right mandibular lesion, a close relationship with piece 4.7 (C) is observed.*

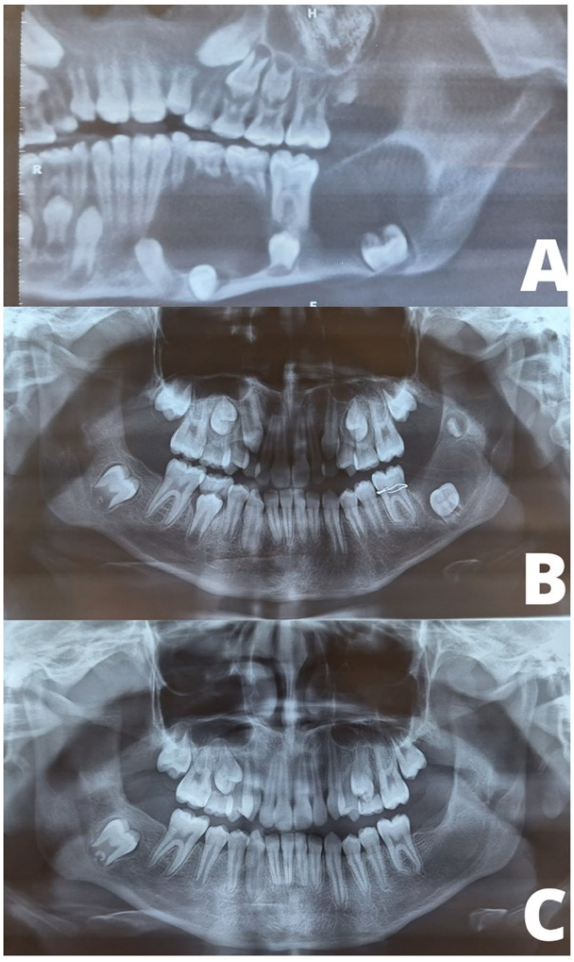

Figure 4. *Evolution of the patient, initial panoramic view (A), injury to the left mandibular body after decompression (B) and control x-ray two years later, where no new injuries are observed (C).*

Discussion

NBCS is characterized by a tumor predisposition, particularly with the development of multiple basal cell carcinomas at a young age, along with odontogenic keratocysts, palmo-plantar fossae, skeletal anomalies, and an increased risk of medulloblastoma.[4]

The criteria reported by Kimonis et al are the most used, this method includes six main criteria (basal cell carcinoma, bone cyst of the jaw, small palmo-plantar depression, calcified falx cerebri, rib anomalies and family history of the disease within the first degree) and six minor criteria (macrocephaly, congenital malformation, skeletal anomalies, radiological anomalies, ovarian fibromas and medulloblastomas). The clinical diagnosis of Kimonis requires the fulfillment of two major criteria, or one major and two minor criteria.[5]

OKCs are benign intraosseous lesions of odontogenic origin that are characterized by aggressive behavior with high recurrence rates. They are the predominant oral manifestation of the NBCS and can be found in 75 to 89% of patients. The average age of onset ranges between 15.5 and 17.1 years, occurring in 60% of patients under 20 years of age and 81% in patients 20 years or older; after 30 years, the rate development of OKCs tends to decrease.[4]

Like other entities that have an odontogenic origin, OKCs originate in regions with teeth, approximately 30% are associated with at least one unerupted tooth, most commonly the third molars, this association occurs particularly in younger patients. According to the literature, they can be located in a periapical, pericoronal or lateral position to the root. 30% of cases are not related to any dental structure. These lesions appear twice as frequently in the mandible compared to the maxilla. When OKCs originate in the mandible, the most common location is in the angle and ramus region. Despite their aggressive behavior, OKCs, in most cases, cause minimal bone expansion due to their propensity to extend along the medullary space "growing along the bone", in asymptomatic patients extensive lesions, which cause significant erosion of the cortices and even perforations in them, along with displacement of the surrounding structures.

On the contrary, large lesions in the maxilla more frequently present hydraulic expansion of the alveolar bone with remodeling, thinning, scalloping and perforation of the cortices. Furthermore, when OKCs originate from the alveolar bone underlying the maxillary sinus, their floor is raised and the space is occupied.[1]

Management of these injuries aims to minimize morbidity, while reducing the risk of recurrence. Currently, there is no consensus on what the best treatment modality is. For this, different factors intervene, among which we find the size and location of the lesion, unilocularity or multilocularity, the presence of cortical perforation, association with teeth, soft tissue involvement and the age of the patient. Several surgical options have been considered, including simple enucleation or associated with complementary measures (ostectomy, Carnoy solution, cryotherapy), marsupialization and decompression, marginal or segmental resection.[1]

The literature reports an overall recurrence rate of 16.6% with 8% for resection, followed by 23% for enucleation alone and 32% for marsupialization alone. Complete or partial resection has the lowest recurrence but is associated with significant morbidity. Therefore, treaters often opt for a less invasive approach, preferably with the lowest recurrence rate. Enucleation is associated with the least morbidity, but also with the greatest recurrence. To reduce this recurrence rate, multiple adjuvant therapies can be applied to the remaining bone defect after enucleation, with recurrence rates for enucleation with peripheral ostectomy (PO) of 17%, marsupialization with enucleation of 15%, enucleation with 15% cryotherapy and enucleation with 11% Carnoy solution.[6]

Carnoy's solution (CS) has been widely used as an adjunctive treatment with a recurrence rate of approximately 11%, applied for three minutes to minimize side effects. The main adverse effect is paresthesia in the dermatome innervated by the inferior alveolar nerve. The results showed a general transient paresthesia ranging from 9 to 78% and a permanent paresthesia ranging between 11 and 22%.[7]

A version without chloroform called modified Carnoy solution is currently used in some countries. (MCS), since its use has been prohibited, due to the possible carcinogenic effects of chloroform. but its effectiveness remains controversial.[6]

5-Fluorouracil is an antimetabolite that targets DNA synthesis in rapidly proliferating cells causing cell apoptosis and has been widely used as a chemotherapeutic agent for various neoplasms, it appears to be an effective method with promising results, but needs further research.[8]

Recurrent OKCs may be due to incomplete elimination of the epithelium that covers the cavity or that found around the teeth that extended into the cyst cavity, which is why some authors recommend the extraction of the teeth contained in the cavity or apicoectomy. . of roots that extend into the lumen of the cyst and interfere with complete removal of the cyst walls.[9]

It is mentioned that most recurrences occur within the first 5 years after surgical intervention, although this observation could be due to the fact that most of the studies have a follow-up of only 1 to 5 years.[10]

Some research has suggested that early-stage marsupialization or decompression followed by enucleation minimized damage to adjacent structures and reduced the recurrence rate when used for large or extensive OKCs. Therefore, it seems appropriate to perform this two-stage surgery if there are multiple affected teeth, however, preserving an affected tooth in the OKC may compromise adequate enucleation of the lesion and increase the chance of recurrence. Therefore, the surgeon should consider extracting the affected tooth if there is any doubt that pathological tissue may remain. However, as OKC is more common in young patients, tooth extraction may not be a widely accepted treatment, from aesthetic reasons to possible occlusal complications.[9]

Regarding marsupialization, studies suggest an average duration of 14.6 months with measures of relative size/volume reduction ranging between approximately 37 and 81%. Regarding the decompression technique, the average duration of the intervention was approximately 9.5 months and the mean measures of relative size/volume reduction ranged from approximately 4 to 97%.[11]

Although tissue biopsy remains the Gold Standard in the diagnosis of OKC, advances are being made in complementary tests that could help in early stages of the development of OKC or help in the early detection of recurrences, in sequencing images. MRI could help differentiate with other tumor diagnoses or other cystic lesions, since the content of these lesions presents an intermediate and heterogeneous signal intensity. It has also been reported that Hounsfield unit (HU) values on CT are significantly higher. lower for OKCs than for other odontogenic cysts, which may provide background to make a more accurate diagnosis at an early stage to prevent recurrences at a later stage.[12]

This could be complemented with immunohistochemistry with p53, the which reveals significantly higher levels of abnormal p53 in OKC than other epithelial cysts and oral mucosa. Therefore, the locally invasive behavior and high recurrence rate of OKC may be attributed to the presence of mutant or inactive p53 protein.[2]

The recommended follow-up for OKCs is once a year during the first 5 postoperative years. As recurrences of new-onset OKCs can also present clinically late, follow-up every 2 years seems to be a reasonable policy. Follow-up is recommended, mainly with panoramic radiographs, every 6 months for 2 years, every year for 5 years and every 2 years for 10 years in asymptomatic patients.[13]

Conclusions

OKC are lesions that mainly affect the mandible in the region of the angle and ramus, which extend through the medullary portion of the bone structures with the possibility of perforating the cortex, displacing adjacent structures and generating large increases in volume. They are usually associated with Gorlin Syndrome, so it is advisable to perform a rigorous clinical and imaging examination in search of major and minor criteria for its diagnosis.

The treatment of choice for these lesions is complete enucleation of the lesion followed by chemical treatment of the surfaces of the bone defect.

If an extensive lesion of more than 3 cm is present, marsupialization or decompression is recommended until a size reduction is achieved that leads to less morbidity when performing enucleation. Irrigations of the cystic cavity should be performed twice a day (with 0.12% chlorhexidine gluconate and saline) through the inserted cannula with clinical and/or radiographic monitoring every 2 months or until starting the second stage of treatment. After radiographic confirmation of a considerable decrease in lesion size and obvious bone formation, the tube is removed and enucleation of the lesion is performed with emphasis on removal of the overlying mucosa to completely remove the remaining clumps of Epithelial islands and microcysts that may be present between the mucosa. and cystic lining. This should be followed by a peripheral osteotomy and treatment of the bone defect with Carnoy's solution (with or without chloroform), liquid nitrogen, or 5-FU at the discretion of the treater.

Post-surgical follow-up is suggested every 6 months for 2 years, annually for five years and routinely every 2 or 3 years.

Conflict of Interest

The authors declare no conflict of interest.

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