

Decompression Associated with Irrigation with Elixir Sanativo® Before Enucleation of Odontogenic Keratocysts: Report of Two Cases

Descompresión Asociada a Irrigación con Elixir Sanativo® antes de la Enucleación de Queratoquistes Odontogénicos: Reporte de Dos Casos

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ABSTRACT: Odontogenic Keratocyst (OKC) is an aggressive cystic lesion of the jaws and one of the most common odontogenic cysts, usually affecting the posterior region of the mandible. Recurrences are frequently recorded and may be directly related to the treatment modality adopted. Two patients presenting OKC were treated by combining decompression and intralesional irrigation with the drug Elixir Sanativo® for 8 months before enucleation surgery. In both patients, the association between decompression and irrigation with Elixir Sanativo® represented a safe and effective method to reduce the preoperative lesion dimensions.

KEY WORDS: odontogenic cysts, conservative treatment, phytotherapy.

INTRODUCTION

Odontogenic Keratocyst (OKC) is an aggressive lesion, that shows slow growth and a high recurrence rate. Commonly, the individuals are affected during the 2nd and 3rd decades of life, being observed with a slight predilection for males (Kinard *et al.*, 2019; Geletu *et al.*, 2023). Commonly, it appears as a unilocular or a multilocular image, with a radiolucent appearance and well-defined sclerotic margins (Geletu *et al.*, 2023). In general, the posterior region of the mandible is the most affected anatomical area (de Castro *et al.*, 2018; Geletu *et al.*, 2023). Depending on its presentation, differential diagnoses may include ameloblastoma, dentigerous cysts, lateral periodontal cysts, and radicular cysts (Sharif *et al.*, 2015).

The pathogenesis of the lesion is unclear, although some authors point to remnants of the dental lamina as the main embryonic factor. Unlike others

odontogenic lesions, such as ameloblastomas, OKC shows no frequent mutation in BRAF (Gomes *et al.*, 2023). However, the PTCH1 mutation is already well established, especially in those cases associated with the nevoid basal cell carcinoma syndrome (Guimarães *et al.*, 2021; Gomes *et al.*, 2023). In 2017, World Health Organization (WHO) in its Head and Neck Tumor classification, reincluded the lesion in the odontogenic cysts section due to insufficient evidence to sustain its neoplastic origin (Wright & Vered, 2017). In the recent classification of 2022, OKC remains as a cystic lesion (Vered & Wright, 2022).

Given the high recurrence rates of OKC, adjuvant therapies have been considered in association with enucleation. These therapies include peripheral ostectomy, chemical cauterization by Carnoy's solution, and cryotherapy with liquid nitrogen (Sharif *et al.*, 2015).

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Similarly, to these adjuvant therapies stands out Elixir Sanativo® — a phytotherapeutic drug composed of hydroalcoholic extracts of different plants — seems to be a promising drug to act on the injured tissue for its antiseptic and healing properties (de Lima *et al.*, 2006).

This study aims to describe two clinical cases of OKC in the posterior region of the mandible treated under decompression and intralesional irrigation with the drug Elixir Sanativo® for 08 months previous to its enucleation. Also, we aim to provide an alternative and adjuvant therapy for the treatment of aggressive odontogenic lesions.

CASE REPORTS

These clinical case reports have a descriptive, exploratory, and qualitative approach. The patients presented signed the terms of consent for disclosure of their images and data, as well as the stages related to diagnosis and all their treatments. Even so, it is fair to say that all the ethical principles of the Declaration of Helsinki were respected.

CASE 1. A 20-year-old female was referred to the oral and maxillofacial surgery department for evaluation of a swelling in the left mandible in March 2020. Chief complaints were pain and chewing difficulty. The extraoral examination revealed slight facial asymmetry on the left side, while the intraoral examination revealed a small bulging in the region of the lower molars. Medical history revealed no abnormalities.

The panoramic radiograph showed an extensive, radiolucent, unilocular left-sided lesion, with well-defined limits by a radiopaque line ranging from the body region to the mandibular ramus, associated with the crown of an impacted third molar, extending to the roots of the second molar (Fig. 1).

Aspiration of the contents of the lesion revealed a creamy and whitish liquid. Based on these clinical findings, it was raised diagnostic hypotheses of OKC, dentigerous cyst, and ameloblastoma. An incisional biopsy was carried out, under local anesthesia, and the material was sent for histopathological analysis, confirming the diagnosis of OKC.

Thus, treatment planning consisted of decompression before enucleation to preserve the patient's function and esthetics. The decompressor device used was a 01 mL syringe that had the phalangeal parts sectioned (Fig. 2A), and the lateral flaps

perforated, to enable a firm suture on the mucosa. Due to its antiseptic and healing properties, Elixir Sanativo® (Fig. 2B) was added as an adjuvant to decompression. To extract the best of its effects, the patient was instructed to dilute 01 mL of the drug to 10 mL of filtered water (1:10) and irrigate the lesion through the orifice of the decompression device three times a day.

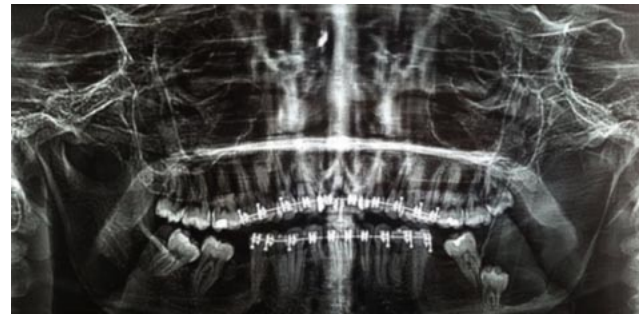


Fig. 1. Initial panoramic radiograph showing a well-delimited radiolucent lesion in the mandibular body and ramus on the left side.



Fig. 2. A- phalangeal sectioned; B- Elixir Sanativo®. A follow-up panoramic radiograph was taken at approximately 8 months, which showed a reduction of the cystic lesion and bone neoformation.

Under general anesthesia, enucleation surgery associated with two transoperative adjuvant therapies was carried out. Initially, through intraoral access in the anterior region of the mandibular ramus, teeth removal, cystic enucleation, and curettage were performed. Then, a peripheral ostectomy was performed with a multilaminated drill and Carnoy's solution was applied with gauze soaked in the solution for 5 minutes and inserted into the bone store. The surgery and postoperative recovery were uneventful. One year after surgery, a new radiograph was taken, and bone neoformation was observed (Fig. 4). The patient is being followed up, with no recurrence.



Fig. 3. Panoramic radiograph taken 08 months after enucleation exhibiting decreased cystic extensions.



Fig. 4. Panoramic radiograph taken one year after enucleation. Evidence of bone neoformation and no signs of recurrence.

Case 2. A 16-year-old male presented to our service of oral surgery in April 2020. On clinical examination the patient exhibited swelling and local pain in the right mandibular region, complaining of yellowish secretion and fetid odor in the oral cavity for approximately 4 months. The past medical history was not contributory.

As a conduct, it was requested a panoramic radiograph. The imaging exam showed a multilocular radiolucent cystic lesion associated with the impacted third molar crown, involving the roots of the second and first molars on the right side and extending to the condyle (Fig. 5).

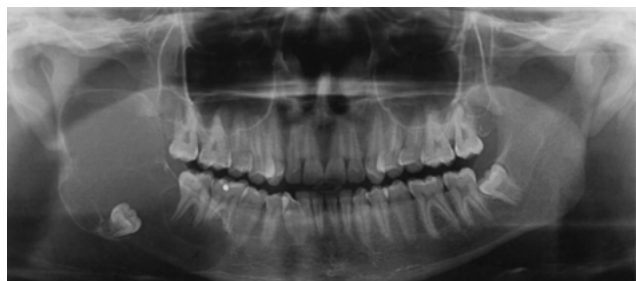


Fig. 5. Initial panoramic radiograph showing a well-delimited radiolucent lesion in the body and ramus of the mandible on the right side.

Thus, aspiration punctures were performed, showing creamy and whitish contents. An incisional biopsy was conducted, and the material was sent for histopathological analysis. Clinical diagnosis included ameloblastoma, odontogenic keratocyst, and dentigerous cyst, as similarly discussed in the anterior case. Histological analysis of the hematoxylin and eosin (HE)-stained slides confirmed the diagnosis of odontogenic keratocyst.

Since it was an extensive cystic lesion, decompression was chosen. The decompression device used was the same as in the previous patient, a 01 mL syringe with a cut in the phalanges and perforated flaps. The drug Elixir Sanativo® was diluted in filtered water (1:10) and applied three times a day (Fig. 2).

After 8 months of decompression, a preoperative radiograph was requested, where a decrease in the lesion dimensions and bone neoformations could be observed (Fig. 6). In the operating room, the unerupted third molar in the lesion was removed. Peripheral osteotomy and Carnoy's solution application were also performed.



Fig. 6. Panoramic radiograph taken 08 months after enucleation suggesting decreased cystic extensions.

At the one-week follow-up visit, the oral mucosa showed signs of normal healing, with no reports of complications within this period. In new visits after one month, no esthetic or functional deficits were observed, and the radiographic examination showed satisfactory bone neoformation (Fig. 7). The patient is also being followed up.



Fig. 7. Panoramic radiograph one year postoperatively. Evidence of bone neoformation and absence of lesional tissue.

DISCUSSION

The pathological cystic or neoplastic nature of the OKC is still controversial. In its last edition, the WHO (2022) maintained the OKC among jaw cysts because of its complexity, similarly established in 2017 (Vered & Wright, 2022). In addition, it has been discussed that the failures of surgical and rehabilitative therapies as well as recurrence and aggressive phenotype observed in this lesion are associated to its histological pattern and presence of genetic alterations (Gomes *et al.*, 2023).

Morphologically, OKC is characterized by the corrugated epithelium of homogeneous thickness lining the inside of a cystic cavity, with the capability of a detachment of its fibrous capsule as well as the presence of remnant lamina dental or invasive satellite cysts in the bone adjacent, which may contribute to incomplete eradication of cellular components (Robinson *et al.*, 2017; Titinchi, 2022). Another relevant finding is the presence of mutations in the PTCH1 gene. This gene may be expressed in sporadic and nevoid basal cell carcinoma-associated OKC, commonly associated with an increased proliferative cellular activity and apoptosis escape alternatives (Tenório *et al.*, 2018; Gomes *et al.*, 2023).

Due to its clinical behavior, therapeutic modalities indicated for the treatment of odontogenic keratocysts usually include radical surgery, marsupialization, and chemical curettage with Carnoy's solution (Sharif *et al.*, 2015; de Castro *et al.*, 2018; Kinard *et al.*, 2019). Despite the clinically satisfactory results obtained in some cases of OKC, the optimal treatment of this lesion type remains a matter of debate, especially the negative impact caused by such interventions on the patient's aesthetic and potential morbidity risk (Oh *et al.*, 2018). Therefore, the use of adjuvant therapies aims to minimize the main disadvantages inherent to surgical treatments alone. The treatment of OKC varies according to their clinical and imaging presentation (Geletu *et al.*, 2023). Lesions of large extension need more invasive treatment modalities, such as en bloc resection, causing significant aesthetic and functional deficits, and also a significant impact on the patient's social and emotional life (Jung *et al.*, 2021; Titinchi, 2022). In these cases, prior marsupialization or decompression is recommended, facilitating enucleation, limiting the risks of pathologic fracture, and preserving valuable anatomical structures (Dias *et al.*, 2017; Oh *et al.*, 2018).

Nevertheless, another relevant aspect is the positive response to conservative treatment like

marsupialization/ decompression that is associated with reversion of the epithelium to normal and the consequent lower recurrence rates (Cserni *et al.*, 2020). Marsupialization, the treatment chosen for the cases described here, not only decreased the intracystic pressure but also favored the preservation of important anatomical structures such as the inferior alveolar nerve (Tabrizi *et al.*, 2019). However, attention is needed to the limitations of this technique, such as long follow-up, poor positioning of the decompressor device, and the need for patient cooperation concerning the irrigation protocol (Ozkan *et al.*, 2021). Furthermore, to avoid trauma to adjacent tissues, the decompressor model employed in our study successfully met the criteria of a comfortable stay, low cost, easy adaptation, and minimal irritation (Catunda *et al.*, 2013).

The clinical effectiveness of marsupialization in the treatment of this lesion type has been proven by several authors. In your metabolomic's study, Leite-Lima *et al.* (2022) demonstrated through liquid chromatography-mass spectrometry the presence of expressive phenotypic alterations in the epithelial lining of odontogenic keratocyst after marsupialization in comparison with pre-marsupialized lesions, possibly justifying metaplastic changes induced by this conservative technique. Similarly, Consolo *et al.* (2020) through the analyses of different histological sections, identified expressive changes in OKC treated with marsupialization, cystic volume, and decreased inflammatory response, as well as the occurrence of fibrosis. Overall, these findings contribute to the validation of this conservative therapy. Alongside, the application of Elixir Sanativo® as demonstrated in our case reports, jointly with cellular alterations induced in the epithelium of OKC through marsupialization, may explain the success obtained in the treatment of the patients.

Elixir Sanativo® is an herbal national medicine that has been widely employed to treat wounds, burns, throat inflammation, and injured epithelial tissues (de Lima *et al.*, 2006). To our best knowledge, this is the first work in the literature reporting the use of this drug in the treatment of OKC. Therapeutically, its pharmacological properties include a healing effect, astringent, anti-inflammatory, and antimicrobial action, making it an adjuvant agent for preoperative care. Besides, this elixir shows in its composition 20 % of *Schinus terebinthifolius* Raddi (aroeira), 20 % of *Piptadenia colubrina* Benth (known in Brazil as angico), 1.7 % of *Physalis angulata* Linné (camapu) and 1.7 % of *Cereus peruvianus* Miller (mandacaru) (de Lima *et al.*, 2006). All these bioactive products have anti-inflammatory, antimicrobial,

anticarcinogenic, antimutagenic, and antioxidant activities, mainly *S. terebinthifolius* also used as a mouthwash to control dental plaque and gingivitis (Santi *et al.*, 2021; Freires *et al.*, 2013).

In contribution, herbal medicines have demonstrated expressive results in different areas of dentistry, from endodontic infections treatment to the control of autoimmune diseases and malignant neoplastic processes, such as lichen planus and oral cancer, respectively (Ghahremanlo *et al.*, 2019; Dehghani Nazhvani *et al.*, 2020; Karobari *et al.*, 2022). Although its action mechanism has not been studied in odontogenic lesions, probably, the bioactive substances presented in Elixir Sanativo® may influence bone healing by reducing the inflammatory response and stimulating the osteoblastic activity, as observed in the radiographic evolution of our cases. Collectively, these findings added to the marsupialization technique encourage new perspectives on therapies and further research on the use of herbal medicines in the treatment of aggressive oral diseases, including odontogenic lesions.

CONCLUSION

Given the aggressiveness and associated high recurrence rates, the treatments of OKC are challenging. The lowest morbidity and recurrence rates seem to come from the union between several therapeutic approaches. Based on the same premise as other adjuvant methods of acting on the lesional tissue, the use of Elixir Sanativo® was proposed as an alternative to optimizing the effects of decompression. In both patients of this study, the association between decompression and irrigation with Elixir Sanativo® represented a safe and effective method to reduce the preoperative lesional dimensions and morbidity associated with the following surgical procedures.

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RESUMEN: El queratoquiste odontogénico (QO) es una lesión quística agresiva de la mandíbula y es uno de los quistes odontogénicos más frecuentes, que suele afectar a la región posterior de la mandíbula. Las recidivas se registran con frecuencia y pueden estar directamente relacionadas con la modalidad de tratamiento adoptada. Presentación del caso: Dos pacientes que presentaban OKC fueron

tratados combinando descompresión e irrigación intralesional con el fármaco Elixir Sanativo® durante 8 meses antes de la cirugía de enucleación. En ambos pacientes, la asociación entre descompresión e irrigación con Elixir Sanativo® representó un método seguro y eficaz para reducir las dimensiones de la lesión preoperatoria.

PALABRAS CLAVE: quistes odontogénicos, tratamiento conservador, fitoterapia.

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