

## Educational Article

# Decompression: a first-intention treatment for “large” non-syndromic odontogenic keratocysts

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**Abstract** – Though odontogenic keratocysts (OKCs) are benign lesions, they have a high recurrence rate. Because of their aggressive behavior, they have been classified as tumors by the WHO until 2017. Main differential diagnoses are ameloblastoma and dentigerous cyst. Anatomopathological examination can reach a final diagnosis. Several treatments have been proposed: curettage, resection, enucleation (alone or together with peripheral ostectomy) and decompression. Decompression aims to decrease the volume of the lesion of “large” OKCs, in order to prevent surgery-related fractures and to preserve the surrounding important anatomical structures such as the inferior alveolar nerve. It could lead to a complete regression. If not, secondary enucleation can be performed in better conditions: a reduced volume to remove, a thicker epithelium to detach, a lower risk to damage neighboring anatomic structures and a lower recurrence rate. Long-term follow-up however remains necessary. Nowadays, minimally invasive surgery prevails. And since OKC was returned into the odontogenic cysts group in the WHO classification, decompression should be considered as the first intention treatment. The purpose of this paper is to provide an update about OKC features and biological mechanisms, to review the different treatment options and to provide a step-by-step protocol for decompression.

## Introduction

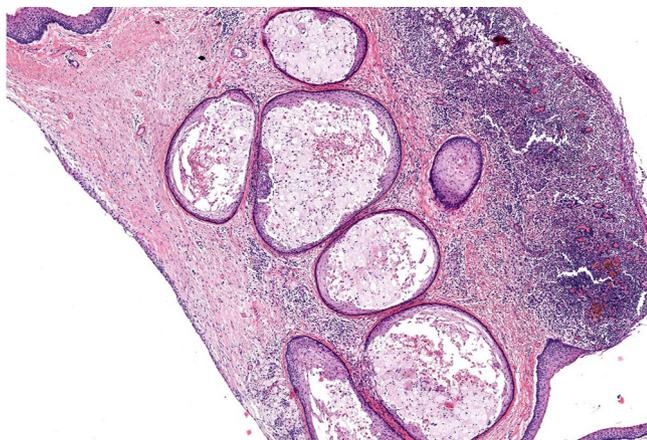
The odontogenic keratocyst (OKC) is a benign intraosseous odontogenic cyst lined with parakeratinized stratified squamous epithelium [1]. It was first described in 1855 by Maisonneuve as “buttery cyst” but finally named as “odontogenic keratocyst” in 1956 by Philipsen [2,3]. It originates from dental lamina remnants or from the overlying epithelium basal cells [4]. The OKC can be unique or multiple, and sometimes associated with a basal cell nevus syndrome (previously known as Gorlin or Gorlin-Goltz syndrome) [5,6]. It then appears necessary to systematically look for this syndrome when an OKC is discovered in young people, to address any aggressive basal cell carcinoma or other neoplasm. A systematic review found OKC to be 11.7% of the 18 297 odontogenic cysts reported between 1993 and 2005 (when the WHO classified OKC as cysts) and 14.3% of the 8129 odontogenic tumors reported between 2005 and 2011 (after WHO classified OKC as tumors) [7]. OKC mainly affects people around 25–34 years (gender predominance changing depending on studies). It has a predilection for the posterior part of the mandible, distal to the canine [4].

One-third of the patients are asymptomatic and usually diagnosed during a routine dental examination [8]. There are not pathognomonic clinical or radiological features of OKC.

OKC local behavior is described as aggressive and infiltrative. After a first surgery, its recurrence rate may extend up to thirty percent [9]. Indeed, it does not respect either the cortical bone or the surrounding soft tissues [10,11]. Clinical cases even report penetration of the skull base [12] and some others extension to the infratemporal fossae or the orbit cavity [13]. Some studies also show the development of primary intraosseous carcinoma arising from an OKC [14]. In 2017, the Fourth Edition of the WHO Classification of Head and Neck Tumors defined the OKC as a cyst and not a tumor anymore [15]. The final conclusion sustained about the clinical findings: an odontogenic keratocyst can completely regress after decompression, which is incompatible with a tumor behavior [16].

OKC’s clinical and biological behavior could be explained by the microenvironmental hypoxia (over expression of NOTCH1, ADAM-12 and HBEGF) more intensive in OKC compared to the normal oral mucosa, the calcifying odontogenic cystic, or the orthokeratinized odontogenic cyst [17]. The molecular background of OKC is not completely understood. BRAF V600E point mutation has been identified as the most

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**Fig. 1.** Histological section of an OCK wall (10× magnification, Haematoxylin and Eosin staining). Daughter cysts can lead to recurrences.

oncogenic driver mutation in malignant melanoma. Recent studies have reported the presence of BRAF or RAS, or FGFR2 mutation in ameloblastoma and subsequent activation of MAPK pathway, providing new treatment options for targeted therapeutics [18–20]. BRAF V600E mutation was found with variable frequency in some odontogenic tumors: ameloblastic fibro-odontoma, ameloblastic fibroma, ameloblastic carcinoma. BRAF V600E mutation was also found in OKC, without, however, any relation between its mutational status and size, location or recurrence rate [21].

The OKC is mainly characterized by its ortho- or parakeratinized epithelium with columnar cells in the basal layer which show focal reverse polarization [22]. Its epithelium is uniformly 5–10 cells thick with parakeratosis. Keratinaceous debris fill the lumen. Focal areas may be covered by orthokeratin. This thin and friable epithelium represents a major challenge for the surgeon, as any remnant can lead to recurrences due to daughter cysts (Fig. 1). As a consequence, enucleation alone is generally not sufficient [5].

Decompression reduces cystic lumen and thickens the epithelial wall, thus facilitating enucleation [23]. It can also be assumed that decompression changes oxygen level in the tumor, decreasing hypoxia and favorably modifying the microenvironment, and thus disadvantages OKC progression. Decompression therefore appears as a first-choice therapeutic option for large keratocysts.

The aim of this article is to describe in detail the different treatment of odontogenic keratocyst and especially highlight the interest of decompression.

## Treatment evolution

Historically, several treatments have been described. At first, two treatments conflicted: curettage and resection.

### Curettage

The purpose of curettage is to surgically scrap the wall of the cyst cavity and remove its contents. Due to recurrences, surgery was recommended every 5–10 years.

### Resection

Mainly proposed at the mandible, resection consists in a segmental bone removal to provide large margins. As this technique can lead to a loss of bone continuity, marginal resection could be favored in order to preserve one of the border of the mandible [24].

These two approaches appeared extreme: one not sufficient and leading to a high recurrence rate and the other associated with an important morbidity.

### Enucleation

Some surgeons then started to perform enucleation: removing the whole intact lesion by detaching the epithelium without cutting. However, with the thin and friable epithelium, a complete removal did not seem feasible. To distinguish the parts left in place, methylene blue could be used as a marking agent. Even so, enucleation was not considered a reliable option, as leaving any parts of the epithelium can lead to recurrence [25].

### Complement to enucleation

Adjunctive measures were published to complement the enucleation in a single intervention:

- A chemical technique: application of “Carnoy’s solution” made up of ethanol (6 ml), chloroform (3 ml), glacial acetic acid (1 ml) and ferric chloride (1 g). This tissue fixative was applied on the bone cavity after enucleation. It was promoted because of the morbidity decrease compared to the resection technique [26]. But vital surrounding anatomical structures such as the inferior alveolar nerve needed to be protected because of its toxicity. That is why, even if some practitioners perform it, this procedure has fallen into disuse and is even forbidden in most centers.
- A physical technique: liquid nitrogen cryotherapy is also reported in different studies: its freezing power devitalize tissues resulting in cell death to a depth of 1.5 mm [27,28].
- A mechanical technique: peripheral burring of the bone cavity with the purpose of removing any part of the remaining epithelium, to ensure a secure minimum margin [29].

### Decompression

The first articles suggesting decompression and marsupialization as treatments for jaw cysts are found in the German literature published in 1892 and 1910 by Partsch [30,31]. Decompression implies any technique to relieve the intra-cystic pressure which causes the expansion of the cyst. It is performed by making an aperture into the cyst wall. Most frequently, decompression techniques use a drain to maintain the cyst cavity open [32]. As a variant, marsupialization aims to exteriorize the internal contents of the cavity, by converting the cyst into a pouch: the superficial wall is resected and its cut

edges sutured to adjacent mucosa. The cavity is packed with medicated ribbon gauze (impregnated with Whitehead's varnish for instance) and changed every ten days until complete healing of the wound [33].

Therefore, with any methods of decompression, the cyst loses its independent functioning. Decompression, with a drain or by marsupialization, may lead to OKC complete disappearance of the lesion [16].

But most of the time, decompression will imply a two-stage surgery: first, marsupialization or decompression to decrease the volume and the proximity with close vital anatomical structures, and then enucleation.

A Cochrane systematic review was carried out in 2015 to compare the effectiveness of the different interventions. The conclusion was that there is no consensus about OKC treatments [34]. However, the last reviews and systematic analysis agree about:

- Segmental or marginal resection is the least conservative treatment but also the one with the lowest recurrence rate: almost zero according to the studies [35]. Because of its morbidity and the benign nature of the lesion, resection does not appear as a first intention treatment. They should be reserved for the multiple recurrence cases [8].
- Nor should only enucleation be prioritized, as this method has the highest recurrence rate [8,35].
- For an OKC with accessible margins, enucleation with adjunctive methods is preferable.
- For a "large" OKC, decompression should first be undertaken, followed if necessary by an enucleation.

### Decompression protocol

OKC diagnosis is generally suspected after radiological findings. Medical history should look for any eventual previous treatment or recurrence of jaw lesions. Of course, a complete clinical examination must then be conducted, notably palpation of a potential swelling. Sensitivity of all involved teeth should be tested. It must also be looked for paresthesia or dysesthesia in the mandibular or the maxillary nerve territory, that may occur as a result of nerve compression by the cyst.

An initial orthopantomogram can provide a first overview of the lesion. It will be especially useful for the follow up afterwards. However, only a three dimensional examination can give a proper evaluation of the real volume of the lesion (major axis measurement) [36]. It will also determine the accurate proximity with any important anatomical element, for instance the teeth, the mandibular canal or the infraorbital nerve (Figs. 2 and 3). Biopsy is mandatory before any treatment decision, as only anatomopathological examination can reach a final diagnosis. In the present case, biopsy material can be conveniently harvested from the resected tissue when performing the decompression.

Decision for a decompression protocol is chosen in case of an expected benefit (See Fig. 4). Even if the clinical situation is favorable, not all patients are eligible for a decompression protocol: indeed, the patient must be motivated to perform a

rigorous oral hygiene and a specific flushing one or twice a day for several months.

Using a simple draining rubber tube sutured to the mucosa can lead to drain loss or displacement [37]. An appropriate design should prevent its displacement. Drains can easily be produced in the dental laboratory. Essentially, there are two types of situations. When the location of the cyst opening matches with the dental collars, a straight thermoformed cannula can be used (Fig. 5); different copies of various lengths should be available at the time of surgery to allow the best choice. In other situations, an individual resin device must be manufactured from an impression taken after the surgical intervention (Fig. 6).

The operating steps can be as follows:

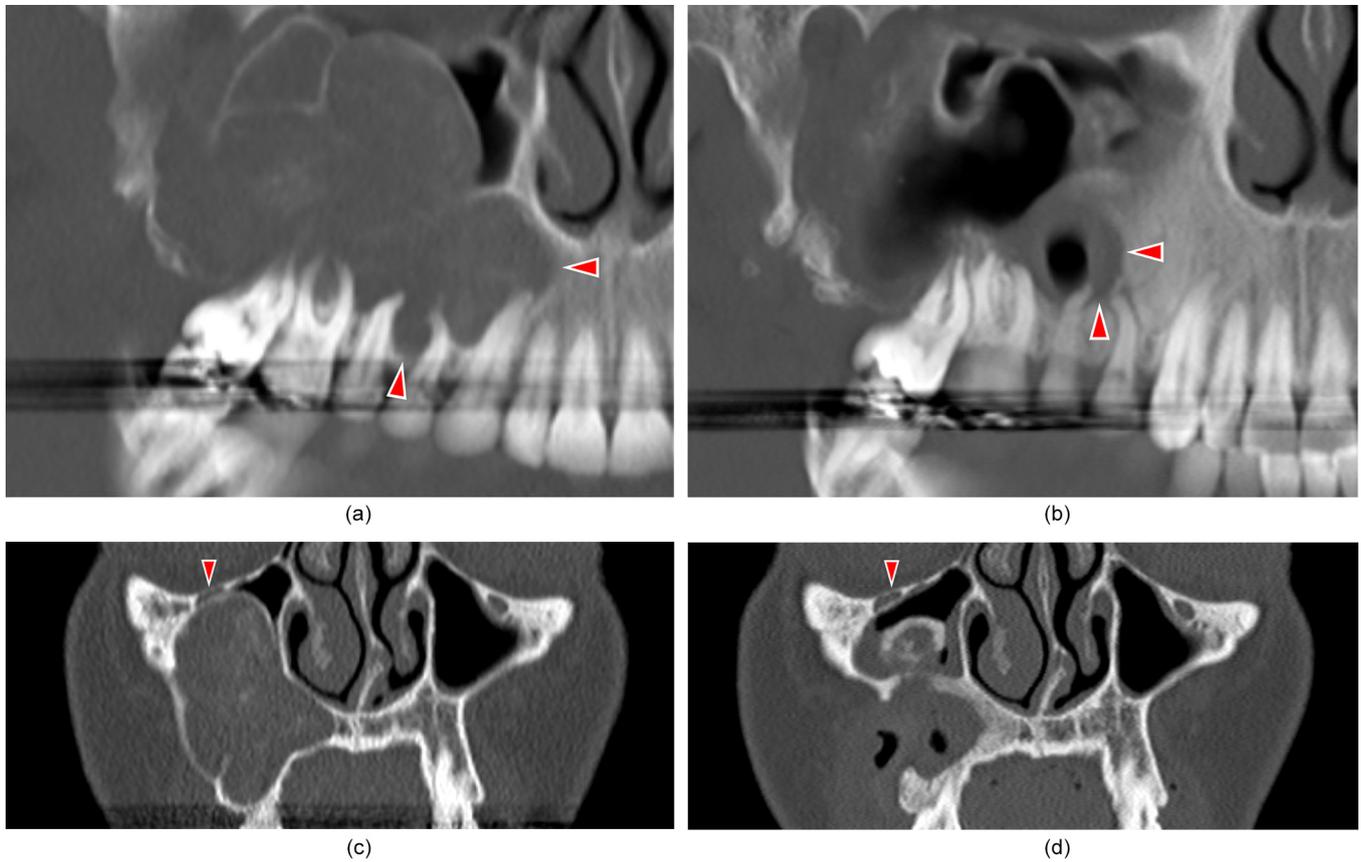
- tissue antisepsis
- local or loco-regional anesthesia
- incision of the mucosa and the periosteum (if any), facing the cyst
- mucoperiosteal flap rise
- if needed, osteotomy of the thinned bone using gouge forceps or rotary round bur and bone edges rounding
- cystic membrane resection
- transmission of the sample to the anatomical pathology laboratory
- insertion of the cannula into the cyst cavity
- stitch to the surrounding mucosa

The operating time is around thirty minutes, and postoperative morbidity is generally minimal [38].

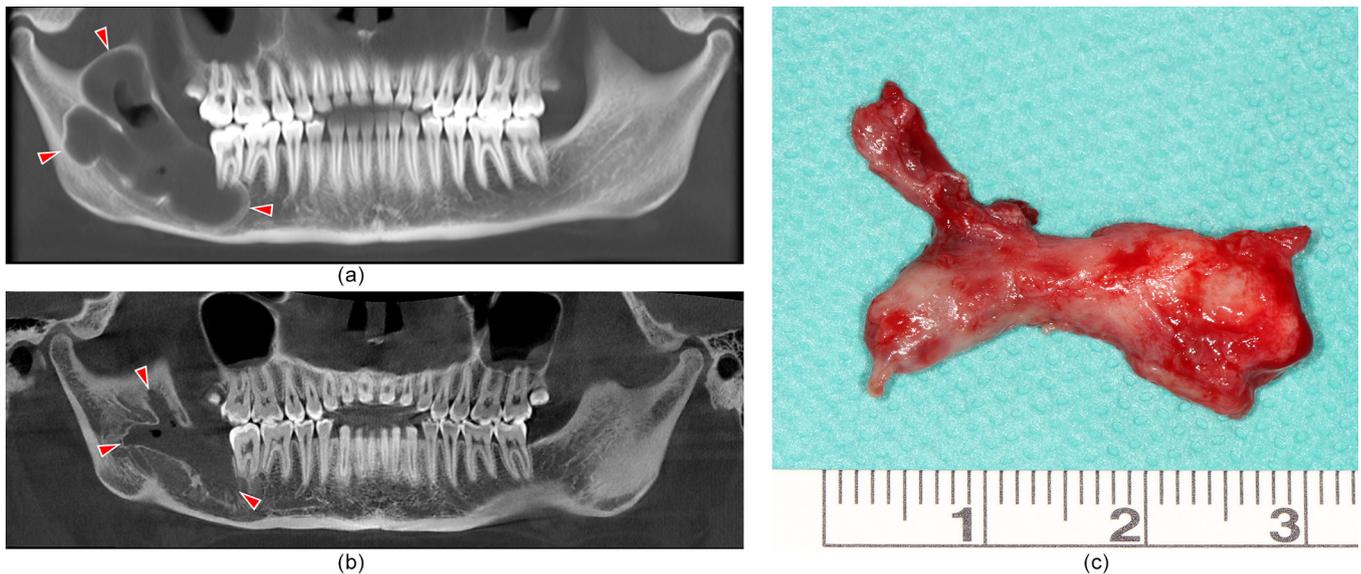
Just after the procedure, the surgeon must make sure that the patient is able to perform the rinse protocol efficiently. A demonstration in front of a mirror may help for the patient education. For the flushing, a flexible catheter attached to a syringe head can be used. The patient can rinse with physiological saline solution or a chlorhexidine mouthwash solution in the beginning, and switch to drinking water after a couple of weeks.

Every 2 months, the evolution of the lesion is monitored through radiological and clinical examinations. In particular, the position of the drain is checked. As a result of the decrease of the intracystic pressure, new bone formation along the periphery of the cystic wall can be noticed on the radiological follow-up examinations: decompression allows the lesion to be gradually replaced by bone, putting distance between the lesion and noble anatomical structures [39].

Depending on the initial size of the lesion and its reduction rate, decompression time can reach as high as 20–33 months [40,41]. A half volume shrinkage has been reported to be achieved on average in 6 months [37] or 9 months [42]. Decompression appears significantly faster in younger patients [37,41]. And shrinkage is faster when the initial size of the cyst is larger [43]. No difference of shrinkage speed has been noted between maxilla and mandible [37].



**Fig. 2.** 3D imaging of a right maxillary OKC in a 37-year-old female. (a) Before the protocol, the lesion extended to the centerline of the second incisor; lobes crept into the alveolar bone down to the tooth collars. (b) After 14 months of decompression, both the incisor and the canine are away from the OKC. Only the apices of the 4 posterior teeth still have their apices inside the cyst. After root filling of these teeth, the next step was enucleation of the lesion, together with apicectomies of these teeth for a better peripheral burring of the cavity. Without the decompression protocol, 5 teeth would have been lost in a one-step surgery. Notice the presence of air in the cavity, because of the drain. (c) Before the protocol, the infraorbital nerve was flattened by the OKC. (d) After 14 months of decompression, surgery could be performed with a lower injury risk to the infraorbital nerve, away of the lesion.



**Fig. 3.** 3D imaging of a right mandibular OKC in a 18-year-old female. (a) Before decompression protocol, the lesion spread from the swollen apex of the mandibular coronoid process to the centerline of the distal root of the first molar (major axis 55 mm). There was high risk of nerve injury because of an intimate relation of the cyst to the inferior alveolar nerve. (b) After 12 months of decompression, the OKC had significantly shrunk. (c) Enucleation did not harm the inferior alveolar nerve.

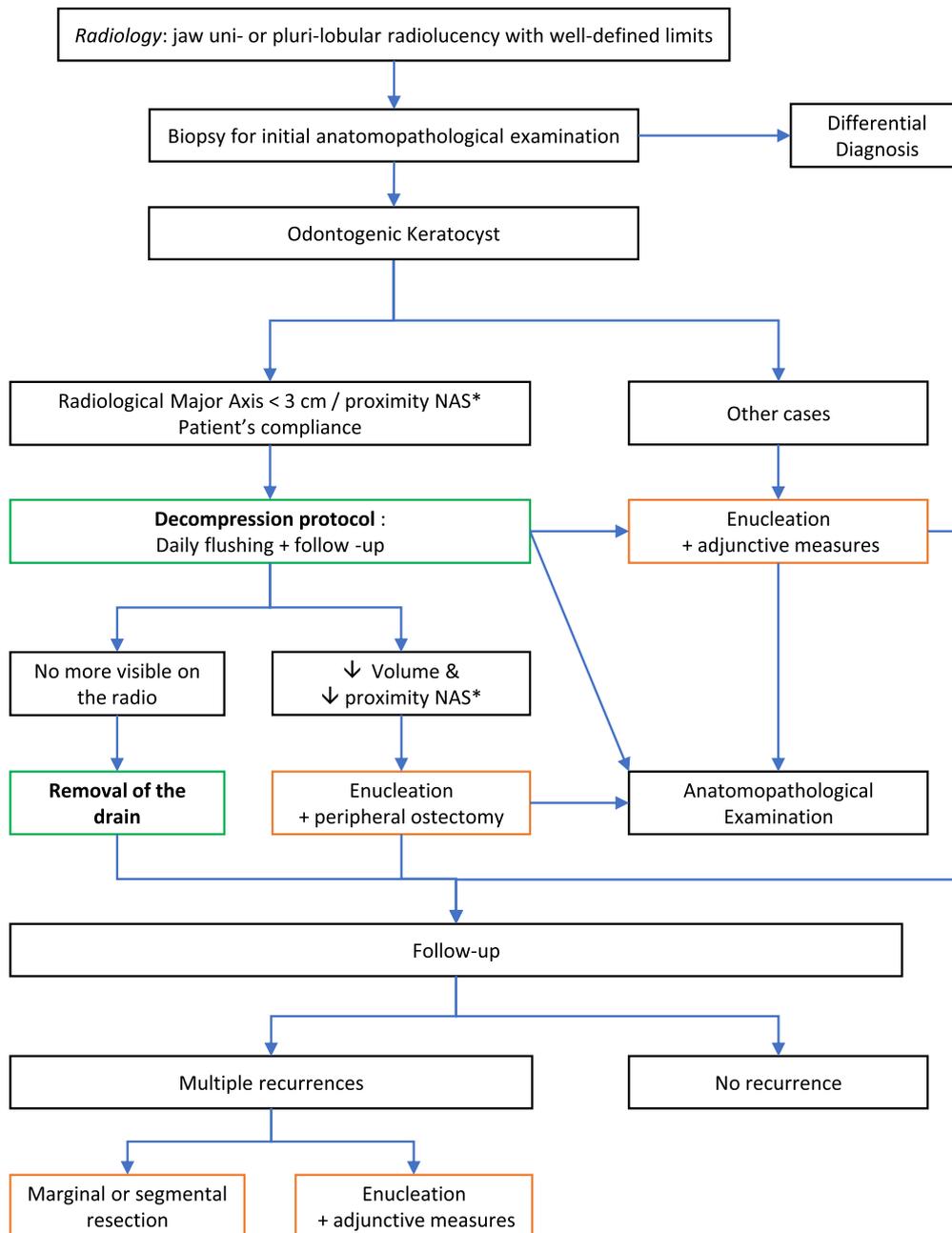


Fig. 4. Decision tree. \*Noble anatomical structures.

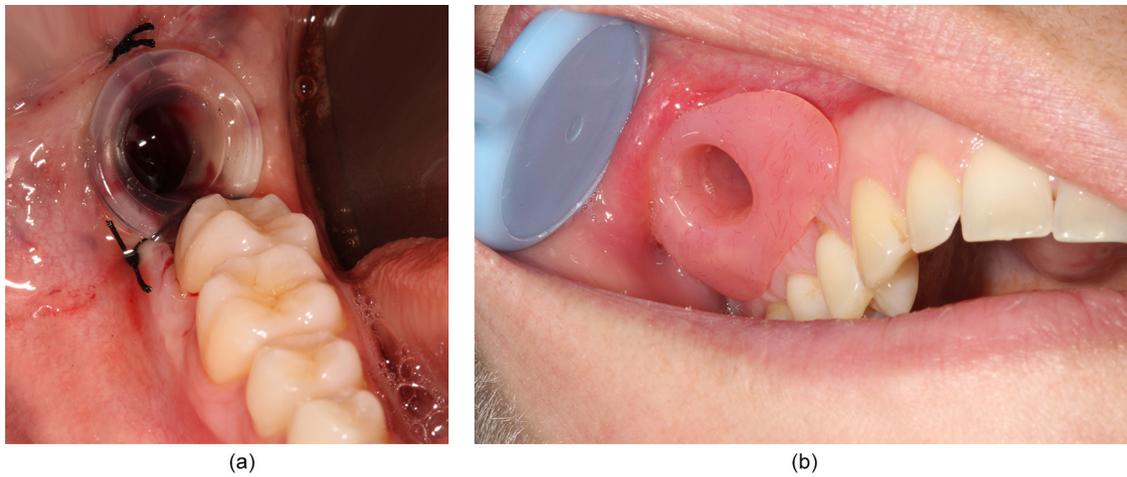
Though complete regression of OKCs have been reported as a result of decompression [15], enucleation is most commonly required. The surgeon will decide the end of the decompression treatment when the volume has decreased sufficiently for enucleation to be performed without damages to the important surrounding anatomical structures [43].

After a decompression protocol, the epithelium becomes thicker: in a study based on 34 OKC, the thickness of the epithelium showed a 9-fold-increase during a 10-month decompression. These changes are mainly related to the inflammation [23]: the epithelium changes to hyperplastic stratified squamous with a dense connective tissue infiltrated of inflammation cells (Fig. 7).

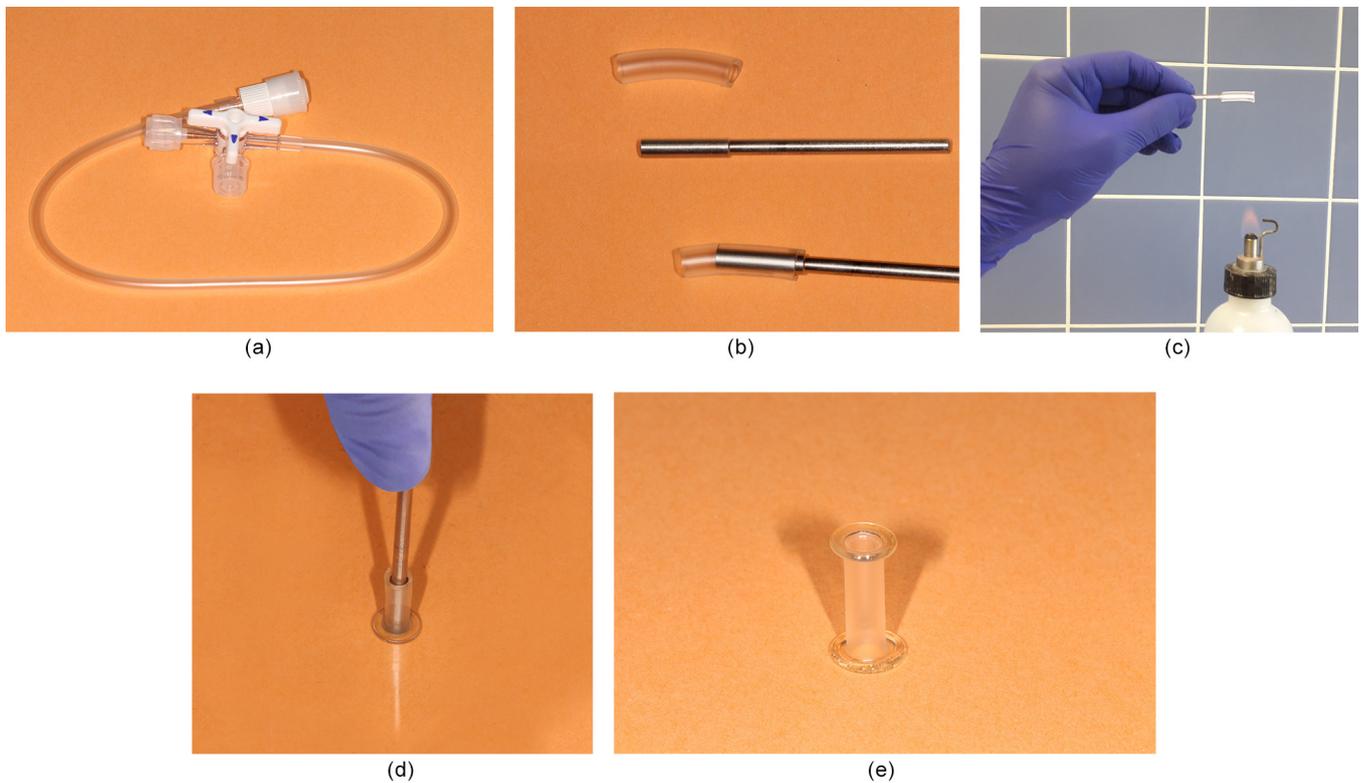
When required, endodontic treatments need to be conducted before OKC enucleation. Any overextension of endodontic filling material would be removed during the surgery time. Likewise, if some apices are still within the OKC, root resections must be conducted at the same time to allow a complete enucleation of the cyst wall.

Even if the cyst wall is thicker, enucleation surgery remains tricky. The cyst and all its epithelium should be removed: dissection to detach without cutting must be prioritized.

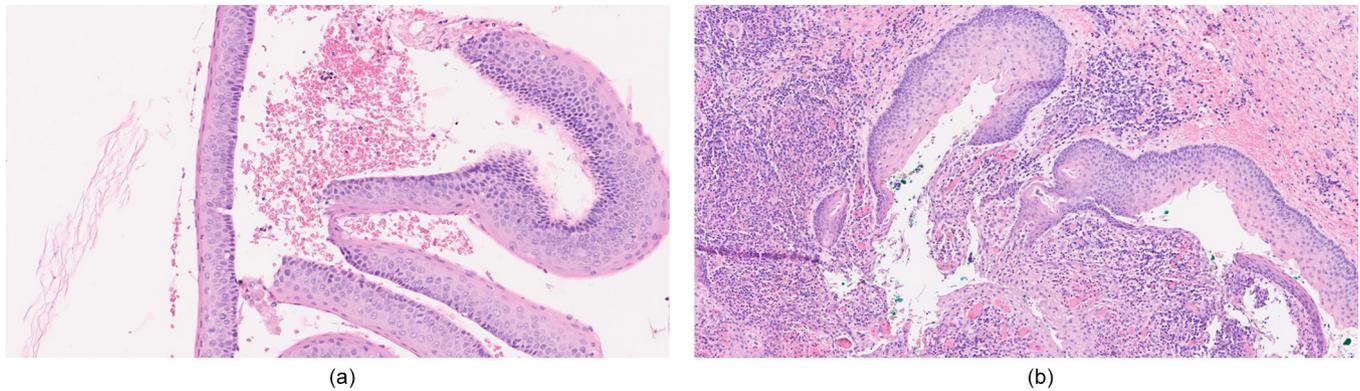
To reach a lower recurrence rate associated peripheral ostectomy is recommended [44]. A rounded bur with abundant saline irrigation can be used.



**Fig. 5.** Examples of decompression cannulas. (a) Thermoformed cannula in a position in line with the dental arch. This cannula has been prepared before the first surgery time (cyst opening and biopsy) and installed during the intervention. Stitches concern only the surrounding mucosa to “trap” the drain during healing. As an option, if the tube is not flanged, stitches can also transfix the drain. (b) Individual resin cannula in a case of decompression above the maxillary teeth apices. This cannula has been manufactured from an impression taken a week after the first surgery time, and installed afterwards.



**Fig. 6.** A method for manufacturing a decompression cannula. The idea is to shape a flange at each end of the tube to prevent the cannula from falling outside, or inside the cyst. Depending on the diameter required, any thermoplastic medical plastic tube can be used (intravenous infusion line, nasogastric tube, surgical suction pipe). When the OKC contents is very thick, a wider internal diameter should be chosen to allow the white lumps to be flushed out. (a) In this example, a polyvinyl chloride (PVC) intravenous infusion line can easily be cut to the appropriate dimension. (b) A metal mandrel is inserted in the tube, to handle it and maintain its shape while soft. The use of a mandrel represents an improvement of the technique initially described by a Danish author (Dr A Nielsen) in 1988 [40]. The mandrel diameter should be the same as the internal diameter of the infusion line. (c) The end of the tube is held above a flame, while rotating the mandrel to distribute the heat. (d) When soft, the tube tip is pressed against a glass plate until it cools. (e) The same process is repeated on the other end to get a double flanged tube. Before surgery, the tube is soaked in paracetic acid and thoroughly rinsed with distilled water.



**Fig. 7.** Histological sections of an OKC before and after decompression (20× magnification, Haematoxylin and Eosin staining). Thickening of the membrane is not significant in this case, but an important inflammatory change can be seen. (a) Before decompression protocol. (b) After decompression protocol.

Of course, the final resection specimen is also sent for anatomopathological examination.

In all cases, a long-term follow-up is necessary, beyond 10 years [45].

Besides OKC, the decompression protocol has also been reported to be efficient in patients with other cystic lesions, like dentigerous cysts and unicystic ameloblastoma [43]. In the three types of lesions, no differences were noted in the velocity of shrinkage [43]. However, the decompression option remains controversial when dealing with a tumor such as an ameloblastoma.

## Conclusion

All in all, decompression appears to represent a minimally invasive and preservative treatment of OKC. It should be proposed as the first option in cases of large cysts that constitute a threat of surgery-related fractures and/or damage to the surrounding important anatomical structures. Decompression protocol should be reserved for patients sufficiently motivated and skilled enough to perform daily flushing for months and to attend control consultations.

Anatomopathological analysis of the lesion tissues resected during the decompression intervention is an indispensable step to avoid missing the diagnose of a malignant process.

In the vast majority of cases, a secondary surgical intervention is needed. It is expected to be easier, at lower risk and with a lower recurrence rate. However, recurrences are always dreaded, and a long-term follow-up is always mandatory.

**Conflicts of interests:** The authors declare that they have no conflicts of interest in relation to this article.

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