

## Case report

# Recurrence challenge in odontogenic keratocyst variants, two clinical cases

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### Key words:

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**Abstract – Introduction:** After radicular and follicular cysts, odontogenic keratocysts are the third most common cyst of the jaws. They can be unique or multiple when included in basal cell nevus syndrome. The odontogenic keratocyst is known for its high recurrence rate and local aggressiveness. It has been classified into two histologic variants: orthokeratinized or parakeratinized. The aim of this report is to highlight the clinical and radiological characteristics, the histopathological features, as well as the risk factors for recurrence of odontogenic keratocysts.

**Case report:** Two clinical cases of odontogenic keratocysts with different histologic features are reported.

**Discussion:** Radiological and histological features, localization, extension and evolutionary aspect of the lesion are risk factors for recurrence, and therefore have an impact on the treatment of keratocysts. Through critical analysis of the first case report, the authors identify therapeutic errors to avoid, particularly when histologic confirmation of the lesion has been obtained.

### Mots clés :

kératokystes /  
histologie / radiologie /  
récidive / traitement

**Résumé – Introduction :** Après le kyste périapical et le kyste folliculaire, le kératokyste odontogène est le troisième plus fréquent des kystes des maxillaires. Il peut être unique ou multiple s'il est associé à la naevomatose baso-cellulaire. Le kératokyste a un risque élevé de récurrence et une agressivité locale. Il a été classé en deux variétés histologiques : orthokératinisé ou parakératinisé. **Observation :** Deux cas de kératokystes odontogènes sont décrits sur un plan clinique, radiologique et histopathologique. **Discussion :** Le type histologique, l'image radiologique, la localisation, l'extension et l'aspect évolutif de la lésion sont des facteurs de risque de récurrence. Ces facteurs doivent être pris en compte dans la décision thérapeutique. À travers une analyse critique du premier cas, les auteurs mettent en exergue les erreurs thérapeutiques à éviter, notamment lorsqu'une confirmation histologique a été obtenue.

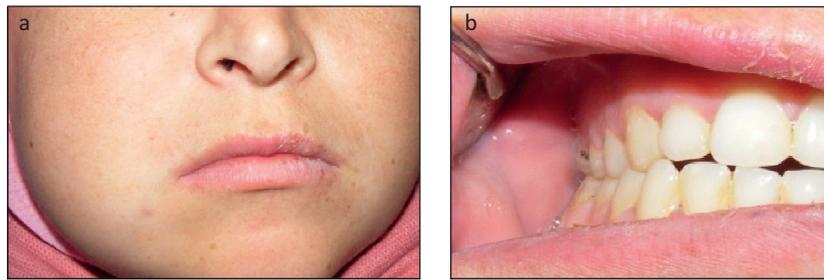
## Introduction

The odontogenic keratocyst was first described by Philipsen in 1956 to designate an odontogenic keratocyst with a parakeratinized epithelial surface. This lesion has a very aggressive nature and high recurrence rate, which makes it distinct from the other keratinized odontogenic cysts. In 2005, the World Health Organization (WHO) [1] reclassified the keratocyst from a cyst to a "keratocystic odontogenic tumour", which is defined as a benign, uni- or multi-cystic, intraosseous tumour of odontogenic origin, with a parakeratinized stratified squamous epithelium, and aggressive behaviour. Before this classification, the odontogenic keratocyst was classified into two

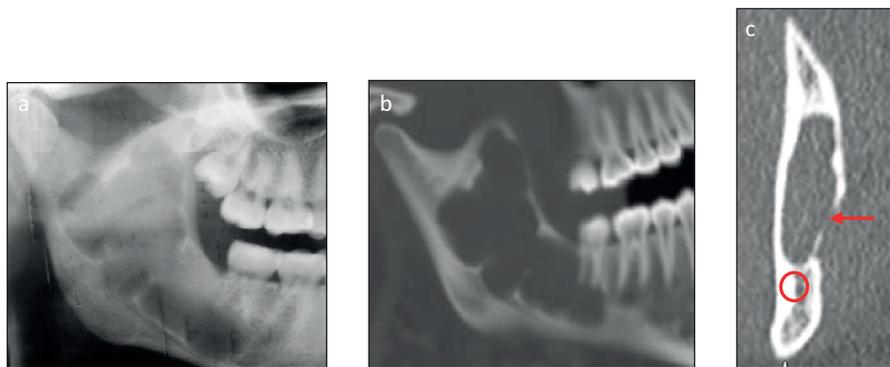
histologic variants: orthokeratinized and parakeratinized. Afterwards, research showed that the orthokeratinized variant not only lacks the typical characteristics of the parakeratinized one, but also has different biological characteristics and consequently a much lower recurrence rate. Radiological and histological features, the lesion topography and numerous other features can constitute risk factors of recurrence. Therefore, they should guide the therapeutic choice.

Taking these data into consideration and based on two clinical case reports, the aim of this article is to report the main characteristics of this lesion and their implications on treatment, and also to highlight some therapeutic errors to avoid through critical assessment of the first case report.

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**Fig. 1.** a: extra-oral clinical aspect, b: intra-oral clinical aspect.  
*Fig. 1. a : aspect clinique extra-oral, b : aspect clinique intra-oral.*



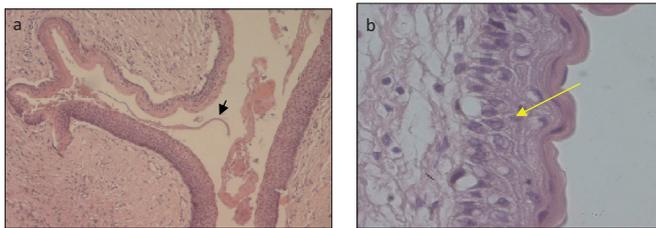
**Fig. 2.** Radiologic aspect of the lesion. a: panoramic radiograph, b: sagittal computed tomography reconstruction, c: oblique coronal reconstruction showing the absence of invasion of the mandibular canal and the perforation of the lingual cortex (arrow).  
*Fig. 2. Aspect radiologique de la lésion. a : radiographie panoramique, b : reconstruction scanographique sagittale, c : reconstruction coronale oblique montrant l'absence d'invasion du canal mandibulaire et la perforation de la corticale linguale (flèche).*

### Clinical case reports

**Case report 1:** A 20-year-old patient with non-contributory medical and surgical history was referred for the appearance of right lower facial cellulitis, developing one week earlier. The dentist prescribed antibiotics and non-steroidal anti-inflammatories for a week that resulted in no improvement. On initial examination in our department, painful cheek tumefaction and limited mouth opening were noted. Intraoral examination revealed purulent discharge from the retromolar region and second-degree mobility [2] (horizontal mobility exceeding 1 mm) of the second mandibular molar, which tested positive for vitality (ethyl chloride vitality test) (Fig. 1). Palpation of the lingual and vestibular bone did not reveal any deformity. A well-defined radiolucent multilocular image with peripheral bone condensation and polycyclic contours spreading to the posterior part and the right mandibular angle and avoiding the condyle was observed on the panoramic radiograph. Considering the aspect of the lesion, the possible diagnoses were odontogenic keratocystic tumour or ameloblastoma. Computed tomography revealed a hypodense image breaking the lingual cortex with a dense liquid content (Fig. 2). The initial treatment consisted in simple enucleation of the lesion under

general anaesthesia without extraction of tooth 47. Histological examination concluded that an odontogenic keratocystic tumour of a parakeratotic type was present (Fig. 3). However, recurrence was noted four months later and revision of the cystic cavity was performed with a more thorough curettage of cystic walls, without extraction of the last inferior molar. The lesion remained stable for three years after the second surgical intervention (Fig. 4)

**Case report 2:** A 50-year-old patient without any medical history was referred for incidental discovery of a radiolucent mandibular image located at the apices of the lower incisors (Fig. 5). Only the right central incisor reacted negatively to the vitality test. Panoramic radiographic examination revealed a unilocular radiolucency with well-limited corticated borders located at the apices of the resorbed inferior incisors and canines (Fig. 6). Following these findings, a periapical cyst, a keratocyst, an essential bone cyst or an ameloblastoma were suspected. First, the patient underwent endodontic treatment of the necrotic tooth followed by surgical enucleation of the cyst. Finally, incisors and mandibular canines were extracted due to insufficient bone support and the intra-operative presence of keratine (Fig. 7). Histological examination concluded



**Fig. 3.** Histological aspect: a: at low magnification (x10), b: at high magnification (x50). The cyst wall is lined with parakeratinized squamous epithelium (yellow arrow); Light is filled with keratin lamellae (black arrow).

*Fig. 3. Aspect histologique : a : à faible grossissement (x10), b : à fort grossissement (x50). La paroi kystique est entourée par un épithélium squameux parakératinisé (flèche jaune) ; la lumière est remplie de lamelles de kératine (flèche noire).*



**Fig. 4.** After three years of follow-up; panoramic radiograph: reossification signs and the persistence of a radiolucency surrounding the roots of the tooth (47).

*Fig. 4. Radiographie panoramique après trois ans : des signes de réossification avec persistance d'une radioclarité entourant les racines de la 47.*

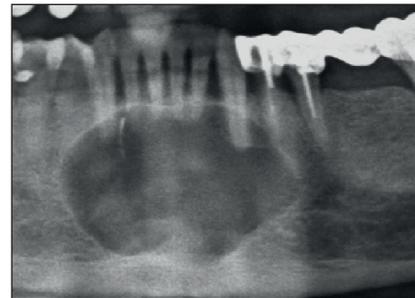
that an orthokeratinized keratocyst was present (Fig. 8). The lesion was stable for three years after surgery (Fig. 9)

## Discussion

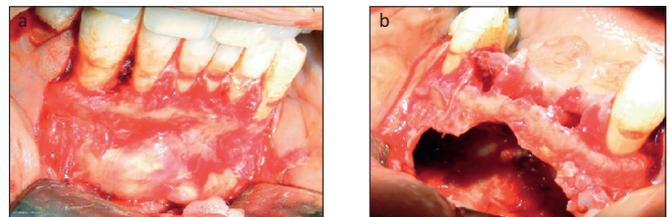
The odontogenic keratocyst or epidermoid cyst as it was previously called, arises from the cell rests of dental lamina or proliferation of epithelial rests [3]. Its frequency among cysts of the jaws is 10 to 20% [4]. It is more common in the second and third decades of life and it can appear earlier when it is associated with basal cell nevus syndrome. The majority of these cysts are found in the ascending ramus of the mandible [5]. Histologically, the WHO designated two different variants of odontogenic keratocyst in 1992, an orthokeratinized and a parakeratinized one. The parakeratinized form, often found in the basal cell nevus syndrome, consists in a basal layer made



**Fig. 5.** Intra-oral clinical aspect.  
*Fig. 5. Aspect clinique intra-oral.*



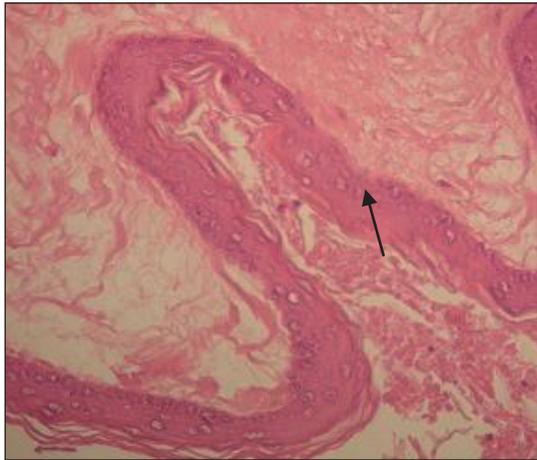
**Fig. 6.** Radiologic aspect of the lesion: panoramic radiograph showing unilocular radiolucency with well-limited corticated border.  
*Fig. 6. Aspect radiologique de la lésion : radiographie panoramique montrant une radioclarité bordée par un liseré d'ostéocondensation.*



**Fig. 7.** Intraoperative aspect of the lesion: lesion which tends to externalize with persistence of fine bone wall without adherence to periosteum, presence of keratin intraoperatively. a: After flap release, b: after enucleation of the lesion.

*Fig. 7. Aspect per-opératoire de la lésion : tendance à l'extériorisation avec persistance d'une fine coque osseuse sans adhérence au périoste, présence de kératine. a : après décollement du lambeau, b : après énucléation de la lésion.*

of cubic or cylindrical cells lacking acanthosis and rete ridge proliferation. It is covered by five to eight layers of squamous epithelium lining. The epithelium is characterized by a wavy or corrugated parakeratinized surface layer. Some signs of dysplasia may be observed. The basal layer of the tumour might be budding into the supporting connective tissue, forming "daughter" cysts at the periphery. If inflammation occurs, the fibrous capsule in the wall of the connective tissue thickens.

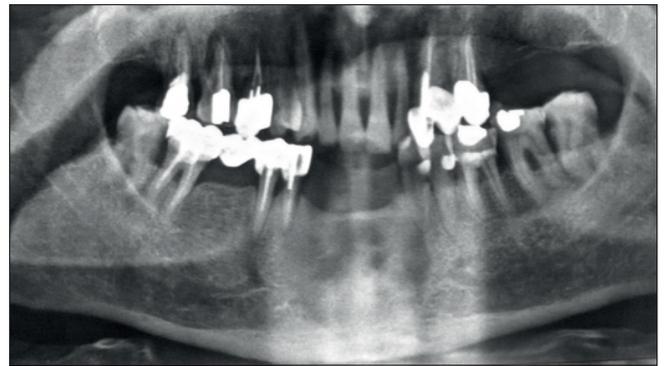


**Fig. 8.** Histological aspect: cystic wall lined by an orthokeratotic epithelium (arrow).

*Fig. 8. Aspect histologique : la paroi kystique est entourée par un épithélium orthokératinisé (flèche).*

In addition, it may cause ulceration of the epithelium, which acquires well-developed ridges, whereas the keratinization tends to disappear. This capsule can contain dystrophic calcifications or small fragments of cartilage of unknown origin [6].

In contrast, the orthokeratinized variant displays a squamous basal layer, a prominent granular layer, orthokeratinization, as well as a high tendency to spread keratine in the cyst [7]. Symptomatic keratocysts present inflammatory signs on histology. This infiltrate causes cystic epithelium metaplasia giving rise to the formation of stratified non-keratinized epithelium, which may lead in turn to difficulty in diagnosis or a false negative. The reclassification of the WHO [1] in 2005 cast doubt on the cystic nature of the parakeratinized type that was renamed keratocystic odontogenic tumour because many authors found that this form had higher mitotic activity and diminishes tumour suppressor genes [6]. The orthokeratinized variant became part of the odontogenic cysts, which underwent a metaplastic orthokeratinisation, involving the gingival cyst, the residual cyst, the primordial cyst, dentigerous cyst and periodontal cyst. This reclassification was not universally accepted and thus the treatment remains controversial with a relatively high recurrence risk. Guy Le Toux [8] reports a recurrence rate between 3% and 62%, associated with many factors: the histologic nature, the radiologic image, the topography and the extension of the lesion (cortical perforation). Its primary evolutive aspect or recurrence are factors that have to be taken into consideration before proceeding to surgical treatment. Dayhimi [9] compared the biological characteristics of parakeratinized odontogenic keratocysts with those of orthokeratinized odontogenic cysts, including the orthokeratinized keratocyst, using P53 and TGF-alpha (Tumour-Growth-Factor-alpha) as markers. He concluded that these proteins are



**Fig. 9.** Follow-up panoramic radiograph showing reossification signs in the mandibular anterior region.

*Fig. 9. Radiographie panoramique de contrôle montrant des signes de réossification de la région mandibulaire antérieure.*

more frequently found in odontogenic keratocystic tumours. This can explain the aggressive nature and the recurrence tendency noted in the first case report. On the other hand, the orthokeratotic forms are treated like the other cysts of the jaws. A recurrence rate of 42.6% is reported in the literature for the parakeratotic variant compared to 2.26% for the orthokeratotic form [6].

Radiologic images of keratocysts are either unilocular or multilocular, including multiple radiolucent images that are well defined and surrounded by peripheral bone condensation with smooth or polycyclic borders. Singh [10] studied the relationship between the radiographic aspect and the proliferation of epithelial cells using proliferation markers (PCNA: proliferating cellular nuclear antigen). He concluded that unilocular images compared to multilocular images displayed a lower proliferative potential; therefore, it should not be treated as a tumour. The radiologic aspect in the second case was unilocular. After conservative treatment, it did not show signs of recurrence after a three-year follow-up, while the multilocular image of the first case report needed two interventions before being stabilized, thus confirming Singh's suggestion. The author and others [11] suggest that the inflammation increases mitotic activity of the multilocular lesion. The recurrence that occurred in the first case report can be explained by inflammation and secondary infection.

The topography of the lesion seems to be a recurrence risk factor. The angle and ramus lesions are more recurrent: this could be due to difficulty of access during resection, mainly for the multilocular forms [12]. Keratocyst infection may also lead to a higher rate of recurrence [10, 11]. Presence of satellite cysts at the surface epithelium, cortical perforation and extension to soft tissues, were associated with a recurrence rate of 60% in a retrospective study [12]. Eventually, the condition of the tumour excision is a major prognostic factor. Enucleation of a single unit is less recurrent than that of several

fragments. Lesions associated with Gorlin-Goltz syndrome require more aggressive treatment because of a higher recurrence risk [13]. All teeth adjacent to the lesion should be extracted as they may be a source of recurrence risk. In the first case report, the second mandibular molar was not extracted even though its roots reached into the tumour mass; this could be the source of the second recurrence. Follow-up panoramic radiograph revealed persistence of a radiolucency surrounding the teeth roots.

Surgical treatment should be prepared by a complete clinical and radiographic examination (computed tomography), and followed by two clinical and radiologic follow-ups per year. Different surgical techniques have been suggested for the treatment of keratocysts and the most appropriate treatment remains a subject of controversy. Aggressive treatment, such as ostectomy, is necessary in cases associated with cortical effraction, coronal invasion, soft tissue invasion, a multi-recurrent keratocyst, an ameloblastic graft or malign transformation. Complete enucleation is recommended for intra-osseous lesions without cortical rupture. Enucleation associated with marginal resection using a bur is done if the split is difficult. Periosteotomy is involved if the lesion adheres to the periosteal elevator. A posterior mandibular location necessitates enucleation with an excision extended to the adjacent mucosa to limit the recurrence risk that may come from the oral mucosa. "Marsupialization" is better suited for children with mixed denture in order to preserve the permanent teeth buds and also for lesions that resorbed nasal walls, sinus or that develop close to the lower alveolar nerve. Decompression associated with later enucleation is recommended for the infected lesions to reduce their volume and thin their lining [6, 8, 14, 15]. Cao [16], in his clinical study of large mandibular odontogenic keratocystic tumours in adolescents treated by decompression, found no recurrence over a period of 1 to 5 years after operation. Some authors [17] conducted a morphometric analysis of the epithelial lining and fibrous capsule in histological sections of odontogenic keratocystic tumours before and after decompression. They reported a considerable thickening of the tumour's fibrous capsule. This change facilitates the surgical procedure, which may explain the lower level of recurrence.

Some limits of these case reports must be raised. In the first case, radiologic features suggested that this lesion was an odontogenic keratocystic or an ameloblastoma and it spread to the mandible angle, the ascending ramus, and part of the horizontal right mandibular branch and the cornoid process. These two tumours have a high recurrence risk (possibly more than 80% for ameloblastoma [18]). Moreover, other factors of poor prognosis are present: the multilocular nature of the image, cortical breaking and invasion of soft tissues. These conditions justified radical treatment. However, the surgical treatment involved simple enucleation without extraction of tooth 47 and without marginal resection of the mandibular

branch, which was a non-adapted therapy according to the literature. During the second surgery, although the histopathologic result was in favour of a parakeratinized type, the surgeon applied the same surgical treatment (simple enucleation) without removal of the second molar. The lesion was clinically silent for three years. But, follow-up panoramic radiograph showed the persistence of a radiolucency surrounding the roots of tooth 47. The diagnosis of a periradicular condition was ruled out as the tooth responded positively to the vitality test. Periodontal probing did not reveal any distal periodontal pocket. This could suggest that the peri-radicular image corresponded to tumoral tissue incompletely eliminated. This conservative treatment avoided performing large bone resection but the risk of recurrence of the lesion was still present. This patient should have had tooth 47 extracted and curettage of remaining soft tissues. Then, she should have been closely monitored to diagnose any recurrence early. The absence of recurrence in the second case confirms the literature data and justifies our conservative approach (Fig. 9).

Treatment of odontogenic keratocysts depends on their clinical and radiologic features. Teeth in relation with the lesion should be extracted as they may be the source of recurrence. To prevent the risk of malignant transformation [19] or an ameloblastic graft and the recurrence problem, strict follow-up is necessary especially for keratocystic odontogenic tumours.

**Conflicts of interests:** none declared

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