



## Review Article

### Odontogenic Keratocyst

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#### ABSTRACT

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The odontogenic keratocysts are developmental cysts of the jaws that require proper diagnosis due to their potential for local aggressive growth, recurrences, and association with an inherited syndrome. The renaming of odontogenic keratocysts as keratocystic odontogenic tumors in 2005 then, after 12 years, denomination as an odontogenic cystic lesion, by the WHO in 2017, has been one of the most debatable changes in the terminology of odontogenic lesions in recent years. This article reviews the etiopathogenesis, clinical, radiographic, histopathological, immunohistochemical and treatment; with the aim of describing the importance of this lesion.

#### Introduction

Lesions arising from odontogenic tissues of the jaws vary from very common to very rare. Odontogenic keratocysts (OKCs) are relatively frequent cysts of the jaw that originate either from the dental lamina or from the primordial odontogenic epithelium. There has been a great concern in OKC in the last decade. In contrast to other jawbones cysts, OKC has a high recurrence rate after surgical management. (1) OKC has been re-classified in the 2005 edition of the WHO Classification of Head and Neck Tumors, from cystic to neoplastic lesions, and named "keratocystic odontogenic tumors." (KCOT) (2, 3) This has been centered on its aggressive behavior, and PTCH1 gene mutation or inactivation, that was structured as a main cause, obligated the rename of OKC as a tumor.

(4) Though PTCH rearrangements are found in more than 8% of OKCs, they are not distinct, as the loss of heterozygosity (LOH) on the 9q22.3 region (where the PTCH1 gene has been mapped) have been detected in other developmental cysts, including dentigerous cyst. (5) The evidence of allelomorphic loss, mainly in the p16, p53, PTCH, MCC, TSLC1, LTAS2, and FHIT genes, have been found in OKC. (6) During the years, many conservative and aggressive treatments have been proposed to minimize the high rate of recurrence, but none of them has been recognized as the gold standard for this entity. (7) Even, marsupialization is successful management for OKC; moreover, it might be linked with the return of the lining epithelium to the normal condition, and decrease recurrency—traits not generally related to tumor. (8)

The last fourth edition of the WHO Classification of Head and Neck tumors restores the OKC to cysts category and declines the prior name KCOT; it considered as a developmental cyst with more aggressive behavior. (9) The OKC is an unusual cyst compared to other jaw cysts. While most epithelial cysts are thought to grow passively driven by hydrostatic pressure inside the lumen, OKC is believed to grow due to active cellular proliferation. (10) This review is an attempt to report and summarize the available and up-to-date knowledge about this dilemma lesion.

## Literature review

### Keratocyst nomenclature

OKC characteristic marks were firstly represented by Pindborg and Hansen in 1963. For many years, several investigators have been seeking to know the nature, recognition, and treatment, guiding to classifying and re-classifying this lesion, priorly classified under developmental odontogenic cyst of the jaw by WHO in 1971 & 1992. OKC has been re-classified and renamed as KCOT in 2005 WHO classifications of head and neck tumors. Yet, in 2017, the latest WHO classification of Head and Neck Pathology, OKC, is back into the cystic category. (11) Passi et al. (11) summarized OKC nomenclature through years in the following list:

1. "Dental cyst by John Hunter; 1774
2. Dermoid Cyst by Mikulicz; 1876
3. Primordial cyst by Robinson; 1945
4. Keratocystoma by Shear
5. Odontogenic keratocyst by Philisen; 1956 & Pindborg and Hansen; 1963
6. Benign neoplasm by Toller; 1967
7. Odontogenic keratocyst by WHO; 1971
8. True benign cystic epithelial neoplasm by Ahlfors; 1984
9. Odontogenic keratocyst by WHO; 1992
10. Keratocystic odontogenic tumor (Benign neoplasm) by WHO; 2005
11. Odontogenic keratocyst by WHO; 2017".

### Definition

OKC fulfills a cyst definition, that is, a pathologic cavity filled with fluid or semi-solid material lined by epithelium. It can also be reduced in size or even ablated in some cases by marsupialization, which seems to support a cyst classification. However, other factors such as recurrence rate, overexpression of cell cycle proteins, and an association with a proliferation-related genetic mutation suggest OKC perhaps a cystic tumor (KCOT). In any event, the classification of this well-recognized entity as an aggressive cyst or as benign neoplasm is academic. Instead, the real importance is the appreciation of its potential behavior, possible syndrome association, and proper management. (12)

OKC is so named because the cystic lining produces keratin. It is a parakeratin-lined cyst-like lesion within the bone. OKC is one of the rare and distinctive developmental odontogenic cysts, which arise from the dental lamina, filled by clear fluid or a cheesy material resembling keratin debris. (11)

Neville 2019 et al. (13) defined OKC as "a quite common developmental odontogenic cyst which represents about 10% to 14% of entire jaw cysts. Its characteristic microscopic features are specified, including basilar nuclear palisading and keratin production (especially parakeratin). Depend on its probable aggressive behavior and molecular abnormalities; there has been an argument whether

OKC should be categorized as a cyst or a neoplasm. Both terms (OKC and KCOT) recently are being used, although the most recent WHO classification system supports designation as a cyst." (13).

### Etiopathogenesis

OKC develops from the rest of dental lamina in jawbones or may arise from basilar cell layer of covering oral epithelium. Features which might be subscribed to the etiopathogenesis of OKCs involve high proliferation rate, which shows a significantly greater expression of proliferating cell nuclear antigen (PCNA) (Figure 1-A), Ki-67 (Figure 1-B), overexpression of (the antiapoptotic protein) Bcl-2, MMPs 2 and 9 (Figure 1-C and D). (12, 14-16).

Studies on basal cell nevus syndrome (BCNS) and sporadic OKCs have shown "a proofed two-hit genetic structure at two or more chromosome loci, 9q22.3, leading to overexpression of many proteins (cyclin D1 and p53)." Mutations of the PTCH, a tumor-suppressor gene, mapped to chromosome 9p22.3-q31. The defective gene associated with BCNS was homologous to the fruit-fly-Drosophila patched (PTCH) gene. The protein produced from the PTCH gene is a component of the hedgehog (Hh) signaling pathway. It is crucial for embryonic life growth and cell signaling in adulthood. The PTCH gene proteins suppress sonic Hh protein and other signaling proteins, such as smoothened protein. When the PTCH gene is nonfunctional, overexpression of sonic Hh and/or smoothened proteins occurs, leading to increased cell proliferation. PTCH-1 and 2 are cell surface ligands, which suppress Hh-signaling-pathway. PTCH binds Hh ligands (Sonic, Indian, and Desert Hh). If that receptor is absent, PTCH inhibits the smoothened receptor that activates the Hh pathway and downstream glioma-associated oncogene (Gli) transcription factors (Gli1 and 2). Besides its linking with BCNS and OKC, Hh activation, possibly as a result of PTCH mutations, has been found in colon, ovarian, and pancreatic cancer. Thus, researchers proposed a change in OKC terminology to KCOT. Genetic analyses have also demonstrated LOH for various other tumor suppressor genes (p16, p53, MCC, TSLC1, LATS2, and FHIT) in many OKCs. (12, 21) Pathogenetic mechanisms can be summarized in the following points: (12, 22).

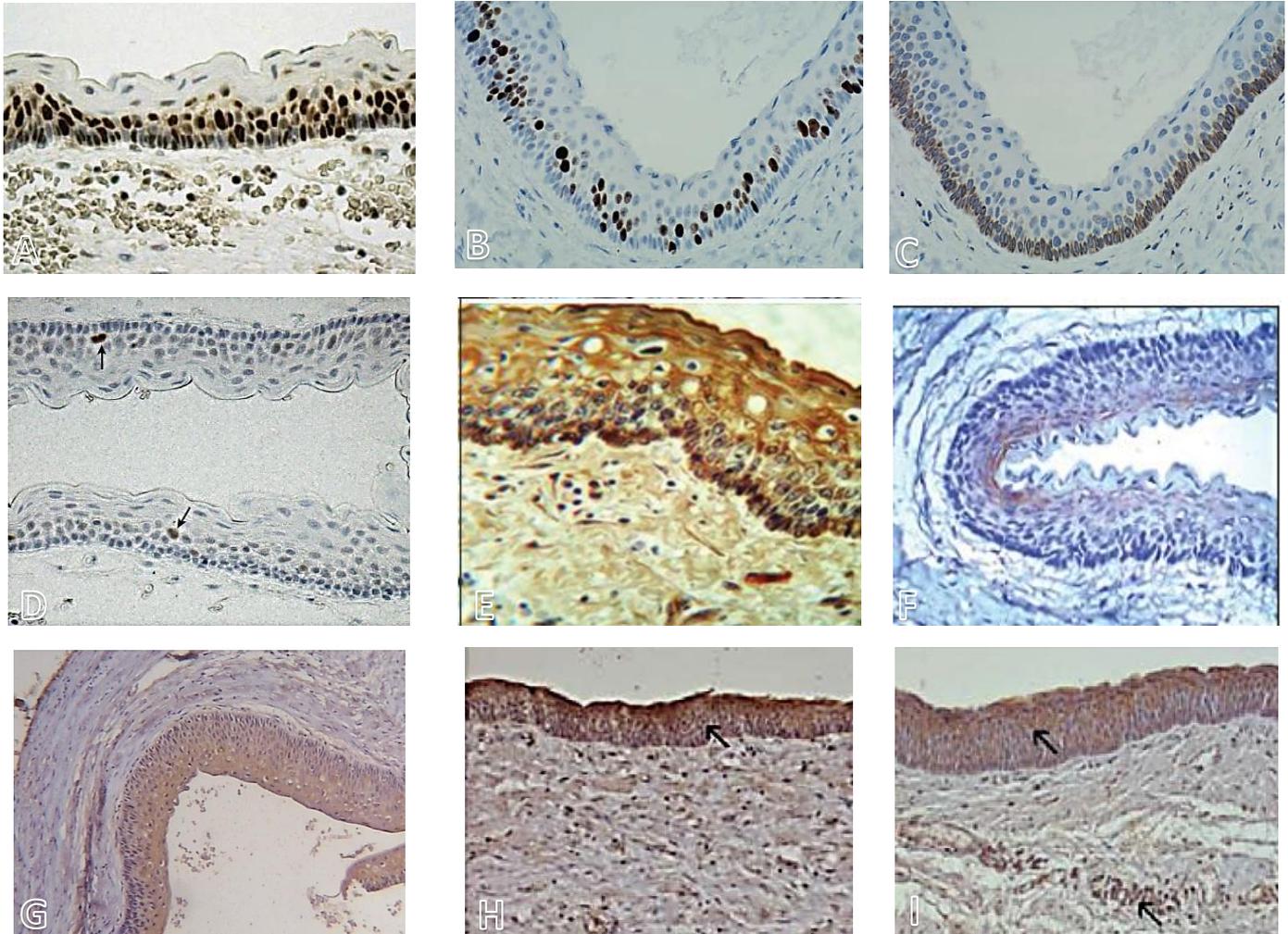
1. High proliferation rate—Ki-67 and PCNA
2. Overexpressing Bcl-2
3. Overexpressing MMPs-2 and -9, TGF, Interleukin-1a, and Inrleukin-6 (Figure 1-G, H, and I)
4. PTCH mutation was found in syndromic and non-syndromic OKCs
5. Found in medulloblastomas of BCNS and basal cell carcinomas.

### Odontogenic keratocyst growth

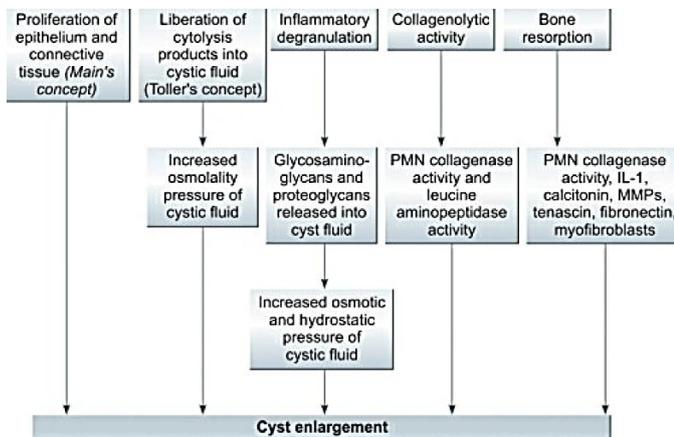
OKCs have a destructive growth manner through bone trabeculae in anteroposterior orientation; (23) this distinguishes OKCs from other jaw cysts that "expand in a unicentric ballooning pattern." Studies suggest various mechanisms of OKC enlargement (Figure 2). The main features thought to cause this are: (24 25)

- *Active epithelial growth* that demonstrates a high mitotic activity. Epithelial lining proliferation is not uniform but tends to occur in clusters, which may account for foldings in the cyst lining and cyst projections into cancellous spaces.
- *Cellular activity in the connective tissue capsule.* Active growth of the capsule occurs in association with the proliferating areas of the epithelium. Osteoclasts tend to be located around the

lining projections tips that are growing into the cancellous spaces.



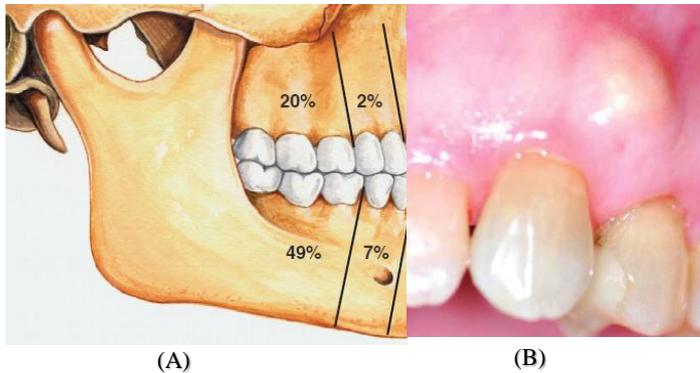
**Figure 1** OKC immunohistochemical staining. (A) PCNA-positive-cells are expressed in the basilar and supra-basilar layers (especially). (1) (B) Ki-67 positive in lots of nuclei. (12) (C) Positive stain (brown) for Bcl-2. (12) (D) p53 positive-cells in the suprabasal layer (arrow). (1) (E) Positive MMP-2 expression. (17) (F) Positive MMP-9 expression. (18) (G) Expression of TGF-β in epithelial and stromal cells. (19) (H) Interleukin-1α (I) and Interleukin-6 expressions in OKC epithelial lining, the inflammatory and endothelial cells (arrows) (20)



**Figure 2** Enlargement of the cyst. (25)

### Incidence and prevalence

OKCs estimate approximately 7.8% of whole jawbones cysts, and incidence varies between 4 and 16.5%. It happens at a wide range of ages, with a peak incidence in the 2nd and 4th decade of life. OKCs of children are multiple cysts, commonly of BCNS. OKC mainly happens in the white population with a male: female ratio of 1.6:1. According to the site, OKCs are found twice in the lower jaw than upper jaw (Figure 3-A). The mandibular cysts usually occur in the angle-ascending ramus area (69 to 83%); furthermore, it crosses the midline. While the upper jaw OKCs may extend to the maxillary sinus, nasal floor, pre-maxilla, and upper wisdom tooth area. It perhaps originates from the temporomandibular joint. OKCs are usually an intra-bony disorder; however, peripheral (extra-bony) cysts have been found in the mandible buccal gum canine area, with a male: female ratio of 2.2:1 (Figure 3-B). (30-26,12,11).



**Figure 3** OKC clinical picture. (A) Relative distribution in the jaws. (21) (B) Peripheral OKC; Initial presentation of a lesion with a yellow nodular appearance. Superficial bony defect present after the cystic lesion was excised and the wound debrided. (31)

**Sign and symptoms**

Clinically, in the vast majority of OKC cases, an absence of any type of symptomatology unless they become secondarily infected, and this perhaps why some OKCs do not appear until the fifties. It is usually discovered during routine imaging exams (Orthopantomography). OKCs grow slowly in an anteroposterior pattern, such they have large sizes without any noticed bone swelling. (24, 32)

Multiple OKCs are related to the basilar cell nevus syndrome (BCNS, Gorlin-Goltz syndrome), inherited as an autosomal dominant trait with many abnormalities (Skin, multiple nevoid basal cell carcinomas, which are not restricted to sun-exposed skin and commonly appear from puberty onwards. Orally, multiple OKCs may arise at varying intervals throughout the patient's lifetime but tend to occur earlier than single sporadic cases. Skeletally, rib abnormalities, vertebral deformities, polydactyly, cleft lip/palate. Central nervous system, calcified falx cerebri, brain tumors (medulloblastoma). BCNS can result from mutations in the PTCH1 gene on chromosome 9q22, the PTCH2 gene on 1p32, or the SUFU gene on 10q24-q25. All of these mutations affect the Sonic Hh pathway. (24, 33)

An essential clinical feature of OKC is recurrence subsequent to surgical removal. It varies from 3 to 60%. (24) Possible reasons for recurrences are: (11).

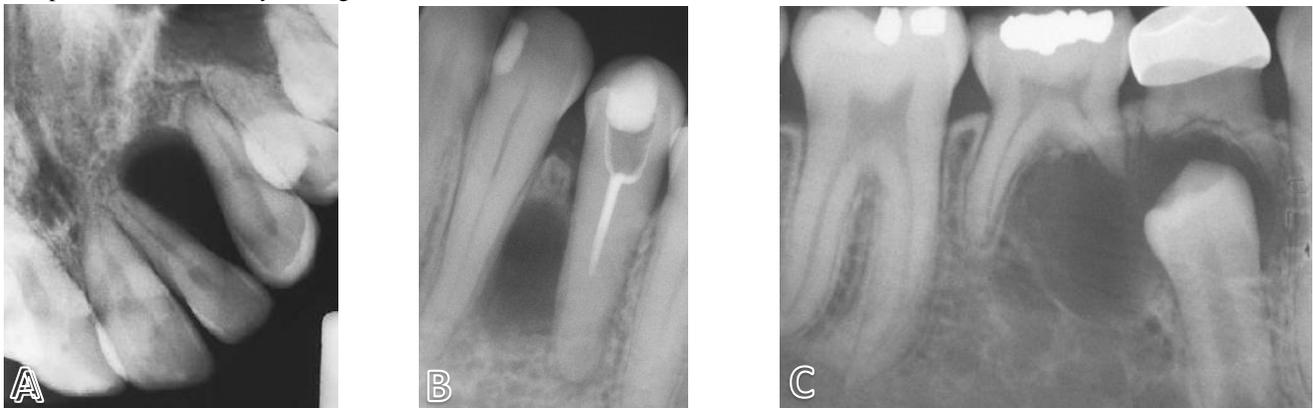
1. Incomplete removal of the cyst lining

2. Thin epithelial lining
3. Increased epithelial cell proliferative activity
4. Budding in the epithelial basal cell layer
5. Bony perforation
6. Adherence to adjacent soft tissue
7. Supraepithelial and Subepithelial separation of the epithelial lining
8. Parakeratinization of the surface layer
9. Remnants of dental lamina epithelium not associated with original OKC and new OKC development in the adjacent area
10. Growth of new OKC from satellite cyst /daughter cyst/remnants/cell rests.

**Radiographical appearance**

OKC often extends into the horizontal and vertical ramus of the mandible, resulting in a dumb-bell-shaped profile. OKC may be unilocular (Figure 4-A, B, and C) but frequently appear multilocular (Figure 4-D) on radiographs. OKCs are usually detected, incidentally, on schedule radiographic screening. Many OKCs are found in an apparent dentigerous (Figure 4-C) relationship with impacted wisdom teeth. Still, the crowns of associated teeth are often separated from the cystic lumen, the pericoronal tissues being continuous with the cyst capsule. OKCs may also present with the radiographic features of a lateral periodontal cyst (Figure 4-B), underscoring the need to submit every cyst that is removed surgically for histopathological evaluation. Most OKCs are found as a single lesion; even in some, 2 or more OKCs might be originated like in BCNS (Figure 4-E). (24, 34)

Solitary OKC remarkably appears as a well-defined radiolucency with fine radiopaque borders. Multi-locular lesion is usually found with more extensive OKC. The mandibular OKCs expand and extend to the other side of the bone by crossing the midline, an essential characteristic feature of OKC. Tooth displacement is commonly seen rather than root resorption. Most lesions, however, are uni-locular, 40% appear in association with a crown of an impacted tooth "like a dentigerous cyst." About 30% of upper and 50% of lower OKCs induce buccal plate enlargement. Mandibular lingual expansion is sometimes presented. Peripheral odontogenic keratocyst shows saucerization of the underlying bone. (12, 25, 36) Depending on radiographic appearance, OKC has the following variants (Figure 5): (25).

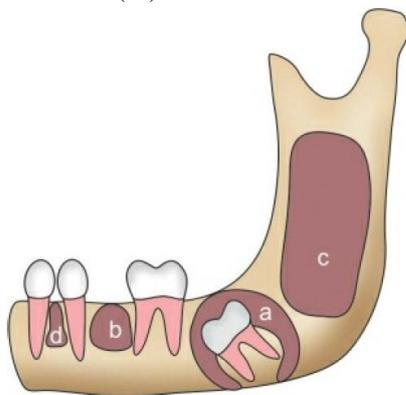




**Figure 4** Radiographical pictures of OKC. (A) Unilocular lesion in the globulomaxillary area. (35) (B) OKC radiographically cannot be differentiated from lateral periodontal cyst, and (C) dentigerous cyst; OKC involves the crown of an unerupted premolar. (21) (D) Multilocular radiolucency of OKC. (24) (E) Multiple OKCs in BCNS (13,33,43,48 regions) (24)

- a. *Envelopmental variant*: Cysts that embrace unerupted tooth (arise from cell rests of Serre).
- b. *Replacement variant*: Cysts that form in normal-tooth region (by degeneration of stellate reticulum in enamel organ).
- c. *Extraneous variant*: Cysts occur in the ascending ramus of the mandible and away from the tooth (Epithelial off-shoots (hamartias) of the oral epithelium from basal layer).
- d. *Collateral variant*: Cysts occur adjacent to the teeth' roots (originate from Epithelial rests of Malassez).

MRI is the only screening that remarked OKC precisely. T2-weighted images show hyper intensity with signal drop out, which is highly suggestive of OKC (85% sensitivity). (37) CT is able to display the main radiological features of an OKC, such as size, shape (hydraulic or scalloping), margins (well-defined and corticated), internal appearance (uni- or multilocular) and effects on adjacent structures (tooth displacement, root resorption, maxillary sinus floor elevation, inferior displacement of mandibular canal). In addition, CT demonstrates other features of OKCs, such as bony changes (expansion in buccolingual/palatal direction and erosion), internal density and extension into soft tissue. Therefore, CT is considered superior to conventional radiography in differentiating OKCs from other unilocular or multilocular osteolytic lesions and in the preoperative assessment. (38)



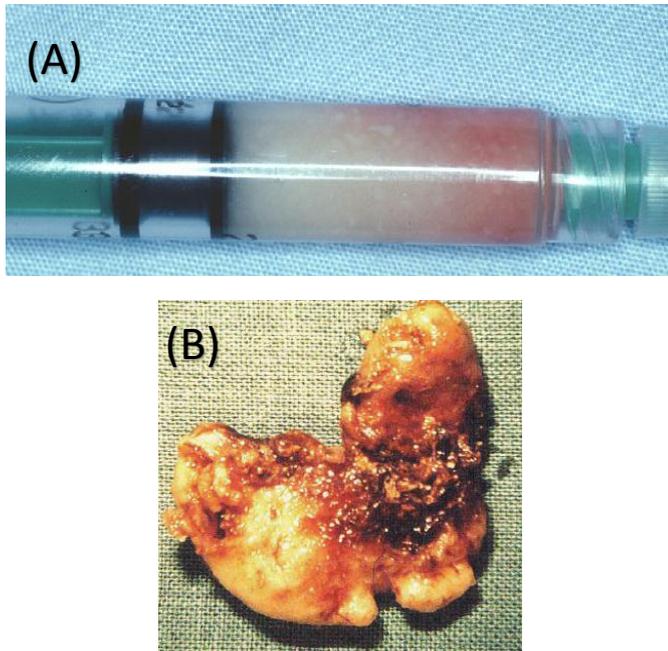
**Figure 5** Radiographival variants of OKC:  
 (a) Envelopmental; (b) replacement; (c) extraneous;  
 (d) collateral. (25)

**Odontogenic keratocyst differential diagnosis**

From a differential diagnosis standpoint, the OKC can mimic various other odontogenic cysts and tumors. 25% to 40% of cases associated with an unerupted tooth's crown, thereby resembling a dentigerous cyst. Dentigerous cysts, however, do not exhibit the regular, palisaded arrangement of cuboidal/columnar basilar cells or the corrugated surface layer of parakeratin. Orthokeratinized odontogenic cysts (OOC) also produce keratin; this keratin consists of orthokeratin associated with a subjacent granular cell layer. Besides, the basilar layer of OOCs does not exhibit nuclear palisading. Cystic ameloblastomas demonstrate a palisaded layer of columnar basal cells that could mimic an OKC. However, the ameloblastoma's basilar cells are usually more hyperchromatic and demonstrate areas with reverse polarization, in which the nuclei are pulled away from the basement membrane. What is more, the upper epithelial layers of cystic ameloblastoma are loosely arranged, reminiscent of the stellate reticulum of the enamel organ. (13, 39) Few cases present in between roots of teeth can be mistaken for lateral periodontal cysts. OKC sometimes develops in the midline maxillary region in older patients, and thus these lesions can be confused with nasopalatine duct cysts. Finally, lesions located beneath tooth roots can mimic periapical cysts. (13) It may mimic other non-odontogenic radiolucent disorders in young patients, such as traumatic bone cyst, central giant cell granuloma, or aneurysmal bone cyst. (12)

**Gross appearance**

The OKC typically shows "a thin, friable wall, often difficult to enucleate from the bone in one piece. The cystic lumen may contain a clear liquid that is similar to a transudate of serum, or it may contain a cheesy material (Figure 6-A) that, on microscopic examination, consists of keratinaceous debris." (21, 39) Unless the cyst is small, the OKCs linings are rarely received intact in the laboratory. Even if one is seen intact, the unequal growth that is responsible for the scalloped radiographic margins may be observed (Figure 6-B). (1) The electrophoretic analysis for aspirated cystic fluids revealed that the soluble protein ratio to total protein content was lower than that in serum. The total protein content is <5 g/100 ml (Albumin; between 2 and 4 g/dl, Globulin; between 0.5 and 2.5 g/dl). (40).



**Figure 6** OKC macroscopically. (A) The cyst aspirate may contain cheesy keratin debris. (39) (B) Gross specimen shows the unequal enlargement induced the scalloped borders. (1).

**Microscopical findings**

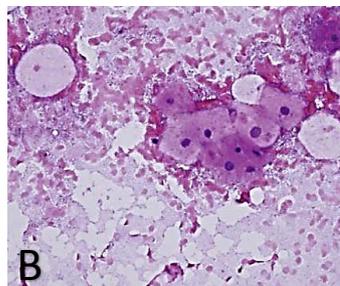
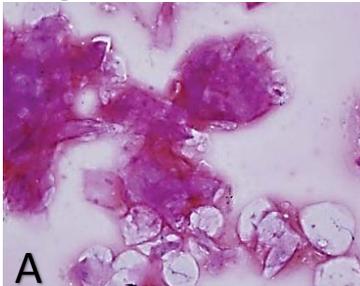
Cytologically, OKC's aspiration is mostly cellular, mainly composed of keratinized cell clusters without nuclei (Figure 7-A). The para-keratinized cells had small pyknotic nuclei and showed less tendency to form groups in a background that contained granular debris (Figure 7-B). Some dyskeratotic parabasal cells may also present, and they exhibited a denser eosinophilic cytoplasm. No evidence of dysplasia, and typically, no inflammation present in a component of the aspirates. In a few cases with numerous inflammatory cells, keratinized cell groups were still easily identified. (41)

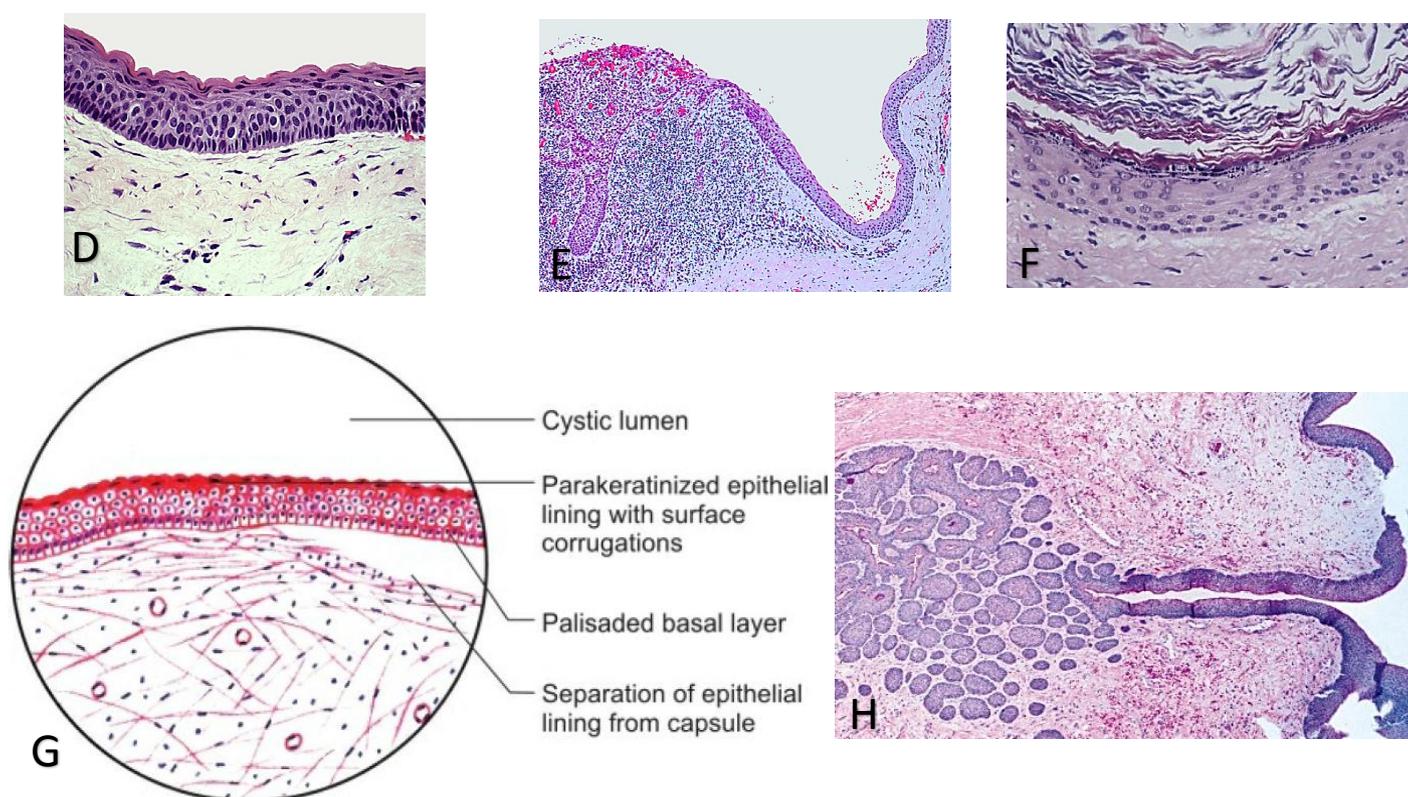
Histopathologically, the cyst wall is usually thin and often folded. It is typically lined by a regular, continuous layer of stratified squamous epithelium between five and eight cells thick (Figure 7-C). The interface between the epithelial lining and the capsule is typically flat smooth. The basal cell layer is well defined and consists of palisaded columnar or occasionally cuboidal cells. The

columnar basilar cells' nuclei in the para-keratinized epithelial lining arranged away from the basement membrane and intensely basophilic in most lesions (Figure 7-D) —critical appearance for differentiation 'true' OKCs from other keratinizing jawbones cysts. (1) The supra-basilar cells look like polyhedral cells of oral epithelia, superficially an immediate transition to more differentiated surface epithelia that produce parakeratin. The cells desquamate into the cyst lumen, where they accumulate. Mitotic activity is higher than in other types of odontogenic cysts, and sparse mitotic figures may be found in basal and suprabasal cells. The fibrous capsule wall of the cyst is usually thin and generally free from inflammatory cell infiltration. If the cyst becomes secondarily inflamed, the epithelial lining loses its characteristic histology, and para-keratinized epithelial surface might be faded. Epithelial lining might be proliferated, producing rete-pegs, losing the characteristic palisading basilar cell layer (Figure 7-E), resembling the lining of periapical cyst. Few epithelial cells cluster, look like dental lamina rests, may be present in the cyst wall, which originates daughter cysts. Satellite (daughter) cysts are more common in cysts associated with the BCNS (Figure 7-H). (21, 24, 42) Microscopical key features can be summarized as follows: (35, 39)

1. Thin epithelium (6-10 cell layers)
2. Refractile, corrugated (rippled) parakeratotic lining on its luminal surface
3. Palisading columnar/cuboidal basilar cells
4. Lack of rete pegs, commonly the cyst exhibits focal separation of the epithelial lining from the adjacent connective tissue
5. Keratin flakes might be present in cystic cavity
6. Epithelial budding at the basal cell layer and remnants of the dental lamina (odontogenic rests), microcyst formation, "daughter cysts."
7. Particular microscopic appearance lost when infected.

The term OKC is never described any odontogenic cyst forming keratin; this term is associated with a unique clinico-pathological condition. Periapical and dentigerous cysts might reproduce keratin due to epithelial metaplastic changes. Still, the lining epithelium is often ortho-keratinized and lacks OKC's distinctive histopathological features. An uncommon ortho-keratinized odontogenic cyst is lined entirely by ortho-keratinized epithelium (Figure 7-F), but this should not be confused with OKC; it is effectively treated by enucleation and rarely recurs. (24).





**Figure 7** OKC microscopically. Aspiration from OKC contains (A) groups of keratinized cells, (B) dispersed ortho-keratinized cells, and a group of intermediate keratinocytes. There is no evidence of atypia. (41) (C) The lining is a uniform layer of stratified squamous epithelia, five to eight-cell wide. There is a split of epithelia from the cyst capsule. (39) (D) The basal cell layer is composed of a palisading row of basophilic columnar cells. A fine, corrugated surface layer is para-keratinized. (39) (E) The characteristic microscopic features have been lost of the cystic lining because of the heavy chronic inflammatory cell infiltrate. (39) (F) Ortho-keratinized odontogenic cyst showed granular-cell layer below keratinized surface and absence basal cell palisading. (12) (G) Diagram of odontogenic keratocyst histopathology. (23) (H) OKC of BCNS with lots of odontogenic epithelial remnants throughout cystic capsule. (21)

False-negative results, histopathologically, may happen when the cyst is inflamed because inflammatory substances make the epithelial lining misplace its crucial features, which might be localized. In most instances, this is due to a non-representative biopsy. In general, when cysts in the tooth-bearing area present with signs or symptoms compatible with those of OKCs, such as no bony expansion, scalloped margins, or even a multilobular appearance, an aspiration biopsy is probably the best option. The presence of keratin flakes or a protein level of less than 4 g per 100 ml is indicative of an OKC. Besides inflammation effects on the epithelial lining, a definite diagnosis might also be close by using this method. (43, 44)

### Management

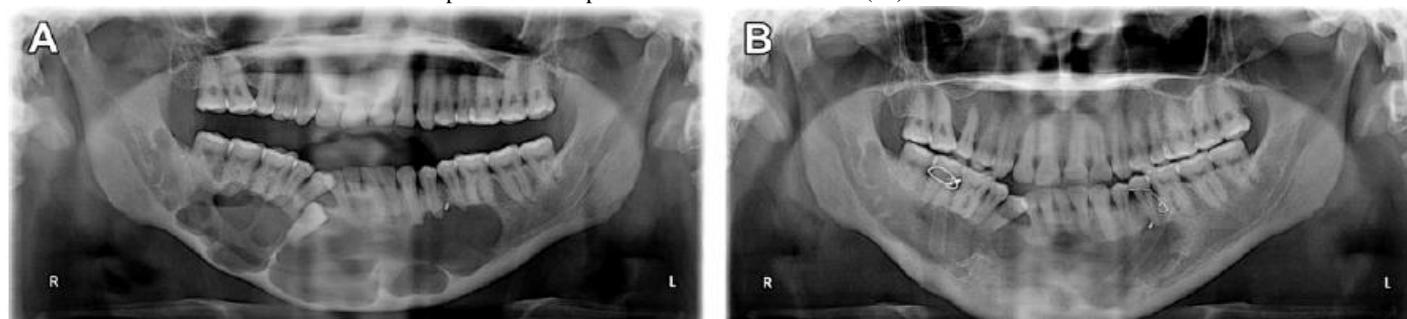
OKC management still a controversial subject in oral and maxillofacial surgery. In spite of several types of research and systematic-reviews on management modalities, there is no agreement on such management protocol. OKC management is related to cystic size, patient age, closeness to mandibular nerve, ease to access, surrounding connective tissue/cortical bone perforation, and whether the cyst is recurrent. (37) Different treatment forms were used, such as marsupialization, decompression, enucleation with adjuvant therapies (Carnoy's solution, peripheral osteotomy, cryotherapy, or electrocautery); (45-

47) however, these methods can cause damage to adjacent structures. Resection provides the least recurrences (0%-8.4% recurrent rate). (37)

Many surgeons recommend peripheral osteotomy, an aggressive form of adjuvant therapy where methylene blue is utilized to stain any cystic remnants of the bony cavity with a bone bur to reduce recurrence frequency. Cryotherapy by liquid-nitrogen induces necrosis of the epithelium (like Carnoy's solution or chemical curettage). (37) Many favor chemical cauterization (by Carnoy's solution) of the bony cavity subsequent to cystic excision (although some hospitals may not permit the use of Carnoy's solution). Intraluminal injection of Carnoy's solution has also been used to free the cyst from the bony wall, allowing easier removal with a lower recurrence rate. It can result in very low recurrence and is an acceptable first line of treatment. Lots of surgeons treat expanded OKCs by inserting a polyethylene-drainage tube to allow decompression and subsequent reduction in the cystic cavity size (Figure 8). Such decompression treatment results in thickening of the cyst lining, allowing easier removal with a lower recurrence rate. (12, 21, 48-51) When OKC is small and easy to access, enucleation is chosen with two adjuvant management protocols. (37, 52, 53) Recurrence rates with different management modalities are mentioned below: (11, 54)

1. Enucleation; 30 %
2. Enucleation + Carnoy's solution; 9 %
3. Enucleation + peripheral osteotomy; 18 %
4. Enucleation + Carnoy's solution + peripheral osteotomy; 8%
5. Enucleation + cryotherapy; 38 %
6. Marsupialization; 33%
7. Marsupialization + cystectomy; 13
8. Resection; 0%

Decompression is "a modified marsupialization technique that causes the cyst to decrease significantly in size, and the cystic lining becomes thicker, resembling oral mucosa that allows for easier enucleation. This method decreases the levels of IL-1 $\alpha$ , which regulates epithelial cell proliferation in OKC; hence, there is immune-histochemical evidence that decompression is superior to



**Figure 8** Decompression of OKC. (A) A large, multilocular OKCs of the mandible on initial presentation. (B) The same lesion nine months later after biopsy, to establish the diagnosis and insertion of two drainage tubes (seen on the radiograph) for decompression. The patient irrigated the drains twice daily with normal saline. The drains were removed after one year. (49)

### Behavior and prognosis

The recurrence rate varies from 10% to 30%, depending on how the lesion is managed, and is also related to several physical factors (mentioned before in section 2.6). In addition, the cyst epithelium's actual biological qualities, like increasing mitotic-index and producing bone-resorption agents, have an association with recurrent. Follow-up evaluation is essential. Patients should be examined for entire cystic excision, newly OKC formed, or BCNS. The majority of recurrent cases show clinical features in the five years of management. Besides cystic recurrency, ameloblastic transformation is reported in some cases. Individuals having multiple OKCs show an elevated recurrence-rate (30%) than patients with solitary OKC (10%). (12) Individuals with OKC must be examined yearly by panoramic-radiography (OPG). MRI could be done two years once to monitor early recurrent lesions. Follow-up ought to be long, at least for ten years. (37, 57-59)

### Summary and conclusions

The biological nature of OKC has been a matter of discussion for a long time. Due to its aggressive behavior, there have always been controversies regarding the cystic or the lesion's neoplastic behavior. The use of FNA, incisional biopsy, and cell block technique may be really helpful to early diagnose OKCs, and to perform more conservative treatment for those lesions without teeth involvement and cortical bone perforation, or more aggressive surgical plan for OKCs with periosteum involvement, up to justify jaw resection for recurred lesions with high aggressiveness. Surgical removal with curettage or osteotomy is the desired management protocol.

enucleation alone. It was reported that the recurrent rate of OKC treated by decompression followed by enucleation be significantly lower than enucleation alone." (37, 55) Another essential things decreasing OKCs recurrence rate are removal of covering oral epithelium, particularly when the cyst is biopsied. Several types of research demonstrate that about whole recurrent OKCs have microcysts in the mucosa covering cortical perforation sites. (48)

Recently some researchers are working on the nonsurgical management of OKC. For more precise therapy, crucially in patients who have multiple, recurrent, or expansive OKC, Hh-pathway inhibitor (Vismodegib) is used orally (150mg/day for 18 months), causing cystic shrinkage. (47) Goldberg et al. (56) cited "the almost full resolution of three OKCs in a patient who had BCNS, who in turn received the Hh pathway inhibitor as a possible treatment, GDC-0449." (56)

However, it advocated that surgical decompression and marsupialization are preferred to induce cyst fading, and then OKC is enucleated. Follow-up ought to be long, at least for ten years.

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