J Oral Med Oral Surg 2024;30:8
https://doi.org/10.1051/mbcb/2024010

https://www.jomos.org

JOMOS
Journal of Oral Medicine and Oral Surgery

Educational Article

Cysts of the jaws and how to make their diagnoses under a microscope: a need for a better communication between clinicians and pathologists

Svyat Strokov[1,2,*], Nathalie Cardot-Leccia[3], Hélène Raybaud[1,2], Sarah Latrèche[1,2], Estelle Guillou[1,2], Nouha Khenissa[1,2], Yves Ponchet[1,2,4], Christine Voha[1,2]

[1] Faculté de Chirurgie Dentaire, Université Côte d'Azur, EA 7354 MICORALIS (Microbiologie Orale, Immunothérapie et Santé), 06357 Nice, France
[2] Institut de Médecine Bucco-Dentaire du CHU de Nice, 28 boulevard de Riquier, 06300 Nice
[3] Laboratoire Central d'Anatomie et Cytologie Pathologiques (LCAP), 30 avenue de la Voie Romaine, 06000 Nice, France
[4] Activité libérale de radiologie dentaire exclusive (Liberal practice of exclusive dental radiology), 35 Rue Rossini, 06000 Nice, France

(Received: 28 December 2023, accepted: 25 March 2024)

Keywords: Jaw cyst / pathological diagnosis / clinical features / radiological features

Abstract – Introduction: Cysts of the jaws constitute an heterogenous group of lesions occurring in the maxillofacial region. Their diagnosis is challenging and necessitating a meticulous correlation of clinical, radiological, and pathological features. Pathologists often face numerous difficulties stemming from inadequate clinical and radiological information, along with limited samples. Nevertheless, clinicians are not always aware of the pathologist's concerns, making difficult to know exactly which pertinent clinical information they should deliver in their request form. The objective of this article is to illustrate the microscopic diagnostic pitfalls associated with cystic lesions of the jaws and enhance communication between oral surgeons and oral pathologist. **Corpus:** This section starts by examining the essential clinical and radiological data necessary for a precise pathological diagnosis. Subsequently, we discuss about the differential diagnosis of jaw cystic lesions, categorizing them into five distinct subsets based on their microscopic features, particularly their histological lining. For each subset, we engage in a detailed discussion concerning the primary diagnostic challenges and their implications for treatment decisions. **Conclusion:** Pathologist and clinicians are not irreconcilables: improved communication, rooted in a mutual understanding of each other's concerns, leads to optimizing the diagnosis and subsequently the treatment of jaw cysts.

Introduction

Cysts are pathological cavities lined by epithelium. Jaw cysts are common lesions, predominantly represented by radicular cysts (constituting 60% of all odontogenic cysts), dentigerous cysts (25%), and keratocysts (10–20%) [1,2]. These lesions are typically asymptomatic and are often discovered incidentally during radiological investigations. Their radiological features are non-specific, necessitating a comprehensive clinical, radiological, and pathological correlation for accurate diagnosis [3]. Histopathological examination is imperative for any jaw lesions to rule out aggressive conditions such as glandular odontogenic cysts, keratocysts, ameloblastomas, or dysplastic/carcinomatous changes in the epithelial cystic lining [4]. Numerous cysts, whether odontogenic or non-odontogenic, can originate from epithelial remnants within the jaw bones. The diverse histological appearances of these lesions are attributed to their pluripotentiality and complex histogenesis [5]. Historically, these cysts were categorized into three types: odontogenic cysts of inflammatory origin, odontogenic developmental cysts, and non-odontogenic cysts. The World Health Organization (WHO) recently unveiled the 5th edition of its Classification of Head and Neck Tumors in March 2022, marking a significant update since the 4th edition in 2017 (Tab. I) [6]. Within this latest edition, discussions concerning odontogenic cysts and tumors have been streamlined into the broader category of "Odontogenic and Maxillofacial Bone Tumors." Despite this reorganization, the core framework remains consistent with its predecessor.

One notable change lies in the restructured section on jaw cysts, now amalgamated into a cohesive group, eliminating previous subdivisions. This strategic realignment

* Correspondence: Strokov.s@chu-nice.fr

Table I. 4th and 5th edition of Classification of Head and Neck Tumors by World Health Organization (WHO) : cysts of the jaws.

4th edition of classification of head and neck tumors (WHO, 2017)	5th edition of classification of head and neck tumors (WHO, 2022)
Odontogenic cysts of inflammatory origin	**Cysts of the jaws**
Radicular cyst	Radicular cyst
Inflammatory collateral cysts	Inflammatory collateral cysts
Odontogenic and non-odontogenic developmental cysts	Surgical ciliated cyst
Dentigerous cyst	Nasopalatine duct cyst
Odontogenic keratocyst	Gingival cysts
Lateral periodontal cyst and botryoid odontogenic cyst	Dentigerous cyst
Gingival cyst	Orthokeratinized odontogenic cyst
Glandular odontogenic cyst	Lateral periodontal cyst and botryoid odontogenic cyst
Orthokeratinized odontogenic cyst	Calcifying odontogenic cyst
Nasopalatine duct cyst	Glandular odontogenic cyst
	Odontogenic keratocyst

reflects the new Blue Book structure, designed to prioritize more aggressive lesions towards the end of each section. Moreover, the Blue Book now supplements each entity with "essential and desirable diagnostic criteria," emphasizing critical clinical or pathological features crucial for accurate diagnosis [1,5].

In a noteworthy addition, the non-odontogenic "surgical ciliated cyst" has been integrated into the category of jaw cysts, despite its well-established recognition. This incorporation signifies a fresh inclusion within this classification, enhancing its comprehensiveness and clinical relevance [1,5]. Furthermore, the sole newcomer to this classification is the "adenoid ameloblastoma," characterized by distinct ameloblastomatous differentiation and the presence of duct-like structures. This novel entity enriches our understanding of tumor diversity within the odontogenic spectrum, underscoring the ongoing evolution and refinement of diagnostic frameworks in the field of head and neck pathology [1,5].

Nonetheless, diagnosing odontogenic cysts and jaw lesions can be challenging for both clinicians and pathologists. Oral surgeons may encounter difficulties when submitting intact cysts for histopathological examination, especially when inflammation is present, resulting in specimens comprising multiple curetted fragments and reducing the predictive value of the histopathological examination.

The objective of this work is to present the key points which you be notify by the oral surgeons and the pathologist to help to the diagnosis of cyst jaw in accordance with the 5th edition of the World Health Organization (WHO) Classification of Head and Neck Tumors.

Corpus

Which clinical and radiological data should be communicated to a pathologist?

According to the recent literature data and our collective experience in the surgical management and pathological diagnosis of jaw lesions, we would highlight the critical importance of clinical and radiological correlation in establishing a diagnosis for any jaw cyst. Effective communication among clinicians, radiologists, and pathologists is essential. To facilitate this collaboration, we suggest implementing a checklist request form for oral surgeons when submitting samples for histopathological examinations. This structured approach ensures the transmission of pertinent clinical and radiological information, fostering an improved diagnostic process and an optimized patient care (Tab. II) [6].

The clinician should provide detailed information regarding the condition of the involved tooth and its spatial relationship to the cyst. However, be mindful that histological techniques involving the decalcification of hard tissues like teeth may prolong sample management and potentially affect histological slide quality due to decalcifying artifacts [7]. To address this challenge, we recommend separating the tooth from its cyst and supplementing with dental radiography, macroscopic photography, or schematic illustrations to elucidate its condition and spatial relationships [5]. Moreover, oral surgeon should exercise caution in using of partial biopsies and Fine-Needle Aspiration Cytology (FNAC) for diagnosing jaw cysts, as they lack accuracy compared to excisional biopsy or enucleation [8,9]. Therefore, we recommend to submit as complete a

Table II. "Check-list" request form for submitting jaw lesions on histological examination.

Clinical data	Radiological data
Identity of the patient/medical records	**Radiodensity**
• Patient's name:.....	• Radiolucent lesion
• Patient's age	• Radiolucent lesion
• Patient's gender:	• Mixed density
• Patient's ethnicity:.....	
• Pertinent medical history/medical records:.....	***Radiological locularity***
	• Unilocular
	• Multilocular
	'Moth-eaten' appearance
Historic data concerning the lesion	***Dimensions of the lesion***
• Duration of the lesion.....	• Size .....
• Previous recurrence:.....	• Well defined margins (with or without corticated border)
• Familial history of jaw lesion?	• Ill-defined margins
	Site of the lesion
Symptomatology	• Intra-osseous, specify:
• Swelling: Yes/No	*Maxillar ? Mandibular ?*
• Nervous manifestations, pain, paresthesia: Yes/No	*Quadrant concerned* :.....
• Adenopathy ?	Tooth number concerned :.....
• Vitality of concerned teeth	• Extra-osseous, specify. .....
• Impacted tooth concerned ?.....	
• Inflamed tooth concerned ?:.....	***Anatomical relationships***
• Resorption of concerned teeth:.....	• Cortical perforation or defect
• Displacement of concerned teeth	• Involvement of inferior alveolar nerve
	• Involvement of sinus floor
Specimen submitted	• Involvement of nasal floor
• Curettage/enucleation	• Other anatomical involvement, specify.
• Incisional biopsy	.....
• Excisional biopsy	
• Surgical resection.	***Schema of the lesion:***
• Needle biopsy/fine-needle biopsy	
• Other, *specify*	
CLINICAL DIAGNOSES	
1	
2	
3	
4	

Table III. Clinical and radiological features of non-keratinized odontogenic cysts [1,2,7].

	Clinical features	Radiological features
Radicular cyst	Most common odontogenic cyst. Invariably associated with a necrotic tooth. It may become residual after removal of the causative tooth without its enucleation.	Well-demarcated unilocular radiolucency at the root apex (apical cyst), or along the lateral root surface (lateral cyst) or found at a site of previous tooth extraction (residual cyst) (Fig. 1A).
Inflammatory collateral cyst	Always associated with a partially or recently erupted vital teeth with historic of pericoronitis or inflammation. Buccal aspect of mandibular molars is the most common location.	Well-demarcated or corticated unilocular radiolucency involving the buccal or distal aspect of a partially erupted molar (Fig. 1B).
Dentigerous cyst	Always associated with an impacted tooth, attached to its cemento-enamel junction	Well-defined unilocular radiolucency, surrounding the crown of an impacted tooth (Fig. 1C).

sample as possible, and if not feasible, consider conducting multiple biopsies, especially before a decompression or marsupialization procedure [5].

Histopathological differential diagnosis of cysts of the jaws

Cysts lined by a non-keratinized Malpighian epithelium

This subset includes inflammatory odontogenic cysts such as radicular cyst and inflammatory collateral cyst, as well as a developmental cyst, the dentigerous cyst.

Clinical and radiological features of non-keratinized odontogenic cysts [1,2,10](Tab. III and Figs. 1A-C).

Histopathological features

Radicular cysts and inflammatory collateral cysts are indistinguishable histologically. The cystic cavity is lined by a nonspecific, malpighian, non-keratinized epithelium of variable thickness, which becomes hyperplastic with an arcading pattern in inflamed areas [1,2,11] (Fig. 2B). Occasionally, the epithelium contains mucous or ciliated cells, or hyaline, curvilinear, or straight lamellar bodies known as "Rushton bodies," which may undergo dystrophic calcification (Fig. 2A). These bodies originate from either hematogenous or odontogenic sources [12]. The cystic wall is typically inflamed and fibrous, featuring chronic inflammation, foamy histiocytes, hemosiderin deposits, cholesterol clefts, and foreign body giant cells [1,2,11] (Fig. 2C).

Dentigerous cyst is lined by a thin, non-keratinized epithelium, occasionally containing mucous or ciliated cells (Fig. 3A). In areas of inflammation, the epithelium undergoes hyperplasia and resembles that of a radicular cyst with occasionally Rushton bodies or dystrophic calcification (Fig. 3B). The cystic wall typically consists of a loose, fibromyxoid, uninflamed connective tissue with scattered odontogenic epithelial rests [1,13] (Figs. 3C and D).

Differential diagnosis and histological pitfalls

These lesions are well-known to clinicians, who can easily differentiate among them. However, pathologists may face challenges due to the overlap of their histological features, particularly in the presence of inflammatory changes. Indeed, when significant inflammation is present, all these lesions exhibit similarities with hyperplastic epithelial lining showing an arcading pattern of rete ridges. The clinician's role is crucial in distinguishing them by providing appropriate clinical and radiological data [5].

Moreover, inflammation can mask the classical histological features of odontogenic cysts, increasing the risk of misdiagnosing a more aggressive lesion such as ameloblastoma or keratocyst. Thorough examination of the entire specimen on additional levels is necessary to identify a less inflamed zone, which provides more confidence in the diagnosis [5,14].

Inflammatory odontogenic cysts lack specific histopathological features. Rushton bodies, cholesterol crystal clefts, dystrophic calcifications, mucous, or ciliated cells may be encountered in many other cystic lesions. The diagnosis should always be supported by strict correlation with clinical and radiological features (association with a non-vital tooth for the radicular cyst, association with an inflamed vital molar for inflammatory collateral cyst) [5,10,14].

The dentigerous cyst can be mistaken for a hyperplastic dental follicle. The general pathologist may not always be familiar with the intricate development of teeth and the microscopic features of all tissues involved in odontogenesis. When the normal dental follicle enlarges, it can mimic a dentigerous cyst on radiographic or histological examination. Some authors suggest reserving the diagnosis of a dentigerous cyst for lesions larger than 3 or 4 mm. Nevertheless, both lesions are associated with an excellent prognosis, with no recurrence after enucleation [15].

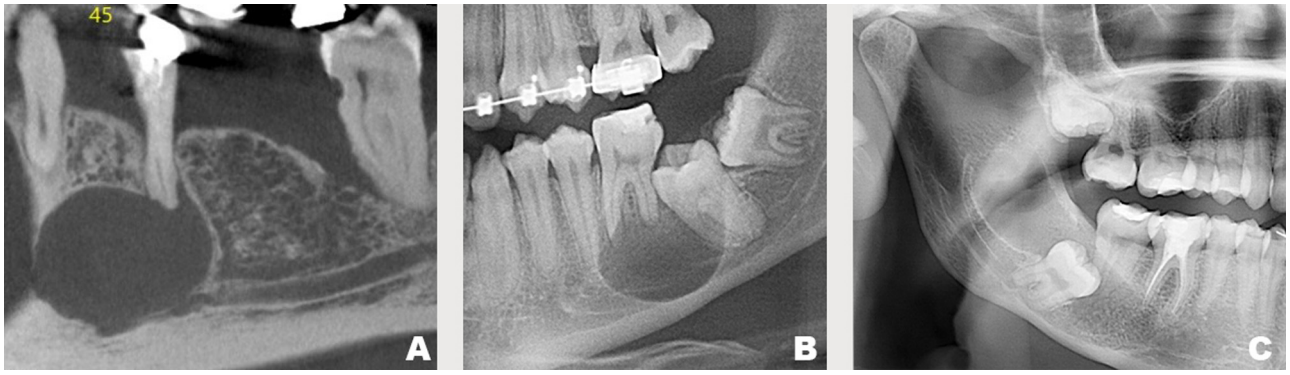

Fig. 1. Radiographic features of odontogenic cyst lined by a non-keratinized malpighian lining. (A) Sagittal section of a cone beam computed tomography (CBCT) showing an unilocular radiolucency at the root apex of tooth 45.The final diagnosis was a radicular cyst. (B) Panoramic view showing a well-defined unilocular radiolucency involving the furcation of a partially erupted molar (37). The final diagnosis was an inflammatory collateral cyst. (C) Panoramic view showing an unilocular radiolucency surrounding the crown of a non-erupted molar. The final diagnosis was a dentigerous cyst.

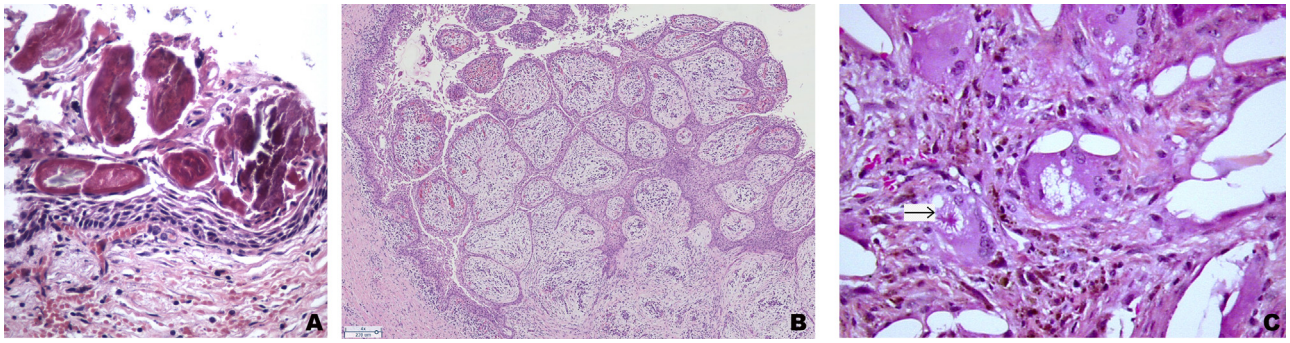

Fig. 2. Photomicrographs showing histopathological features of a radicular cyst. (A) Non-keratinized epithelium contains hyaline laminated Rushton bodies (HE ×400). (B) Non-specific hyperplastic epithelium with arcading pattern of rete ridges (HE ×40). (C) Cholesterol clefts with foreign body giant cell and hemosiderin deposits. Note the asteroid body with the cytoplasm of a giant cell (arrow) (HE ×400).

The fibromyxoid nature of the cystic wall in a dentigerous cyst should not be confused with an odontogenic myxoma, which is an aggressive tumor. The presence of a thin cystic epithelium and its association with a non-erupted tooth allow for the exclusion of a myxoma diagnosis [1,14].

Implications for treatment decisions

Radicular cysts and dentigerous cysts are typically treated with enucleation and the extraction or the endodontic treatment (for small radicular cyst) of the causative tooth. Conservative treatment without tooth extraction is indicated for inflammatory collateral cysts that arise from the furcation of the 1st or 2nd mandibular molars [16].

Cysts lined by a keratinized Malpighian epithelium

This subset is prominently represented by the odontogenic keratocyst, a potentially aggressive lesion known for its tendency to recur after enucleation and its frequent association with Nevoid basal cell carcinoma syndrome (Gorlin Syndrome). It is essential to distinguish this entity from the odontogenic orthokeratinized cyst, which exhibits a lower recurrence rate after enucleation and has not been conclusively linked to Gorlin Syndrome. Another noteworthy odontogenic keratinized cyst is the curious gingival newborn cyst, which emerges on edentulous alveolar ridges of newborns and resolves spontaneously [1].

Clinical and radiological features of keratinized odontogenic cysts [1,2,10] (Tab. IV and Figs. 4A-C).

Histopathological features

The odontogenic keratocyst (OKC) is lined by a malpighian epithelium devoid of rete ridges and covered by corrugated parakeratosis. The basal cells are columnar, hyperchromatic, and palisaded, sometimes displaying reverse polarity features (Fig. 5A). Increased mitoses are occasionally observed within the suprabasal cell layer. Basaloid cells budding, prominent dental lamina remnants, and microcysts in the wall may be encountered, particularly in syndromic cases [1,17] (Figs. 5B and C).

The odontogenic orthokeratinized cyst (OOC) is lined by a thin orthokeratinized malpighian epithelium with a prominent granular cell layer. The basal cell layer is not palisaded, and microcysts within the wall are rare [1,18].

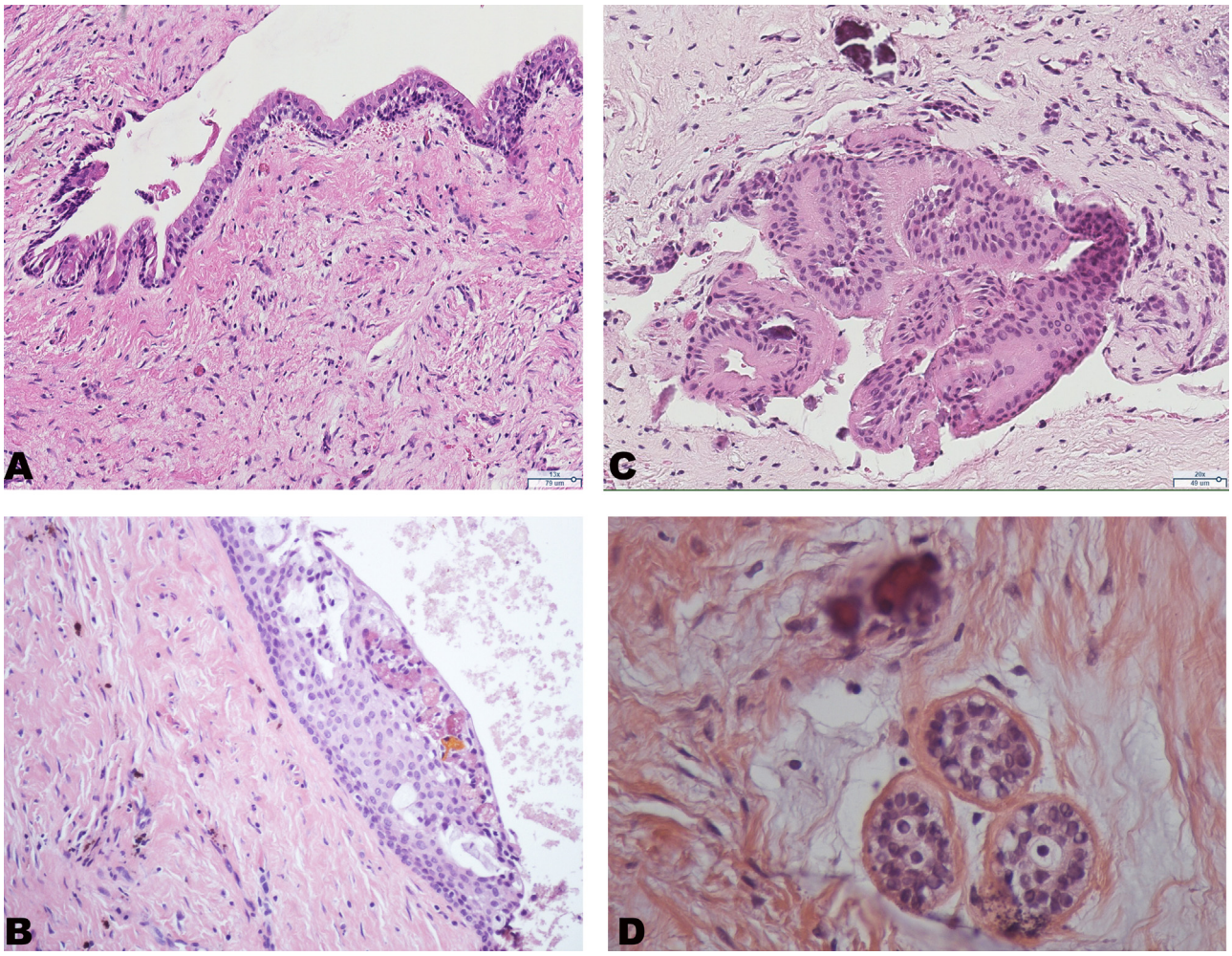

Fig. 3. Photomicrographs showing histopathological features of a dentigerous cyst. (A)Non-keratinized thin epithelium with scattered mucous and ciliated cell (HE ×130). (B) Hyperplastic epithelium with Rushton bodies (HE ×200). (C) Reduced enamel epithelium within a cystic wall of a dentigerous cyst (HE ×200). (D) Odontogenic epithelial rest with dystrophic calcifications within a wall of a dentigerous cyst (HE ×400).

The gingival cyst of the newborn (GCn) is a peripheral cyst lined by a thin keratinized epithelium that sometimes connects to the buccal mucosa. They are rarely biopsied, and their clinical features are generally sufficient to establish the diagnosis [1].

Differential diagnosis and histological pitfalls

The odontogenic keratocyst (OKC) can be easily distinguished from other cysts, especially the odontogenic orthokeratinized cyst (OOC), by its corrugated parakeratinization and the palisaded basal cell layer [5] (Figs. 6A and B). However, a very focal area of orthokeratinization within the lining of OKC or a very focal area of parakeratinization within the lining of OOC may be tolerated [1].

Diagnosing OKC can be challenging if inflammatory changes obscure its histological features. A thorough examination of the entire specimen, along with deeper sections, is necessary [5] (Figs. 6C and D).

While the epidermoid cyst shares histological similarities with OKC, it is a soft tissue cyst mostly found in the floor of the mouth [19]. Superficial necrosis observed in a radicular cyst should not be confused with areas of keratinization.

Implications for treatment decisions

The diagnosis of odontogenic keratocyst may imply more aggressive treatments such as peripheral ostectomy, surgical resection, or even hemi-mandibulectomy for larger lesions. Its high recurrence rate (20–30%) implicates a long-term follow-up. Additionally, clinicians should offer genetic counseling to their patients to detect syndromic cases early on [1,17]. The important distinction between odontogenic keratocyst and orthokeratinized odontogenic cyst lies in the significantly lower recurrence rate (5%) of the latter, its less aggressive treatment (enucleation), and its non-association with Gorlin Syndrome [1].

Table IV. Clinical and radiological features of keratinized odontogenic cysts [1,2,7].

	Clinical features	Radiological features
Odontogenic keratocyst	3rd most frequent cyst of the jaws. Strong predilection for posterior mandibular area. Recurrence rate is 20 to 30%. Syndromic cases are generally multiple and occur at a young age	Unilocular or multilocular well-defined radiolucency, sometimes associated with an unerupted tooth. The potential growth of these lesions may cause large cyst and bone destruction (Fig. 4B and C)
Orthokeratinized odontogenic cyst	Strong predilection for posterior mandibular area, sometimes associated with a non-erupted tooth. Recurrence are rare (< 5%). No association with Gorlin syndrome.	Unilocular well-defined radiolucency, mostly associated with an impacted tooth. Multilocular cases are rare (Fig. 4A)
Gingival cyst of the newborn	Multiple small white nodules on edentulous alveolar ridge occuring in 90% of the neonates (< 3 months)	Absence of radiological manifestations

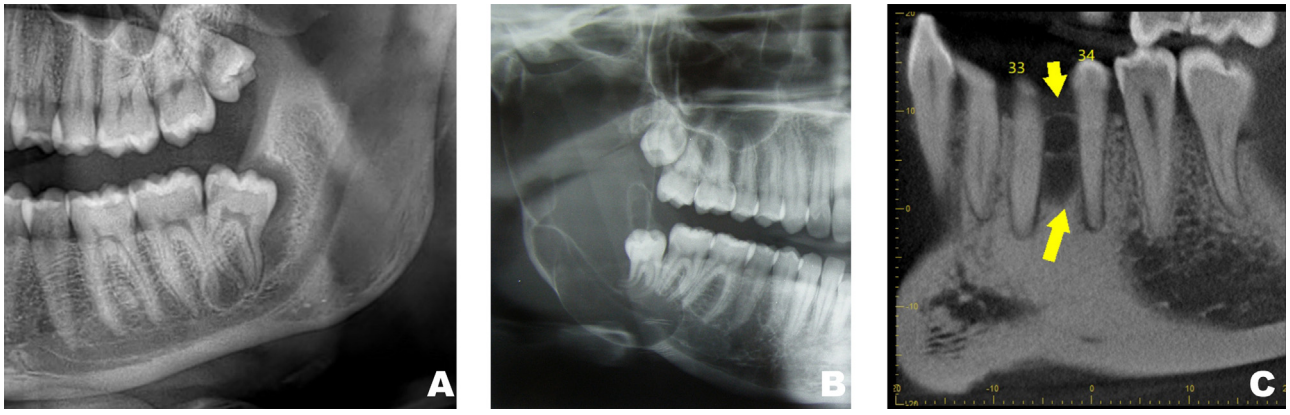

Fig. 4. Radiographic features of keratinized odontogenic cysts. (A) Panoramic view showing an unilocular radiolucency surrounding the distal aspect of a partially erupted molar. The final diagnosis was an orthokeratinized odontogenic cyst. (B) Panoramic view showing an extensive multilocular radiolucency involving the right ascending ramus. The final diagnosis was an odontogenic keratocyst. (C) Sagittal section of a CBCT showing a multilocular radiolucency in a "lateral periodontal" emplacement. The final diagnosis was surprisingly a keratocyst.

Cysts lined by an ameloblastomatous epithelium

This subset comprises only one true odontogenic cyst, the calcifying odontogenic cyst. We include a discussion about the unicystic ameloblastoma, despite it not being a cyst but an odontogenic tumor, due to its significant clinical implications.

Clinical and radiological features of odontogenic cysts lined by an ameloblastomatous epithelium [1,2,10] (Tab. V and Figs. 5A–C).

Histopathological features

The unicystic ameloblastoma is a single cyst lined by a loose epithelium reminiscent of stellate-reticulum, supported by a peripheral basal cell layer with hyperchromatic, columnar, and palisaded cells that may exhibit reverse polarity features. Epithelial papillary proliferations into the lumen define the intra-luminal subtype, while additional epithelial islands proliferating into the wall represent the mural subtype [1,15,20] (Figs. 8A–C).

The calcifying odontogenic cyst is typically unilocular and lined by an ameloblastomatous-like epithelium containing ghost cells that may undergo calcification. These ghost cells appear pale and eosinophilic, retaining cell outlines but lacking a nucleus. They may breach the basement membrane, triggering a foreign body giant cell reaction in the connective tissue. The production of dentinoid or dystrophic calcifications is not uncommon [1,21] (Fig. 8D).

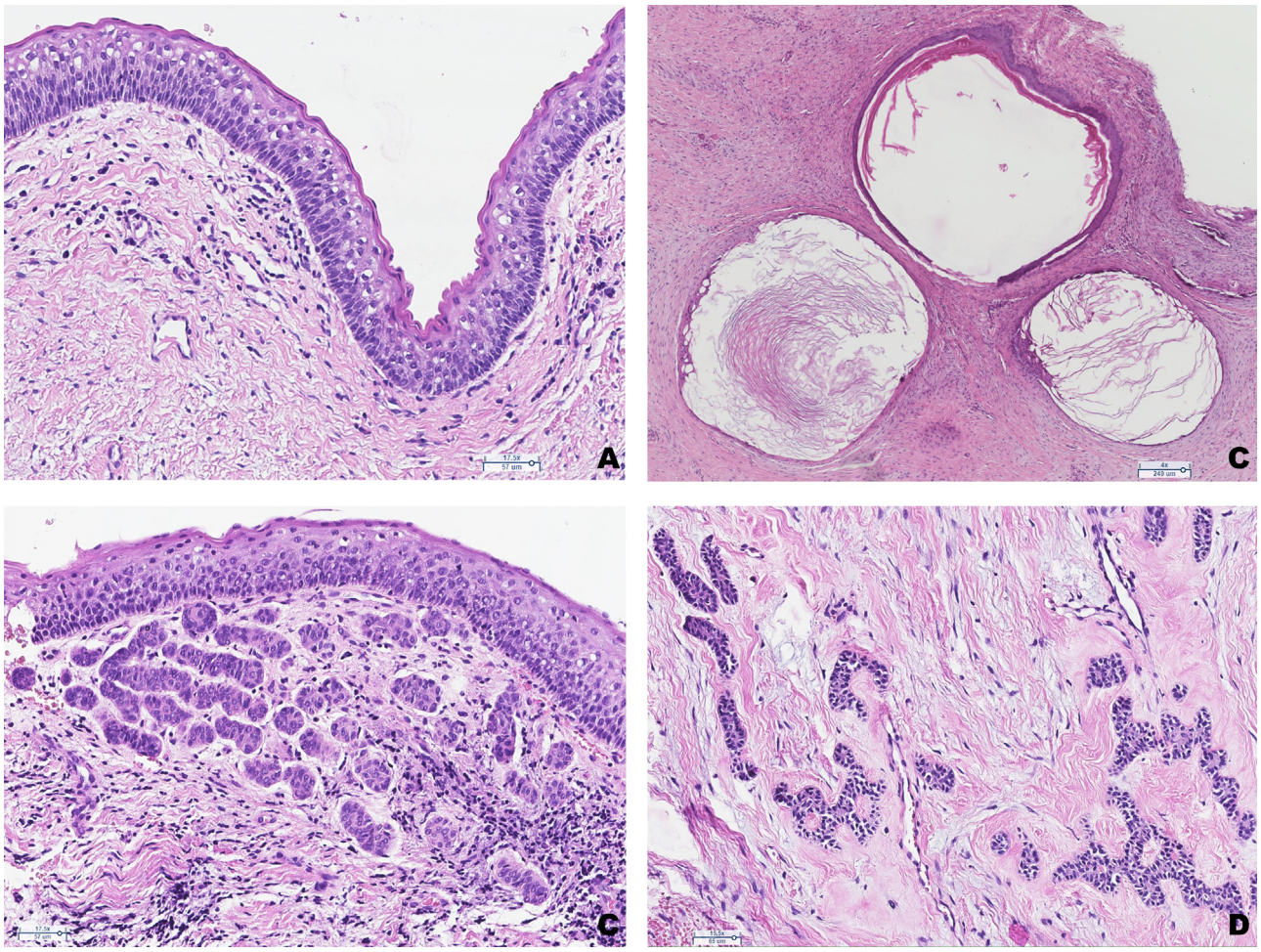

Fig. 5. Photomicrographs of a keratocyst (Gorlin syndrome in a 8-year-old child). (A) Corrugated parakeratosis and hyperchromatic palisaded basal cells (HE ×175). (B) Satellite "daughter" cysts within the cystic wall (HE ×40). (C) Basaloid cell budding in a syndromic case (HE ×175). (D) Prominent odontogenic epithelial rests with hyalinization within the cystic wall (HE ×400).

Differential diagnosis and histological pitfalls

Ghost cells may be observed in various odontogenic and non-odontogenic lesions, including calcifying odontogenic cyst, dentinogenic ghost cell tumor, ghost cell odontogenic carcinoma, odontoma, as well as craniopharyngioma or pilomatrixoma. The intriguing similarity in features among these lesions can be explained by a common molecular pathogenesis linked to aberrations in the Wnt signaling pathway, which is involved in the formation of teeth, hair, and the adenohypophysis [21].

Differential diagnosis is essential, particularly with its solid counterparts, the dentinogenic ghost cell tumor, and the ghost cell odontogenic carcinoma. The dentinogenic ghost cell tumor is a solid odontogenic neoplasm and not a unilocular cyst, while the ghost cell odontogenic carcinoma exhibits architectural and cytological evidence of malignancy, including nuclear pleomorphism, mitotic activity, necrosis, or an infiltrative growth pattern [1].

The presence of a significant number of ghost cells and dentinoid deposits is a key feature for distinguishing it from unicystic or conventional ameloblastoma. Ghost cells have distinctive characteristics and should be easily differentiated from conventional keratinization, which may be observed in ameloblastoma with acanthomatous changes or squamous metaplasia [21,22].

Calcifying odontogenic cyst and adamantinomatous craniopharyngioma share similar histological features, but craniopharyngioma is typically localized to the hypothalamic–pituitary axis [1,21].

Implications for treatment decisions

The calcifying odontogenic cyst exhibits a low recurrence rate following simple enucleation. In contrast, dentinogenic ghost cell tumors or ameloblastomas require more aggressive surgical interventions, such as surgical resection, and are associated with a high recurrence rate, justifying the necessity for long-term follow-up. It is crucial to distinguish it from ghost cell odontogenic carcinoma due to its malignant behavior, even though it is an incredibly rare lesion with fewer than 50 reported cases [1,2].

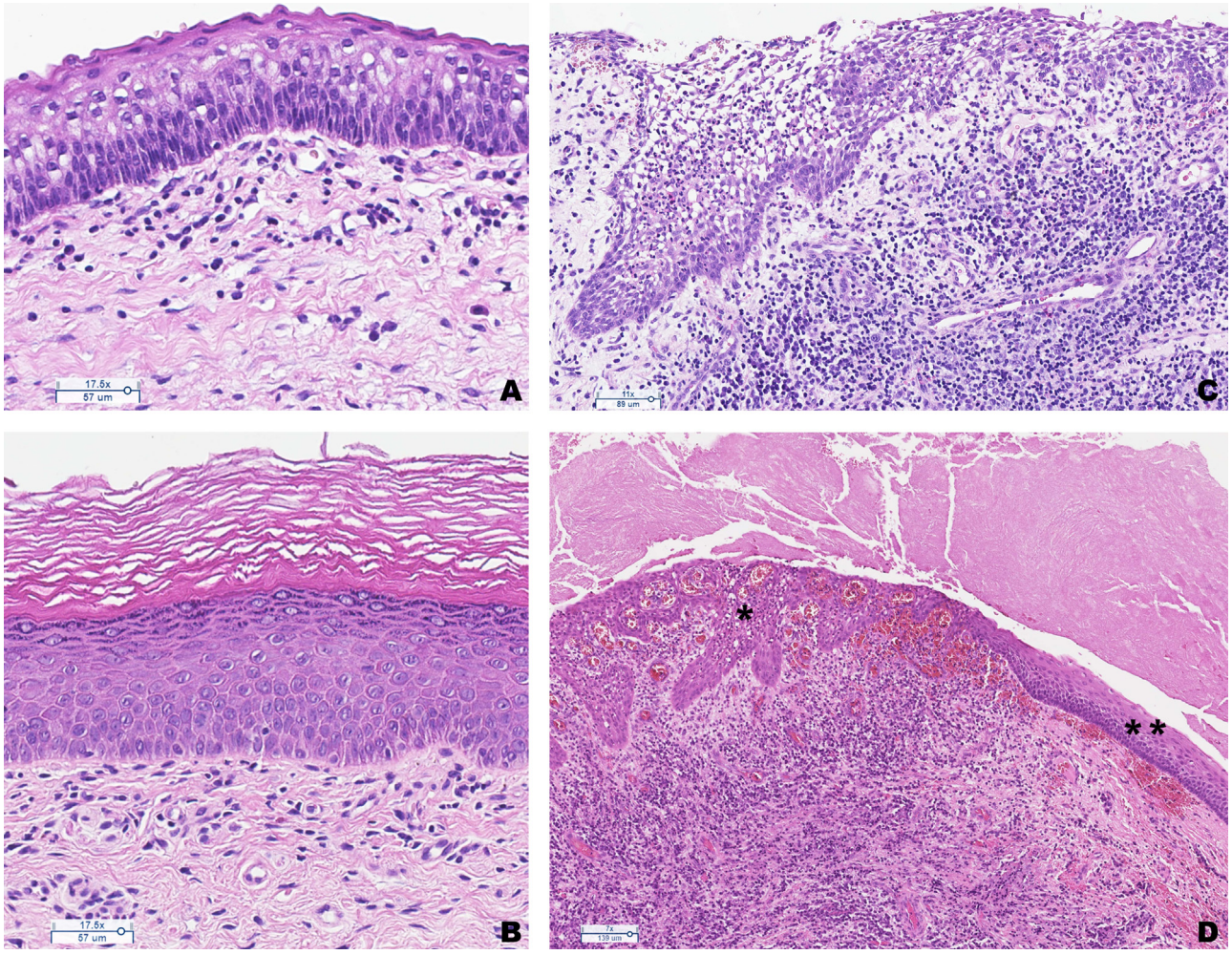

Fig. 6. Photomicrographs showing diagnostic pitfalls for keratinized odontogenic cysts. (A) Parakeratosis and hyperchromatic palisaded basal cells in a keratocyst (HE ×175). (B) Odontogenic orthokeratinized cyst are covered by a lamellar hyperorthokeratosis and don't have polarization features within their basal cell layer (HE ×175). (C) Inflammation mask histological characteristics of keratocyst (HE ×175). (D) Transition between an inflamed non-specific epithelium (*) and a non-inflamed parakeratinized epithelium (**) within a keratocyst (HE ×400).

Cysts lined by an epithelium with plaque-like thickenings

This subset includes 4 developmental odontogenic cysts: periodontal lateral cyst, botryoid odontogenic cyst, gingival cyst of the adult and glandular odontogenic cyst.

Clinical and radiological features of odontogenic cysts lined by an epithelium with plaque-like thickenings [1, 2, 10, 23] (Tab. V and Figs. 9A–F).

Histopathological features

The lateral periodontal cyst (LPC) is a unilocular cyst lined by a thin, non-keratinized epithelium that may exhibit focal whorled plaque-like thickenings, occasionally containing pale clear cells [1,23] (Figs. 10A and B).

The botryoid odontogenic cyst (BOC) represents a multicystic variant of LPC, featuring multiple confluent cystic spaces lined by a non-keratinized epithelium with focal plaque-like thickenings [1,23] (Figs 10C and D).

The gingival cyst of adults (GC) is the peripheral counterpart to LPC [1,23] (Figs. 10E and F).

The glandular odontogenic cyst (GOC) shares histological resemblance to the botryoid odontogenic cyst, presenting multicompartmental cystic spaces lined by a non-keratinized epithelium that produces plaque-like thickenings. However, GOC includes intra-epithelial duct-like spaces and sometimes other glandular features such as mucous or ciliated cells, clear or vacuolated cells, apocrine metaplasia, and papillary projections [1,5] (Figs. 10G and H).

Differential diagnosis and histological pitfalls

The plaque-like thickenings of the lateral periodontal cyst (LPC) are sometimes challenging to discern, and the diagnosis should rely on a robust correlation with radiological and clinical features [23].

The lining of the gingival cyst (GC) is so thin that it may be inconspicuous or mistaken for a dilated thin vessel or a dilated salivary gland duct. The use of a pan-cytokeratins marker may prove useful in highlighting this thin epithelium [23] (Fig. 10F).

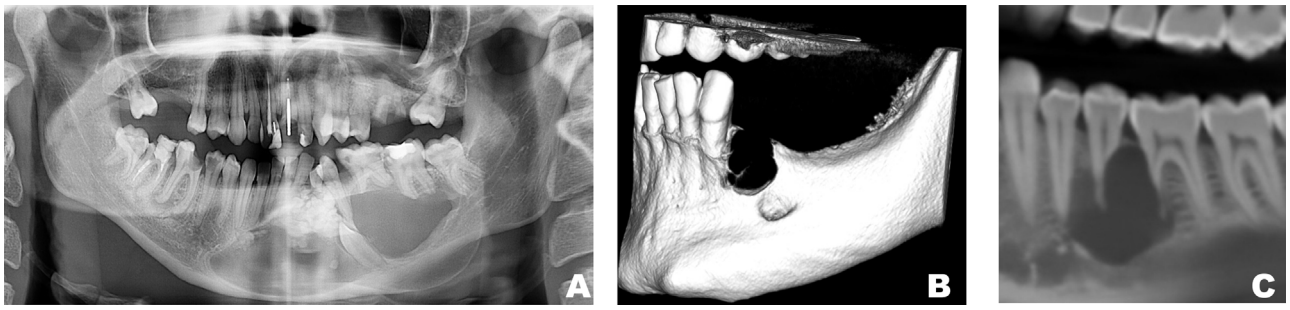

Fig. 7. Radiographic features of "ameloblastomatous-lined" cysts. (A) Panoramic view showing an extensive unilocular radiolucency involving the body of the mandible and including an impacted tooth and calcifications. The final diagnosis was a calcifying odontogenic cyst associated with a complex odontoma. (B) 3D reconstruction of a CBCT showing an pseudo-unilocular radiolucency involving alveolar bone after the extraction of tooth 34. The final diagnosis was an unicystic ameloblastoma. (C) Sagittal section of a CBCT showing an unilocular radiolucency with root resorption of teeth 35 and 36. The final diagnosis was an unicystic amelobalstoma.

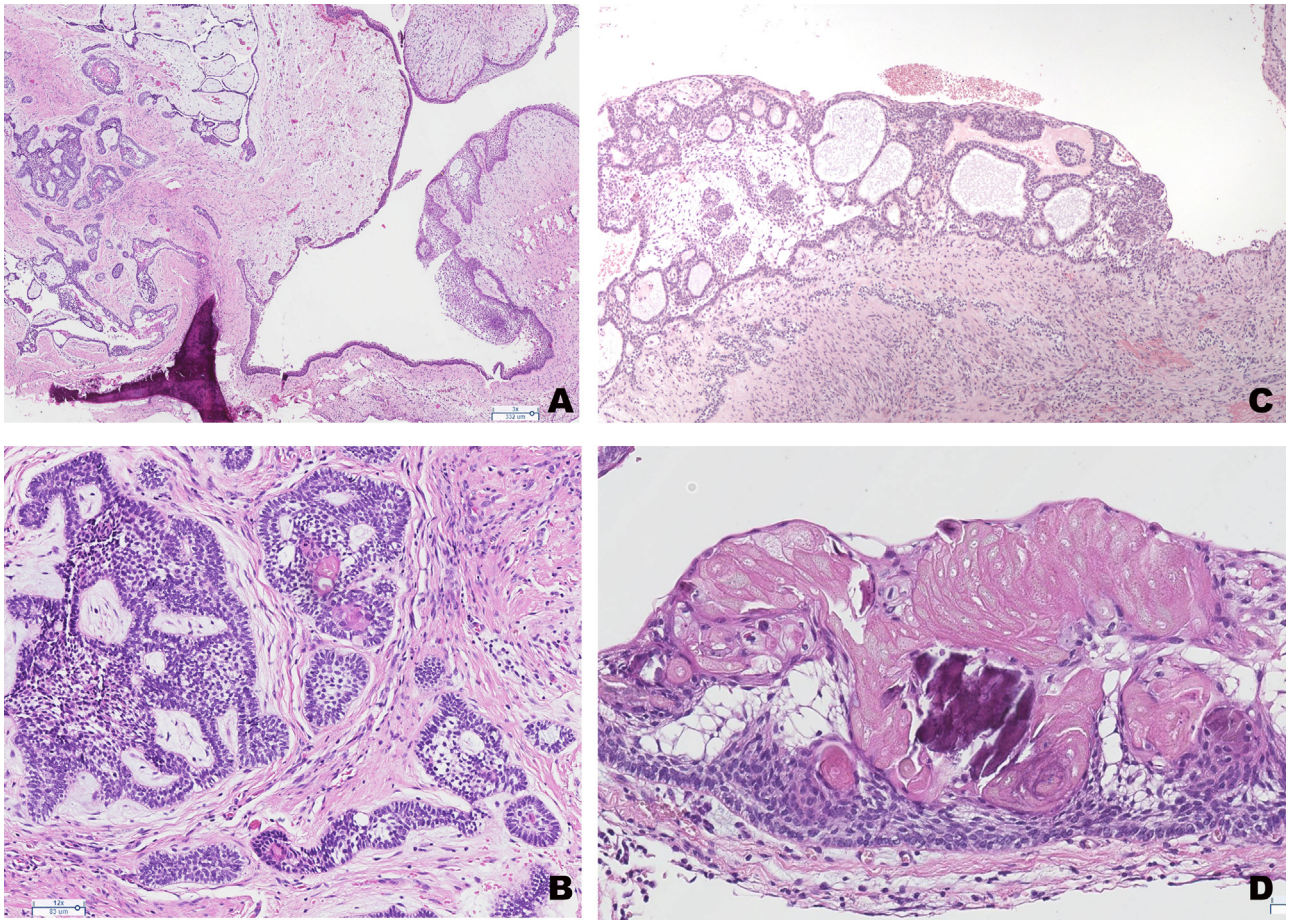

Fig. 8. Photomicrographs showing histopathological features of unicystic ameloblastoma and calcifying odontogenic cyst. (A) Cystic component (right) and mural ameloblastomatous proliferation (left) in an intra-mural unicystic ameloblastoma (HE ×50). (B) Mural proliferation is composed of multiple ameloblastomatous well-differentiated follicules subtented by a palisaded basal cell layer with nuclear polarity reverse features (HE ×120). (C) A pure intra-luminal proliferation of an unicystic amleoblastoma (HE ×100). (D) Ghost cells and dystrophic calcification in a calcifying odontogenic cyst (HE ×400).

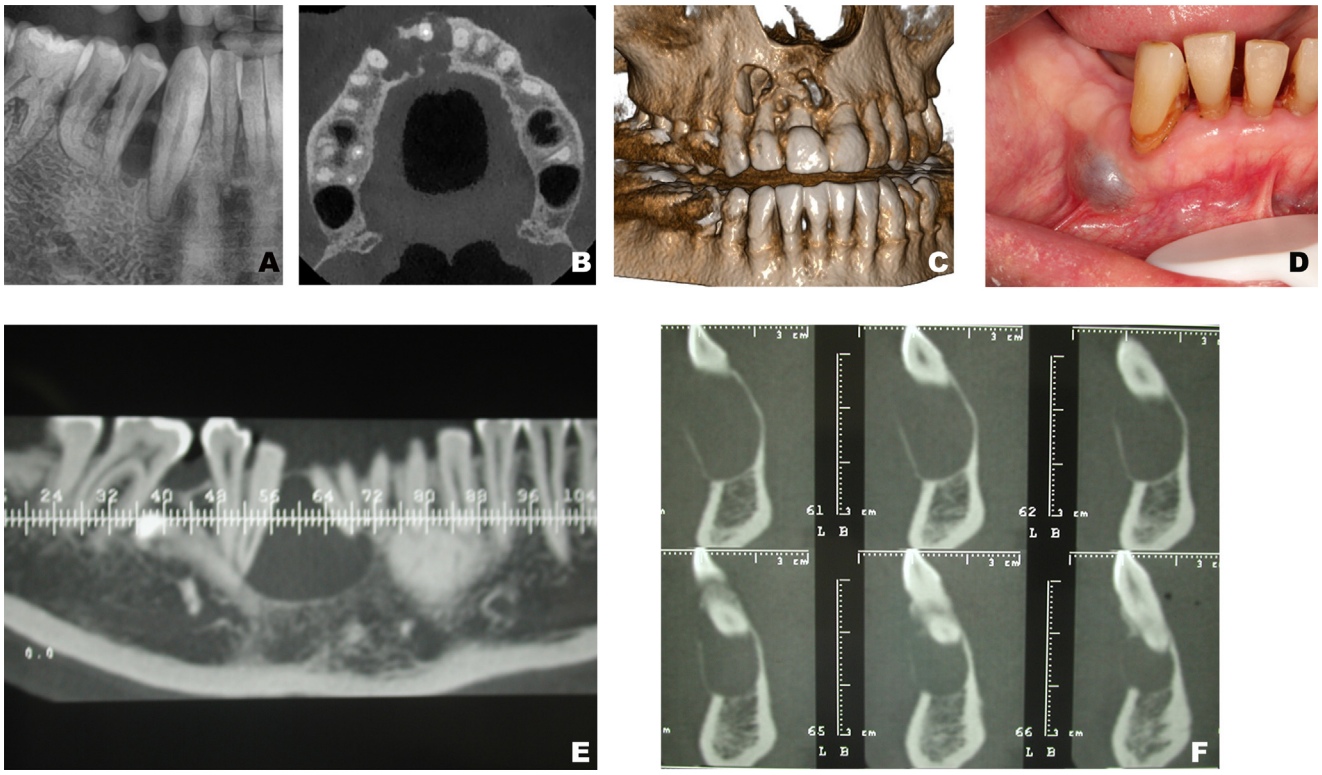

Fig. 9. Radiological features of odontogenic cysts lined by an epithelium with plaque-like thickenings. (A) Panoramic view showing an unilocular radiolucency consistent with a LPC. (B/C) CBCT sections showing confluent multilocular radiolucencies consistent with a BOC. (D) Clinical view showing a bluish nodule consistent with a gingival cyst. (E/F) CBCT sections showing a unilocular radiolucency with tooth displacement. The final diagnosis was a GOC.

Distinguishing between botryoid odontogenic cyst (BOC) and glandular odontogenic cyst (GOC) can be challenging, but GOC displays true glandular spaces surrounded by luminal hobnail cells in all cases [5]. The differential diagnosis should also consider low-grade central mucoepidermoid carcinoma, although it poses significant challenges. Central mucoepidermoid carcinoma is a rare intra-osseous salivary gland tumor with epidermoid, intermediate, and mucous cells, harboring MAML-2 rearrangement, whereas glandular odontogenic cyst is considered MAML-2 rearrangement negative [1,5,14].

Implications for treatment decisions

Careful distinction should be made between indolent lesions, such as the lateral periodontal cyst or gingival cyst, which are highly unlikely to recur after simple enucleation, and more aggressive lesions, such as botryoid odontogenic cyst or glandular odontogenic cyst. These aggressive lesions have a high recurrence rate after enucleation (exceeding 20%) and may necessitate surgical resection for recurrent cases [1].

Low-grade central mucoepidermoid carcinoma is typically treated through block resection, hemi-mandibulectomy, or hemi-maxillectomy, with or without additional treatment such as neck dissection or radiotherapy [24].

Cysts lined by a metaplastic epithelium with mucous or ciliated cells

Mucous or ciliated cells are commonly observed within the epithelium of dentigerous cysts, glandular odontogenic cysts, nasopalatine duct cysts, surgical ciliated cysts, as well as radicular or paradental cysts, keratocysts, and various other odontogenic and non-odontogenic cysts closely associated with the sinus or nasal floor, lined by a respiratory mucosa [5,14]. In this discussion, we focus on two non-odontogenic cysts: the nasopalatine duct cyst and the surgical ciliated cyst.

Clinical and radiological features of non-odontogenic cysts lined by an epithelium with mucous or ciliated cells [1,2,10,23] (Tab. VII and Fig. 11A).

Histopathology features

The nasopalatine duct cyst is typically lined by a non-keratinized malpighian epithelium with focal respiratory changes, such as the presence of columnar, ciliated, or mucous cells. When the cysts are positioned more superiorly within the nasopalatine duct, they tend to be lined by a true respiratory-type epithelium. The cyst wall exhibits normal components of the nasopalatine duct, including prominent nerve bundles, muscular vascular channels, and occasionally cartilaginous rests or mucous glands [1,25].

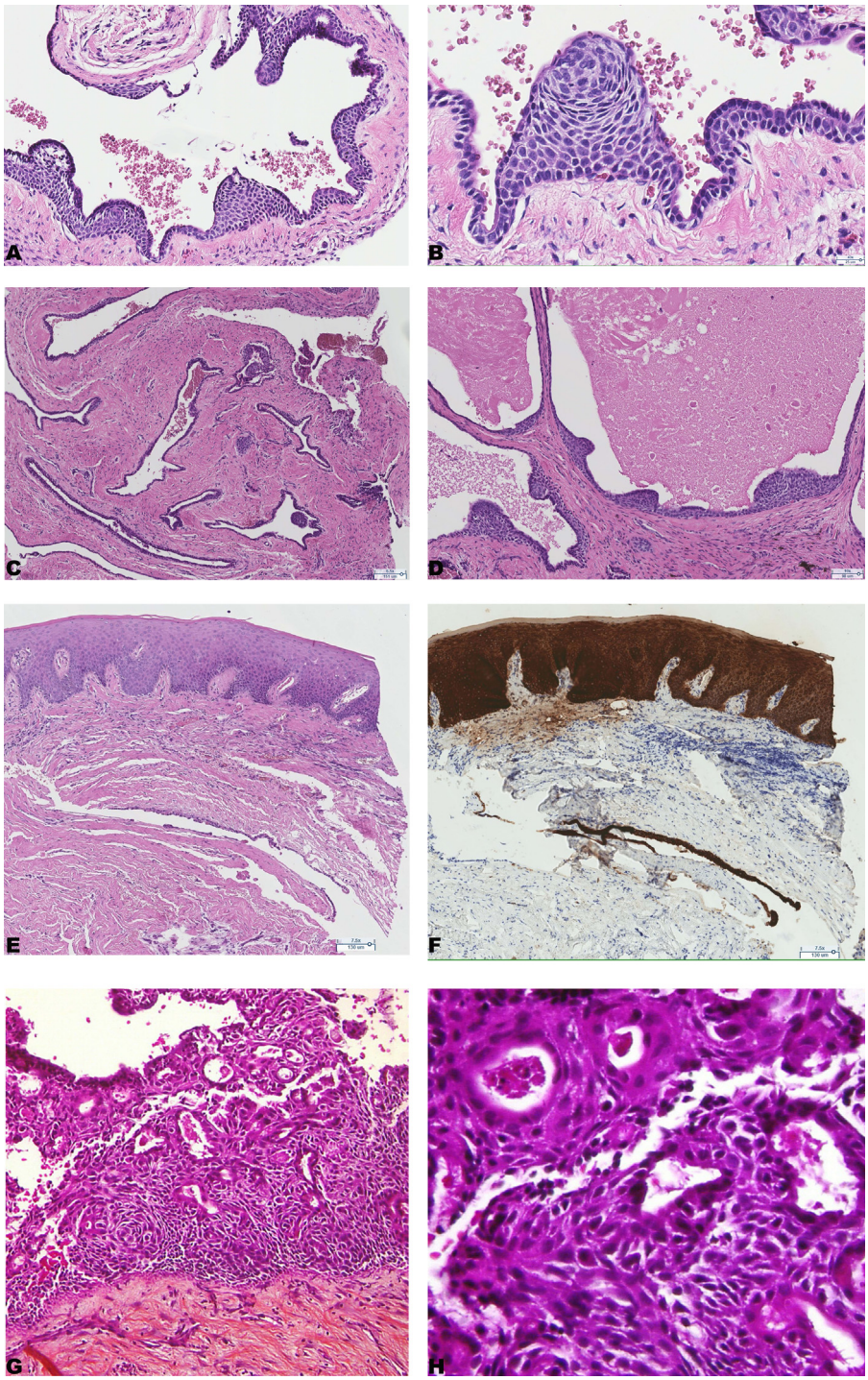

Fig. 10. Photomicrographs of odontogenic cysts lined by an epithelium with plaque-like thickenings. (A) Plaque-like thickenings within the cystic epithelium of a LPC (HE ×145). (B) Whorled plaque-like thickenings in a LPC (HE ×400). (C) Multicystic spaces in a BOC (HE ×65). (D) Necrotic-filled multicystic spaces with plaque-like thickenings in a BOC (HE ×100). (E) Inconspicuous very thin epithelium within the gingival chorion in a gingival cyst (HE ×75). (F) Cytokeratin marker helps to highlight the thin epithelium of a gingival cyst (HE ×75). (G) Glandular structures within the epithelium of a GOC (HE ×200). (H) Secretions within the true glandular spaces of a GOC (HE ×400).

The ciliated surgical cyst is lined by a respiratory-type epithelium reminiscent of the mucosa of the sinus floor. It generally features a pseudostratified ciliated columnar epithelium with mucous cells, and squamous metaplasia or simple cuboidal cells are not uncommon [1,26].

Differential diagnosis and histological pitfalls

Mucous metaplasia is not uncommon, non-specific, and not essential for diagnosing any odontogenic cyst. The presence of mucous cells within the cystic lining can lead to a misleading diagnosis, particularly in the case of the glandular odontogenic

Table V. Clinical and radiological features of odontogenic cysts lined by an ameloblastomatous epithelium [1,2,7].

	Clinical features	Radiological features
Calcifying odontogenic cyst	Rare cyst (< 1%), 2nd – 3rd decades of life. Some cases arise from gingiva. May be associated with an odontoma.	Well-defined unilocular radiolucent or mixed lesion, sometimes associated with an odontoma. Teeth displacement, root resorption, cortical bone thinning are possible (Fig. 7A)
Unicystic ameloblastoma	5–22% of all ameloblastoma, 2nd – 3rd decades of life with predilection for posterior mandible	Unilocular well-defined radiolucency, often associated with an impacted tooth. Root resorption and cortical perforation are frequent (Figs. 7B and C)

Table VI. Clinical and radiological features of odontogenic cysts lined by an epithelium with plaque-like thickenings [1,2,7,20].

	Clinical features	Radiological features
Lateral Periodontal Cyst (LPC)	Predilection for mandibular canine/premolar area, usually localized between the roots of 2 vital teeth that may be displaced	Well-defined unilocular radiolucency usually less than 10 mm (Fig 9A)
Botryoid odontogenic cyst (BOC)	*Multicystic variant of LPC*	Usually confluent multilocular radiolucency (Figs 9B, Figs 9C)
Gingival cyst of adults (GC)	*Peripheral counterpart of LPC* Predilection for mandibular gingiva of canine/premolar area. It appears like an asymptomatic, well-defined and usually bluish nodule on the attached gingiva. (Fig 9D)	This cyst is purely peripheral and is not associated with any radiographic involvement
Glandular odontogenic cyst (GOC)	Rare cyst (<0,5%), slight predilection for anterior mandibular area. Usually asymptomatic slow-growing swelling.	Radiological features are not specifics, and this cyst may appear initially like an unilocular radiolucency that becomes locally aggressive with multilocular features and often tooth displacement, root resorption or cortical perforation. It may cross the jaw midline. (Figs 9E, Figs 9F)

cyst, an aggressive lesion. Mucous cells alone are insufficient for establishing this diagnosis, and the visualization of true glandular spaces is mandatory [5,14].

The neurovascular bundle often plays a crucial role in the diagnosis of the nasopalatine duct cyst, as its epithelial lining is non-specific and may be obscured by inflammation [25].

Diagnosing the ciliated surgical cyst requires careful clinical and pathological correlation, considering the patient's history of previous maxillofacial surgery or facial injuries [1,26].

Implications for treatment decisions

Misdiagnosing the glandular odontogenic cyst may result in inappropriate and unnecessarily aggressive surgical interventions [5].

Conclusion

Cysts of the jaws constitute a heterogeneous group of maxillofacial lesions. Histopathological examination is imperative for all jaw lesions, as potentially aggressive entities like

Table VII. Clinical and radiological features of non-odontogenic cysts lined by an epithelium with mucous or ciliated cells [1,2,7,20].

	Clinical features	Radiological features
Nasopalatine duct cyst	Cyst arising in the midline of anterior hard palatine, in the incisive canal, between the central upper incisors that remain generally vitals.	Unilocular and symmetrical "heart-shape" radiolucency between upper incisors, greater than 6 mm (normal diameter of nasopalatine duct)
Surgical ciliated cyst	Cyst caused by a traumatic or iatrogenic implantation of respiratory epithelium in jaw bones (especially maxillary bone)	Well-defined unilocular radiolucency, that may fill the sinus for largest maxillary lesions

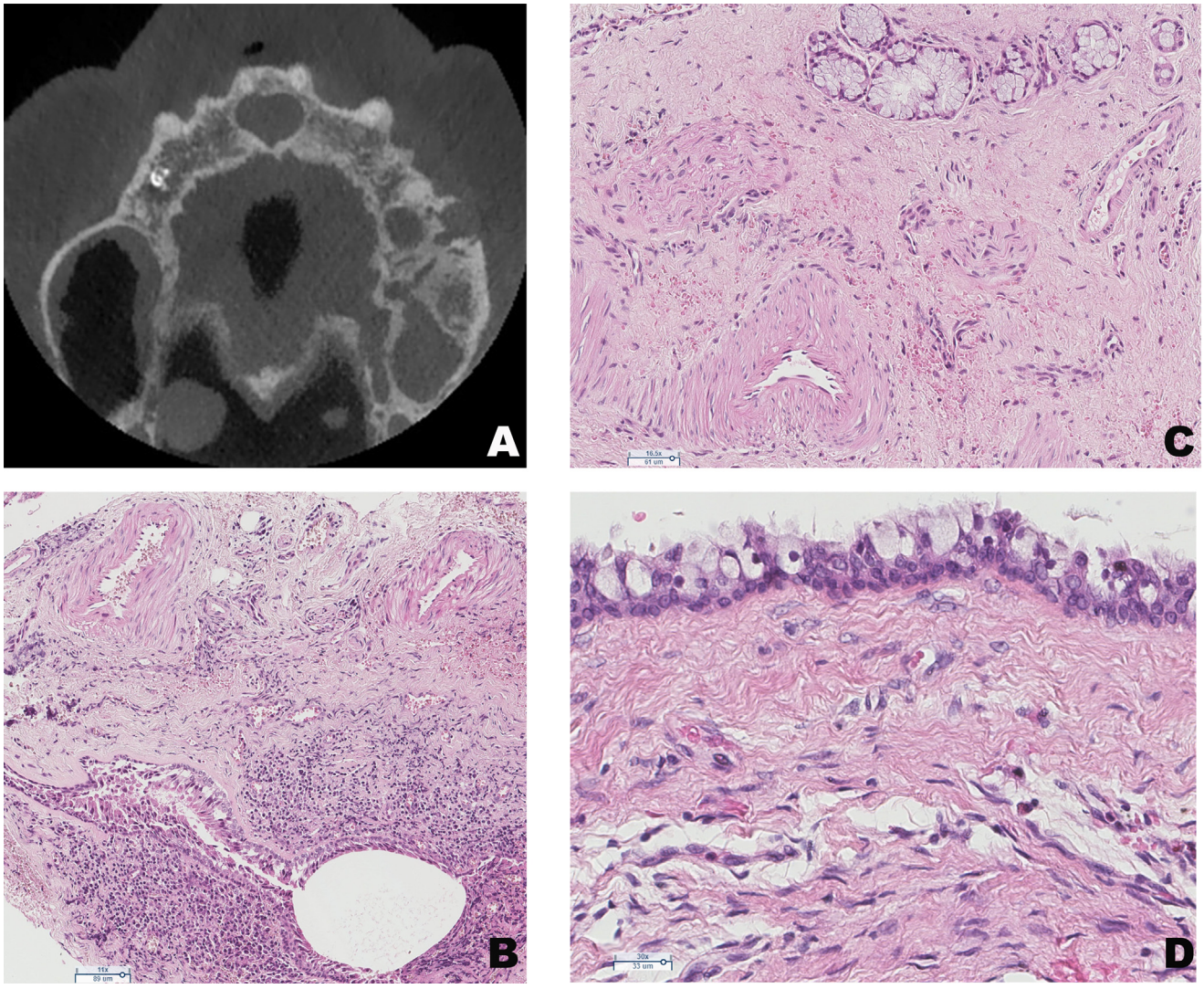

Fig. 11. Radiological and histological features of a nasopalatine duct cyst. (A) CBCT horizontal section showing a "heart-shaped" radiolucency between superior incisors. (B) Pseudostratified cystic epithelium and prominent arteries within the cystic wall (HE ×110). (C) Mucous gland and prominent neurovascular bundles within the cystic wall (HE ×165). (D) Presence of mucous cells within the epithelium of a radicular cyst : these cells are not specific of any odontogenic cysts (HE ×300).

keratocysts, glandular odontogenic cysts, or unicystic ameloblastomas may mimic indolent ones such as radicular cysts or dentigerous cysts. Pathological diagnosis is challenging due to the lack of specific histological morphology, often obscured by inflammation, and the limited utility of ancillary studies. Accurate pathological reporting necessitates strict clinical and radiological correlation, but clinicians may not always be aware of the pertinent data to communicate.

In this article, we propose a model request form for microscopic examination and present numerous photomicrographs to raise awareness among clinicians about the primary pathological diagnostic challenges in jaw lesions. We encourage clinicians, radiologists, and pathologists to enhance their communication skills to improve the quality of their diagnoses.

Funding

This research did not receive any specific funding.

Conflicts of Interest

The authors declares that they have no conflicts of interest in relation to this article.

Data availability statement

The data analysed during the current study are openly available on PubMed Website following the link: https://pubmed.ncbi.nlm.nih.gov/

The WHO's 5th edition of Head and Neck Tumors is available with a one-year subscription on this web-site: https://tumourclassification.iarc.who.int/chapters/52

Author contribution statement

Svyat Strokov = Writing original draft and histological photomicrographs / Nathalie Cardot-Leccia = Conceptualization reviewing and editing, histological examinations/ Hélène Raybaud = Writing original draft / Sarah Latrèche: surgery and reviewing/ Estelle Guillou: surgery and reviewing/ Nouha Khenissa: surgery and reviewing/ Yves Ponchet: radiological procedures / Christine Voha = Writing original draft and final reviewing.

Ethics approval

Ethical approval was not required.

Informed consent

This article does not contain any studies involving human subjects.

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