SMGroup

Odontogenic Cysts

Ioannis Chatzistefanou[1]*, Vassilios Kogias[1] and Konstantinos Antoniades[1]

[1]Department of Oral and Maxillofacial Surgery, Aristotle University of Thessaloniki, Greece

***Corresponding author:** DIoannis Chatzistefanou, Department of Oral and Maxillofacial Surgery, University of Thessaloniki, Papanikolaou General Hospital, Exochi, Thessaloniki, 57010, Greece, Tel: +30 2310 760124; Fax: +30 2310 760124; Email: Ioannis.chatzistefanou@gmail.com

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INTRODUCTION

Cysts are abnormal, closed sac-like lesions within a tissue containing luminal liquid or semisolid substance. They may or may not lined by epithelium. Odontogenic Cysts **(OC)** are epithelial lined cystic lesions of the jaws, that by definition derived from tooth-related apparatus (remnants of dental lamina - rests of Serres; reduced enamel epithelium; remnants of epithelial root sheath - rests of Malassez) [1-3]. Pathogenetically the odonto-genic cysts are classified as inflammatory and developmental [1,4] (Table 1). Given the potential difference in therapeutic approach, accurate differentiation from nonodontogenic cystic lesions (Table 2) or other pathologic entities of the jaws is deemed necessary. The purpose of this chapter is to review the clinico-pathologic features, biological profile and treatment recommendations for the various odontogenic cysts, with aim to assist in accurate diagnosis and proper clinical decision-making.

Table 1: Classification of Odontogenic Cysts.

Inflammatory
Periapical (radicular) cyst
Residual periapical cyst
Buccal bifurcation cyst (Paradental cyst)
Developmental
Dentigerous (follocular) cyst
Erupsion cyst
Gingival (alveolar) cyst Infants
Gingival cyst of adults
Lateral periodontal cyst
Calcifying odontogenic cyst (COC)*
Glandular odontogenic cyst (GOC)

*The term "Calcifying odonigenic cyst" refers only to the noon-neoplastic cystic lesion. According to the 2005 WHO classification the COC is described as an odontogenic tumor.

Table 2: Nonodontogenic Cysts of the Jaws.

Developmental
Nasopalatine duct (incisive canal) cyst
Nasolabial (nasoalveolar) cyst
Globulomaxillary lesion (cyst)
Median Palatal cyst
Median mandibular cyst
Non-epithelial lined cysts (pseudocysts)
Aneurysmal bone cyst
Traumatic bone cyst
Simple bone cyst
Stafne's bone defect (static bone cyst)

ODONTOGENESIS

A clear conception of the tooth development process [2,3,5,6] is required for understanding the pathogenic pathways and the biological behavior of odontogenic cysts. For each tooth, odontogenesis (Table 3) begins with the formation of the dental lamina [Initiation/ Bud stage], an apical proliferation of the oral epithelium (ectoderm). The dental lamina subsequently gives rise to a cup-shaped structure called enamel organ (Proliferation/ Cup stage), while the surrounding mesenchymal tissue gives rise to the dental papilla and the dental sac (ectomesenchyme derived from neural crest cells). The enamel organ consist of four distinct epithelial linings, which are from inner to outer side the inner enamel epithelium, the stratum intermedium, the stellate reticulum and the outer enamel epithelium.

During the next stage (Differentiation/ Bell stage), tooth development proceeds with sequential cellular interactions between the epithelial and the mesenchymal components (Figure 1). The enamel organ will give rise to enamel (ameloblasts derived from the inner enamel epithelium). The dental papilla will give rise to dentin (peripheral cells) and dental pulp (centrally located cells). The dental sac will give rise to cementum, periodontal ligament and alveolar bone. The inner and outer enamel epithelia will form the Hertwig's epithelial root sheath that proliferates apically and eventually gives rise to the root of the developing tooth. After completion of enamel formation, the enamel organ epithelium atrophies to form a flattened layer that covers the enamel of the unerupted tooth known as the reduced enamel epithelium. Remnants of Hertwig's epithelial root sheath may remain in the periodontal ligament (rests of Malassez) [1,2,6] (Table 4).

Table 3: Stages of Odontogenesis.

Initiation (Bud stage)
Proliferation (Cap stage)
Differentiation (Bell stage)
Apposition
Calcification
Eruption

Table 4: Inflamatory and Developmental Odontogenic Cysts.

Type	Age (decade)	Common location	Origin	Radiograph	Management
Periapical cyst	3rd - 4th	Root Apex (necrotic tooth) Anterior maxilla/ Posterior mandible	Rests of Malassez	Unilocular, well-defined radiolucency with a sclerotic border	Enucleation – management of the offending tooth
Rsidual cyst	4th – 5th	Post-extraction edentelous area	Rests of Malassez	Unilocular, well-defined radiolucency - not associated with tooth (solitary cyst)	Enucleation
Buccal bifurcation cyst	1st	Mandibular molars	Rests of Malassez	Unremarkable	Enucleation
Dentigerous Cyst	2nd – 3rd	impacted or unerupted teeth Mandibular 3rd molars/ Maxillary canines	Reduced enamel epithelium	Unilocular, well-defined "tooth containing" radiolucency	Enucleation (marsupialization)
Eruption cyst	1st	Primary tooth	Reduced enamel epithelium	Erupting tooth	Nil unless hindering eruption
Gingival cyst of infants	Infants	Gum pads	Dental lamina rests	Unremarkable	Nil
Gingiva cyst of adults	Any	Gingiva	Dental lamina rests	Unremarkable	Enucleation
Lateral periodontal cyst	Any	Periodontal ligament (95%)	Dental lamina rests	Well- defined, round or teardrop-shaped radiolucency	Enucleation
Calcifying odontogenic cyst	Any	Anterior mandible/ maxilla	Dental lamina / "ghost cells"	Unilocular. well-defined radiolucency with irregular calcifications	Enucleation and curettage
Glandular odontogenic cyst	4th – 6th	Anterior mandible	Odontogenic (tooth germ) and glandular origin	Unilocular or multilocular radiolucency	Enucleation and curettage (30% recurrence)

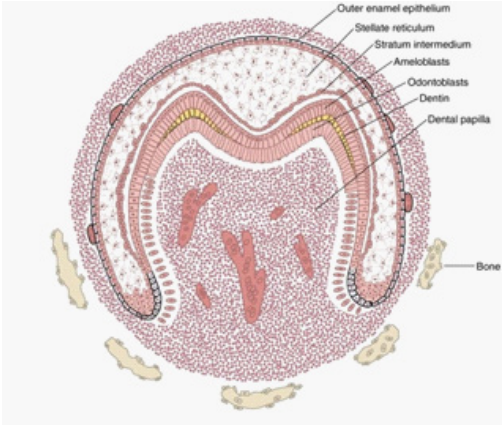

Figure 1: Bell stage of tooth formation [57].

DIAGNOSIS

There is a slight male predilection (57.70% vs. 42.30%) [7]. The mandible is affected almost three times more commonly than the maxilla. Odontogenic cysts are usually asymptomatic and they are often discovered as an incidental finding on imaging. Reaching a considerable size, they give rise to a bony swelling, with or without crackle sensation on palpation. In contrast to a malignant lesion, they are rarely cause cortical bone erosion. Pain is mainly attributed to secondary infection or pathologic fracture. In the mandible, they are characteristically encountered above the inferior alveolar canal [8,9].

Radiographically, an odontogenic cyst is typically appeared as a unilocular, well-defined radiolucency, often with a sclerotic radiopaque border (Table 4). Plain radiographs (e.g. orthopantomograph) are usually enough to evaluate a small-sized OC; however, further imaging, using contrast enhanced CT (multidetector or cone beam) or MRI scans, is generally required for evaluating more extended lesions regarding their size, location and proximity to adjacent teeth or important anatomical structures (e.g. inferior alveolar nerve or maxillary sinus). The location of an OC and its relation to specific teeth are valuable diagnostic tools in clinical routine [8,9] (Figure 2).

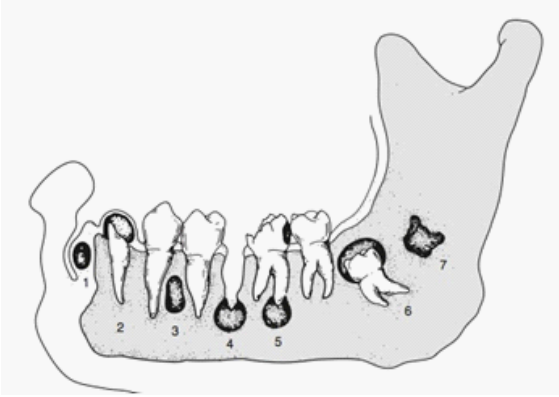

Figure 2: Common OC locations: 1.Gingival cyst; 2. Eruption cyst; 3.Lateral periodontal cyst; 4. Residual cyst; 5. Periapical cyst; 6. Dentigerous cyst; 7. Keratocystic odontogenic tumor [58].

Pulp vitality tests should be routinely performed to differentiate an inflammatory from a developmental cyst and decide on the proper management of the involved teeth. Needle aspiration or incisional biopsy of the cystic wall may also occasionally required to excluding a neoplastic process or other pathologic entity [10-12].

MANAGEMENT

Enucleation (complete cyst removal) with or without curettage is the generally recommended therapeutic approach for the majority of the odontogenic cysts (Table 4), as neoplastic processes (including mucoepidermoid carcinoma, ameloblastoma or squamous cell carcinoma) may occasionally arise from their epithelial lining [8]. Marsupialization (partial removal of cystic wall with aim to convert the close cavity into an open pouch) may alternatively be considered for large sized lesion when there are medical limitations for general anesthesia and/ or a high risk for pathologic fracture or injury to adjacent important anatomical structures [8,13]. Decompression can cause significant reduction in cyst size by peripheral new bone formation [13]. As the healing process may take up to six months, the treating surgeon could potentially decide on removal of the reduced lesion in a second stage, smaller-scale surgical intervention [14]. The fact that not the whole cyst lining is available to histopathological examination and considerable patient cooperation is required for keeping the open cavity clean, are the main disadvantages of marsupialization technique.

Prognosis is good. Recurrence is relatively rare after efficient OC removal. Regular imaging post-surgery re-evaluations are generally recommended to assess healing progress and confirm diagnosis [8,9].

INFLAMMATORY

Periapical Cyst

The Periapical or Radicular **(RTC)** cyst is the most commonly encountered odontogenic cyst (55% of all cases) [1,15]. It arises from proliferation of the epithelial rest of Malassez as a response to chemical inflammatory mediators, secondary to pulp necrosis. As these islands of epithelial cells continue to enlarge, their center gradually degenerates due to lack of adequate blood supply, giving rise to intralesional microcysts. The microcysts subsequently collapse, merge and form a well-defined intraosseous cystic cavity. Given the high protein concentration, following the cellular breakdown, the intraluminal osmotic gradient makes fluid from the surrounding tissue to transudate into the cystic center [8,16]. As long as the inflammatory stimulus persists, the radicular cyst continues to enlarge by unicentric expansion due to the gradually increasing intraluminal hydrostatic pressure [16] (Figure 3).

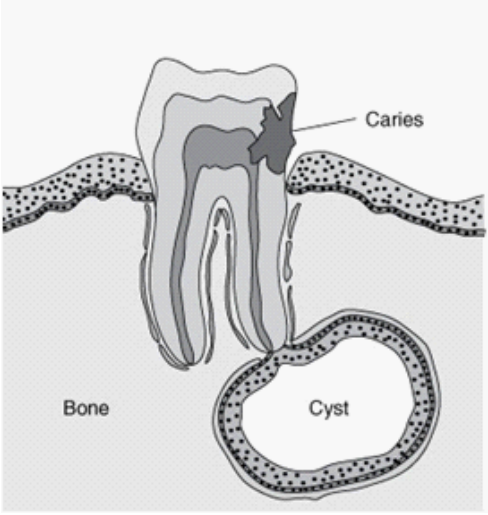

Figure 3: RTC pathogenesis [59].

Clinically the periapical cysts are typically presented as unilocular, well-defined radiolucency with a sclerotic border, around the apex of a necrotic tooth (Figure 2 and Figure 4). Vitality test of the involved tooth is crucial for the clinical diagnosis of a RTC; however histological analysis is required for the final definitive diagnosis. The cystic wall consists of fibrous connective tissue, lined by nonkeratinized stratified squamous cell epithelium of various thicknesses with elongated rete pegs. Cholesterol crystals and hyaline (Rushton) bodies are commonly identified within the cyst fluid [16,17]. Accurate differentiation from periapical granuloma (chronic localized osteitis) based on clinical and radiological features is generally not feasible; although is of limited clinical value, as it doesn't really affect treatment decision-making.

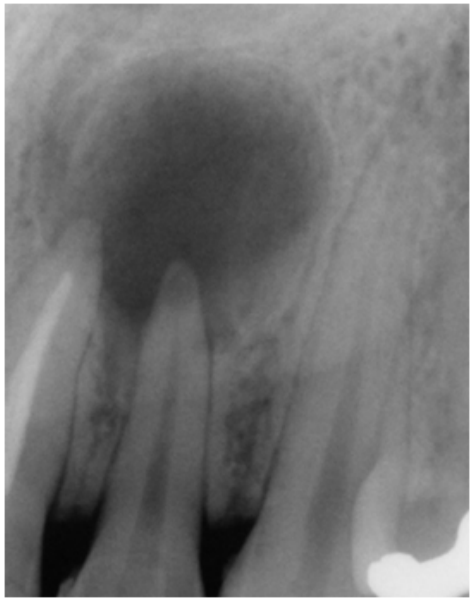

Figure 4: Radiological features of a typical periapical cyst [60].

Enucleation of the cyst and proper management of the offending necrotic tooth (root canal therapy/ apicoectomy or extraction) is the recommended therapeutic approach [8,9].

Residual Periapical Cyst

As Residual Periapical Cyst **(RPC)** is defined as a radicular cyst which was remained in jaw after removal of the associated necrotic tooth [1,8] (Figure 5). Clinical, radiological and histological features are similar of those of a periapical cyst (Figure 6). History of tooth extraction is crucial for the differentiate diagnosis from a primordial odontogenic keratocyst (an odontogenic tumor arising from epithelial elements before tooth formation) (Figure 2). Enucleation of the cyst is usually curative. Histological examination is generally recommended to exclude neoplasia or other significant pathology [8].

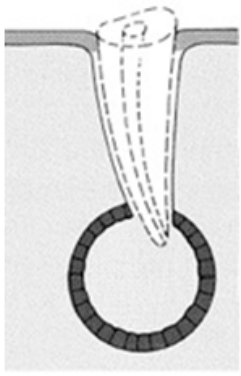

Figure 5: Pathogenesis of a residual periapical cyst [61].

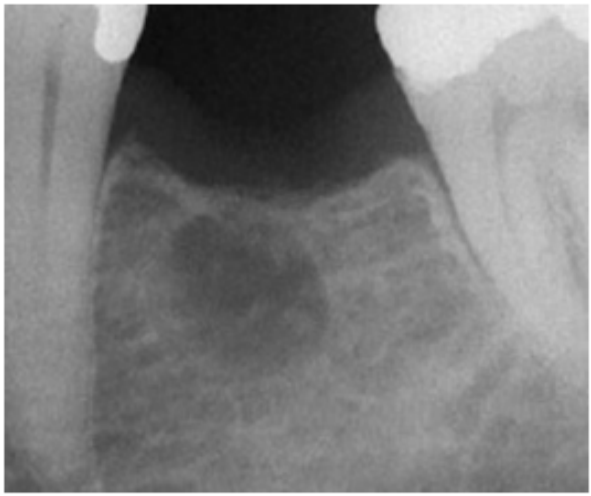

Figure 6: A residual periapical cyst characteristically located at a post-extraction site [62].

Buccal Bifurcation Cyst

Buccal Bifurcation Cyst **(BBC)** is an uncommon inflammatory cyst of uncertain origin (2005 WHO classification) [1,18]. It is typically encountered at the cervical, buccal aspect of a vital multi-rooted tooth (usually mandibular 1st molars) [19,20]. The paradental cyst is mainly associated with a partially erupted third molar complicated with chronic pericoronitis [21]. Enucleation of the cyst is adequate treatment; extraction of the associated tooth is usually not unnecessary [8,19-21,23].

DEVELOPMENTAL

Dentigerous Cyst

Dentigerous (DC, follicular) cyst is the second most common odontogenic cyst (22% of all cases) and the most common of the develop-mental odontogenic cysts [1,15]. They arise from cellular degeneration and fluid accumulation between the reduced enamel epithelium and the crown of an unerupted tooth or between the inner and outer enamel epithelium (Figure 7). Given the intraluminal osmotic gradient, the cyst lesion keeps expanding due to the gradually increasing hydrostatic pressure [9].

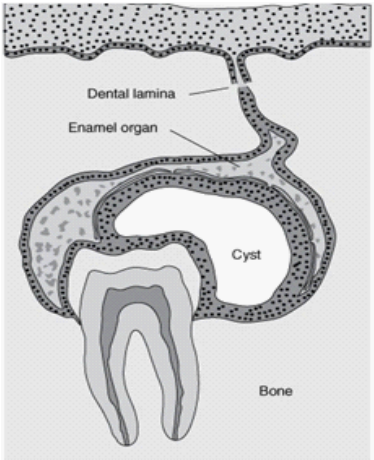

Figure 7: Pathogenesis of a dentigerous cyst [63].

The dentigerous cysts are more frequently associated with impacted or unerupted mandibular third molars (70% of all case) followed by maxillary canines and mandibular premolars [8,24] (Figure 2). They are typically presented as a unilocular, well-defined "tooth containing" radiolucency [24] (Figure 8). Depending on the relationship to the involved tooth, the cyst could be characterized as central, lateral or circumferential [8]. Follicular cysts may become extremely large causing significant displacement of the involved tooth, but in contrast to malignant process they typically do not cause cortical bone erosion. The cystic wall is typically lined by a 2 - 3 layer thick stratified non keratinized epithelium. Usually the contained fluid is yellow to brown in color, unless the cyst is infected. The differential diagnosis includes a hyperplastic follicle (which is usually smaller than 5 mm and cause no tooth displacement or bone expansion) [23,25], keratocystic odontogenic tumor, unicystic ameloblastomas and adenomatoid odontogenic tumor [11,12,26].

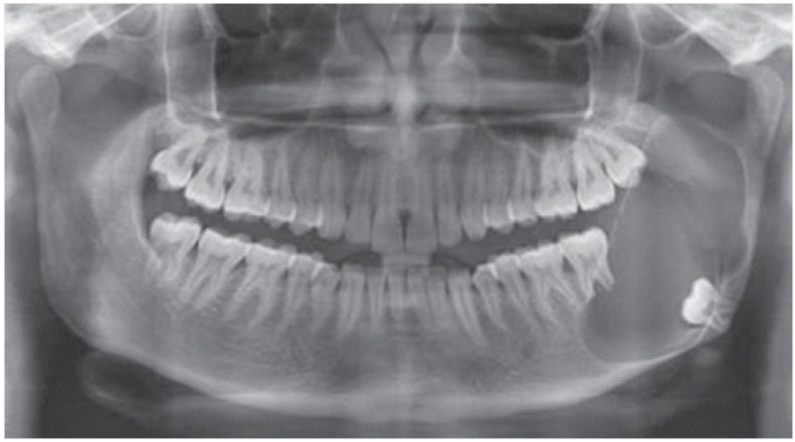

Figure 8: A remarkable displacement of a lower left wisdom tooth associated with an enlarged follicular cyst [64].

Dentigerous cysts are generally recommended to be managed with enucleation and curettage with concurrent removal of the involved tooth. As foci of ameloblastoma [27], intraosseous mucoepidermoid carcinoma [28] or squamous cell carcinoma (carcinoma ex–dentigerous cyst) [29,30] may be arise from the epithelial lining of a dentigerous cyst, marsupialization should be preferably avoided. However, for patients with medical limitations for general anesthesia or for cases predisposing to injury important adjacent anatomic structures or pathologic fracture, marsupialization could be alternative considered [26,29,31-33]. Conservative decompression could also be a reasonable option in pediatric patients with intent to allow for the eruption of the involved tooth [34].

Eruption Cyst

Eruption cyst is a soft tissue variation of a follicular cyst, associated with the dental follicle of an erupting tooth (mainly primary and only occasionally permanent tooth) [1] (Figure 2). It is typically appears as a smooth-surface, translucent, bluish – purple, fluctuant swelling localized on the alveolar ridge, just over the crown of an erupting tooth (Figure 9). The characteristic bluish color is attributed to blood accumulation (eruption haematoma). No treatment is usually necessary, as the majority of the eruption cysts burst spontaneously; rarely, a simple incision or marsupialization is required to facilitate the eruption of the involved tooth [8].

Figure 9: Eruption cyst [65].

Gingival Cyst of Infants

These developmental odontogenic cysts are typically encountered in newborns and believed to originate from dental lamina rests [1]. They present as multiple, firm, small-size, white colored nodules on the edentulous maxillary or mandibular alveolar process [8,18] (Figure 10). No treatment is generally required, as they usually resolved spontaneously [31].

Figure 10: Gingival cysts of infants [66].

Epstein's pearls and Bohn's nodules are rare variations of neonatal inclusion cysts, that typically encountered in the midline or on the lateral side of the palate, respectively [8,18.31].

Gingival Cyst of the Adults

Gingival cysts of adults are very rare soft tissue encounters of the developmental lateral periodontal cysts (0.3% of all odontogenic cysts) [1,35]. They originate from remnants of dental lamina (rests of Serres) and appear as well-defined cystic nodules located typically on the attached gingiva [8,18,31,35] (Figure 2).

Lateral Periodontal Cyst

Lateral periodontal cysts **(LPC)** are rare odontogenic lesions derived from dental lamina rests retained in the periodontal ligament space [1]. They are typically located lateral to the root of a vital tooth (95% between mandibular premolars and canines) [8,31] (Figure 2 and Figure 11). Lateral periodontal cyst is a distinct pathologic entity that should clearly differentiated from lateral radicular or primordial odontogenic cysts [1]. Enucleation with or without bone graft restoration is the recommended therapeutic approach [36].

Figure 11: Lateral periodontal cyst [67].

The botryoid odontogenic cyst is a polycystic variation of the lateral periodontal cyst [31,37] (Figure 12).

Figure 12: Botryoid odontogenic cyst [68].

Calcifying Odontogenic Cyst

The Calcifying Odontogenic Cyst **(COC)** or Gorlin's cyst [38] is relative rare (10% of all cases) [39] developmental odontogenic cyst with potentially aggressive biologic behavior [18]. COCs that show neoplastic potential and an infiltrative growth pattern are described as "Calcifying Cystic Odontogenic Tumors" **(CCOT)** or "odontogenic ghost cell tumor" (OGCT, WHO classification, 2005) [1,18,40-42]. In young patients COCs are often encoundered in association with odontomas or impacted teeth, while the more aggressive variants are more common in elderly patients [8]. Coexistence with recognized odontogenic tumor (adenomatoid odontogenic tumor or ameloblastoma) has also been occasionally reported [42,43]. Clinically, they are usually present as a unilocular well-defined radiolucency with irregular, scattered, dystrophic calcifications, predominantly located in the anterior jaws [44-46] (Figure 13); however, up to 20% of cases may also have an extraosseous manifestation [8,42]. Histologically the presence of the so called "ghost cells" (enlarged epithelial cells with eosinophilic cytoplasm but without other cytoplasmic structures or nucleus) is diagnostically helpful but pathognomonic [42,47-49].

Enucleation and curettage is generally adequate for a benign entity. More aggressive therapeutic approach is generally recommended for the neoplastic variants [8,31]. Recurrence may occasionally occur.

Glandular Odontogenic Cyst

Glandular Odontogenic Cyst (**GOC**, sialo-odontogenic cyst) is an uncommon (1.3%) and recently described cystic lesion of the jaws, that also shows histological evidences of gradual or salivary origin [1,8,18,31,50]. It is characterized by locally aggressive behavior and high propensity to recur (up to 30% of cases) [51-53]. They are typically presented as either unilocular or multilocular lesion of the anterior mandible with a tendency to cross the midline [41,54,55]. The differential diagnosis from a central mucoepidermoid carcinoma may be quite challenging without immunohistochemistry-staining methods [28,56]. Despite some authors recommend resection [51], enucleation and curettage is the most widely accepted therapeutic approach [8,52].

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