

Glandular Odontogenic Cyst: A Challenge in Diagnosis

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Abstract

Glandular odontogenic cyst is a quite rare developmental cyst seen in the jaw area. Clinically, it is most commonly seen in mandibular anterior. Its prevalence is higher in middle aged and old males. In general, it is radiologically observed as a regular bordered uniloculated or multiloculated radiolucent lesion. It is important due to high post-treatment recurrence rate and wide distinctive diagnosis range. Our two cases diagnosed with Glandular odontogenic cyst were presented together with distinctive diagnoses in the light of literature.

Keywords: Glandular • Odontogenic • Cysts

Introduction

Cysts are fluid filled sacs forming in different areas of the body. Cysts with epithelium-covered surfaces are mostly observed in the jaws among the bones in human body. Odontogenic cysts form through the differentiation of odontogenic epithelial residues inside the jaw. Jaw cysts are formed by oral ectodermal structures, mainly oral mucosa epithelium and odontogenic epithelium [1]. Many studies were made on odontogenic cyst classification. World Health Organization (WHO) re-classified odontogenic cysts in 2017 containing glandular structures; glandular odontogenic cysts (GOC) are rarer among developmental jaw cysts.

GOCs were first defined as sialodontogenic cyst [2] as this basis was not provable in this cystic formation claimed to be based on salivary gland, it was defined as Glandular odontogenic cyst [3]. It was first covered in the classification by World Health Organization in 1992 [4] and preserved its place in the last WHO 2017 classification [5]. Its clinical and histopathological significance is high due to its high recurrence rate, aggressive course and wide distinctive diagnosis range [6,7]. Histopathological distinctive diagnosis is important due to its histopathological similarity with mucous metaplasia presenting radicular cyst and dentigerous cyst, lateral periodontal cyst and central low degree mucoepidermoid carcinoma [6-8]. Clinical, radiological and histopathological characteristics of two GOC cases were presented here.

Case Series

Case 1

A 59-year-old male patient referred to Süleyman Demirel University Dentistry Maxillofacial Surgery department with left mandibular posterior area swelling and drooling complaint present for a few months. He defined mild pain and intermittent bloody discharge. A regular bordered, uniloculated radiolucent lesion was radiologically observed in left mandibular posterior (Figure 1). Surgically excised lesion was sent to Süleyman Demirel University Medical Pathology Department. A tooth structure with macroscopic dimensions of 1.6 × 0.6 × 0.4 cm and a thin walled membrane resembling lesion with a diameter of 0.6 cm adjacent to this tooth were observed in the examination. The fluid in the cyst wasn't seen due to fragmented lesion. A cyst which was formed by

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small tissue fragments and had a surface covered by mucinous epithelium was observed in the microscopic examination. Atypia and atypical mitosis wasn't observed in cyst epithelium. Chronic inflammation, free haemorrhage areas and cholesterol clefts were observed on cyst wall (Figure 2). Staining was observed on goblet cells in the histochemical PAS-Alcian Blue performed for distinctive diagnosis (Figure 2). Intense positive immune reactivity stood out in the epithelium based on immunohistochemical CK19. Clinical evaluation of the radiological and histopathological findings showed that the case had Glandular Odontogenic Cyst.

Case 2

A 10-year-old male patient was admitted to Süleyman Demirel University Dentistry Faculty maxillofacial surgery department with swelling and pain complaint around the second molar tooth at maxilla right lateral area (tooth area no 15). The surgically excised lesion was sent to Süleyman Demirel University Faculty of Medicine Medical Pathology Department. A tissue piece with a bright external surface, membrane resembling appearance and dimensions of 1.5 ×

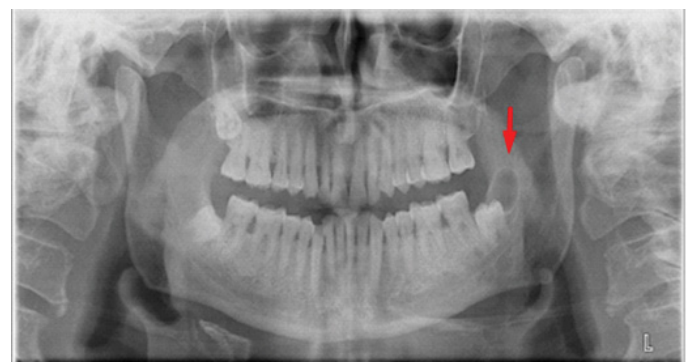


Figure 1. A sclerotic radiolucent lesion with regular borders on the teeth on mandibular left posterior.

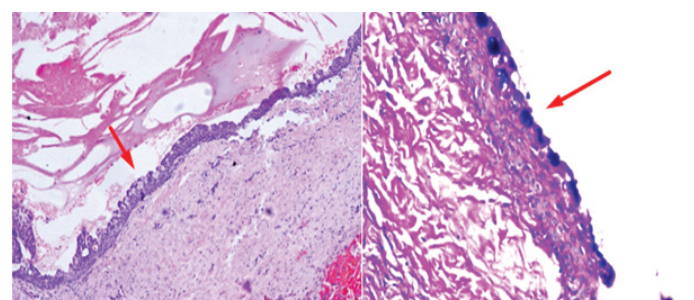


Figure 2. Cyst epithelium where mucinous epithelium covered goblet cells was also observed. Fibrinoid material was observed on cyst lumen. Chronic inflammation findings on cyst wall (10x H&E) Goblet cells (40x PAS-AB).

1.1 × 0.3 cm was observed in the macroscopic examination. A cyst covered by microscopic wall epithelium was observed. Pseudoglandular structures due to epithelial invagination on cyst wall were observed. Intensively activated chronic inflammation was present on the cyst wall (Figure 3). Positive staining was observed on walled epithelium and pseudoglandular structures with PAS-AB in the histochemical examination (Figure 3). Intensive positive immunoreactivity was observed on the epithelium with PanCK in the immunohistochemical examination. When the clinical and histopathological findings were evaluated together, the case was evaluated as glandular odontogenic cyst.

Discussion

Cysts with epithelium-covered surfaces are mostly observed in the jaws among the bones of the human body. Jaw cysts are formed by oral ectodermal structures, mainly oral mucosa epithelium and odontogenic epithelium. These asymptomatic cysts can be noticed as mass lesions felt in the mouth by the tongue as swelling. They may cause bad breath or tasting problems. Cysts located in jaw bones are odontogenic or non-odontogenic based on the originated epithelium. Some studies have been made for the classification of odontogenic cysts but there were conflicts on the real nature and etiopathogenesis of these lesions and this condition reflected on previous WHO classifications. GOC was first defined by Padayachee and Van Wiyk in 1987 [2]. It was first mentioned as sialodontogenic cyst but as the salivary gland basis of the lesion was proven, Glandular odontogenic cyst name was asserted by Gardner in 1988 [3].

World Health Organization (WHO) separated odontogenic cysts into two categories as developmental and inflammatory. Dentigerous cyst, Odontogenic keratocyst, Lateral periodontal (botryoid odontogenic cyst, Gingival cyst, Glandular odontogenic cyst, Calcified odontogenic cyst and Ortokeratinized odontogenic cyst are developmental ones while Radicular cyst is an inflammatory, collateral cyst. GOC is a rare developmental odontogenic cyst in the lower and upper jaw. Among all jaw cysts, its prevalence is between 0.012-1.3 [4]. GOC is generally seen in middle aged or old males. In line with literature, both of our cases were male. GOC is seen in middle or old ages. A Study examined 45 cases that were previously diagnosed with GOC [8]. The age range of 14 and 75 was examined in this study. Different from literature, one of our cases was aged 10. Although GOCs may occur in all areas of the jaws, they are more commonly reported in mandibular anterior area [9].

It was located in mandibular posterior in one of the cases and in maxilla lateral area in the other. This is another aspect of our cases different from literature. GOCs may emerge in very different types microscopically. These are intraepithelial microcysts, crypts, goblet cells, glandular and pseudoglandular structures, hobnail resembling cell extensions, papillary projections, basal and parabasal clear cytoplasmic cells [6,7]. Studies have prepared guidelines including histopathological co-criteria for GOC diagnosis. Major and minor criteria were formed in these guidelines. Presence of flat keratinized squamous epithelium, Microcysts and cords or focal luminal proliferations, Superficial cubic eosinophilic cells or hobnail cells, Intraepithelial mucus / goblet cells including / not including crypts covered by mucus producing cells, intraepithelial glandular microcystic or canal resembling/pseudoglandular structures constitute major criteria. Minor criteria are papillary proliferation, brush border cells, multicystic or multiluminal architecture, clear or vacuolized cells in basal or spinous layer.

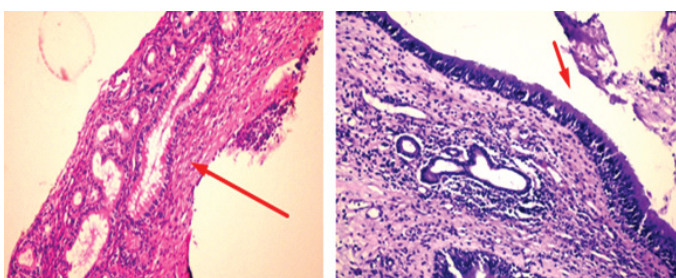


Figure 3. Mucinous glandular structures observed due to the cyst wall invagination of surface epithelium (20x H&E). Positive staining in favor of mucin in walled epithelium and glandular structures (20x PAS-AB)

Table 1. Head and neck - Differential diagnoses in surgical pathology 2016.

Variables	Glandular Odontogenic Cyst	Central Mucoepidermoid Carcinoma
Age	5-7. decade	4-6. decade
Location	Most commonly anterior mandibula	Most commonly posterior mandibula
Symptoms	Swelling and pain	Swelling, pain, paresthesia
Findings	Sclerotic bordered uniloculated/ multilocular radiolucent lesion	Irregular bordered uniloculated/ multilocular radiolucent lesion
Etiology	Unknown	Ectopic salivary gland tissue or previous odontogenic cyst
Histology	Mucinous cells, cuboidal cells, microcystic structures	Both solid and cystic structured
	No solid component.	Invasion on the cyst wall
	Focal proliferation in the epithelium.	
Private studies	No MAML2 rearrangement	MAML2 rearrangement
Treatment	Marginal resection due to recurrence risk	Marginal resection conservative treatment
Prognosis	Benign but has high recurrence rate (50%).	May present local recurrence, rare distant metastasis

The presence of at least one of the main criteria is compulsory based on these guidelines; presence of minor criteria supports the diagnosis [6].

The study reported that at least seven out of 10 histopathological characteristics are required for GOC diagnosis [5]. Presence of Intraepithelial microcysts, pseudoglandular structures, intraepithelial mucin, hobnail resembling cells, eosinophilic columnar cells, flat squamous epithelium, walled epithelium and papillary projections in our cases is in line with this study. Distinction from low grade mucoepidermoid carcinomas is important as GOCs present microscopic similarities. Since the lesion is not completely visible especially in small biopsies, glandular odontogenic cysts can cause difficulties in the distinctive diagnosis of glandular odontogenic cysts and mucoepidermoid carcinomas. Mucin-rich goblet cells and small glandular structures can be present in cyst epithelium. Small and cystic glandular structures can be present below the epithelium. Surface epithelium of GOC is formed by mucin including cells (Table 1).

Studies showed the increased expression of bcl-2 which an antiapoptotic protein is making us consider that the biological behaviour of GOC is related to the irregular cell death on surface epithelium. Many studies support that the offensive behaviour and recurrence tendency are due to the increased cell kinetic in the surface epithelium [10]. Dentigerous cyst, Odontogenic keratocyst, Lateral periodontal (botryoid odontogenic cyst, Gingival cyst, Glandular odontogenic cyst, Calcified odontogenic cyst and Ortokeratinized odontogenic cyst are developmental ones while Radicular cyst is an inflammatory, collateral cyst. Although GOC has specific histopathological characteristics, mucous metaplasia containing radicular and dentigerous cysts, lateral periodontal cyst botryoid cyst (polycystic lateral periodontal cyst) with similar histopathological characteristics should be considered in its distinctive diagnosis.

Most important of all, it should be distinguished from low grade mucoepidermoid carcinoma. It should be considered as the whole lesion is not visible especially in small biopsies. Neoplastic formation wasn't observed in cyst epithelium in both our cases: atypia and atypia mitosis wasn't observed in epithelium. High recurrence rate in GOCs can be explained probably by the separation tendency of multilocular structure and thin epithelium from the underlying bond tissue capsule and thus its removal during the operation gets more difficult. Conservative treatment method is another factor responsible for increased recurrence rate [6].

Glandular odontogenic cysts are clinically and radiologically similar to lateral periodontal cysts. It is defined as a radiolucent lesion with radiologically regular bordered or indented, uniloculated or multiloculated appearance. Our cases were similar with literature and were radiologically uniloculated. Also the radiological similarity to Odontogenic keratocyst constitutes diagnostic difficulties [6]. Thus the mutual evaluation of radiological, clinical and histopathological examinations is important for distinctive diagnosis.

Conclusion

GOCs are quite important for their rareness, distinctive diagnoses, aggressive courses and high recurrence rates. This lesion was misdiagnosed for years and it was observed that they were correctly diagnosed in case of recurrence. These cysts can be distinguished from other lesions if their clinical and radiological findings are known well. Together with clinical and radiological findings, histopathological examination is highly important for the diagnosis of the cysts. GOC cysts are most correctly diagnosed when evaluated together with clinical, radiological and histopathological findings. Correct examination of these lesions, determination of the criteria to provide histopathologically correct diagnosis in GOCs, choosing the radical surgical approach to lower recurrence rate and necessity of postoperative long-term follow-up constitute the characteristics of this cyst which should be known.

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