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Carrera de Odontología

“QUISTE ODONTOGÉNICO GLANDULAR: REPORTE DE CASO Y REVISIÓN DE LA LITERATURA”

Trabajo de titulación previo a la obtención del título de Odontólogo


Autores:

Arianna Nicolle Espinoza Ganchozo

Gabriela Fabiana Andrade Bravo

Director:

Diego Mauricio Bravo Calderón

ORCID:  0000-0003-1813-8051

Cuenca, Ecuador

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Resumen

El quiste odontogénico glandular (QOG) es una entidad patológica que se desarrolla con mayor frecuencia en la región anterior de la mandíbula y que puede mimetizar otras lesiones incluyendo otros quistes, tumores odontogénicos y hasta lesiones malignas de origen glandular. Por lo tanto, el objetivo del presente manuscrito es reportar un nuevo caso de QOG tratado de forma conservadora y discutir sus aspectos clínicos, imagenológicos, anatomopatológicos y terapéuticos.

Palabras clave: quiste sialodontogénico, quiste odontogénico, odontogénico, quiste mandibular



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Abstract

The glandular odontogenic cyst (GOC) is a pathological entity that most commonly develops in the anterior region of the mandible and can emulate other lesions, including other cysts, odontogenic tumors, and even malignant lesions of glandular origin. Therefore, the aim of this manuscript is to report a new case of GOC treated conservatively and discuss its clinical, radiological, histopathological, and therapeutic aspects.

Keywords: Sialo-odontogenic cyst, odontogenic cyst, cyst, odontogenic, jaw cyst



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Introduction

The glandular odontogenic cyst (GOC), also known as sialo-odontogenic cyst or mucoepidermoid odontogenic cyst, was extensively described by Padayachee and Van Wyk in 1987. According to the 2022 World Health Organization classification, it is defined as "a developmental cyst where the epithelial lining resembles glandular tissue" (WHO 2022; Padayachee y Van Wyk, 1987; Sadeghi *et al.*, 1991).

The GOC is a rare entity, and as such, it is seldom included in the differential diagnosis of other radiolucent lesions affecting the jaws (WHO, 2022). Therefore, understanding its clinical, radiographic, and pathological characteristics contributes to distinguishing it from more common pathologies, including other odontogenic cysts and/or tumors. Thus, the purpose of this manuscript is to report a case of GOC and provide a narrative review of the literature on this lesion.

Case report

A 67-year-old male patient presented to a private consultation with the complaint of a volume increase in the lower right region of his face, with an approximate duration of two and a half years. During the intraoral clinical examination, the following findings were noted in the region: gums with a color similar to the adjacent mucosa, teeth with slight mobility, and crepitation of the vestibular cortical bone upon palpation. The lesion was asymptomatic and, radiographically, it appeared as a multilocular radiolucency extending from the right mandibular angle to the left mandibular body; distal to tooth 3.3 (Fig. 1). The established diagnostic hypotheses included odontogenic cyst, conventional ameloblastoma, and odontogenic myxoma.

The patient was instructed about possible treatments and expressed a preference for a conservative management, regardless of the definitive diagnosis. Consequently, the removal of the lesion was performed under general anesthesia, involving curettage with adjunctive cryotherapy applied at the level of the bone margins (Fig. 2). The obtained material was sent for histopathological analysis. Macroscopically, fragments of soft tissue were observed, containing cavities filled with serous, translucent, and slightly viscous fluid (Fig. 3). As shown in Figure 4, microscopic analysis revealed various cystic cavities mostly lined by epithelium ranging from stratified squamous to cuboidal, resembling the reduced enamel organ epithelium. In some regions of the epithelial lining, columnar-shaped superficial cells, cilia presence, papillary projections towards lumina, intraepithelial microcysts, clear cells, and some

epithelial plaques were noted. Additionally, the cavity content consisted of eosinophilic mucoid material, and the connective tissue lining exposed a moderately focal mononuclear inflammatory infiltrate and some trabecular bone fragments. Based on clinical, radiographic, and histopathological characteristics, the definitive diagnosis of glandular odontogenic cyst was established. Currently, the patient is under clinical and imaging follow-up, and no recurrence has been detected after a period of three years and six months (Fig. 5)

Materials and methods

This literature review was based on the analysis of observational studies and clinical case reports retrieved from the PubMed, Google Scholar, Scielo, and Latindex databases spanning from 1987 to 2023. The search utilized the following terms: sialo-odontogenic cyst, glandular cyst, odontogenic cyst, jaw cyst, and odontogenic lesion.

Discussion

The term "sialo-odontogenic cyst" was coined by Gardner in 1984 and adopted by Padayachee and Van Wyk in 1987 to describe cystic lesions exhibiting histopathological characteristics of both botryoid odontogenic cyst and mucoepidermoid tumor (Gardner *et al.*, 1988; Padayachee & Van Wyk, 1987). Subsequently, in 1991, lesions with these characteristics were termed mucoepidermoid odontogenic cysts by Sadeghi *et al.* due to the entity being composed of both mucin-producing cells and epidermoid cells. Additionally, in 1988, Gardner reported another eight similar cases and designated them as glandular odontogenic cysts (Gardner *et al.*, 1988; Sadeghi *et al.*, 1991). Of all the proposed names, the World Health Organization (WHO) in its 2022 classification recommends the terminology "glandular odontogenic cyst," discarding the prefix "sialo" because the histogenesis related to salivary glands has not been proven, and the histological characteristics suggest an odontogenic origin, specifically arising from cellular remnants of the dental lamina (WHO, 2022).

The GOC typically develops in the mandible, most frequently in the anterior region, with no gender predilection. It can occur in patients of different age groups, although a higher incidence has been observed in adults between the fifth and seventh decades of life (Grossman *et al.*, 2007; WHO 2022). The present case aligns with these epidemiological characteristics. However, due to the extent of the lesion and the absence of previous images, it cannot be definitively confirmed or this missed that it originated in the anterior region of the mandible.

Regarding the most common clinical and radiographic features, the lesion typically presents as

a painless augmentation. Radiographically, it appears as a well-defined and scalloped uni- or multilocular radiolucent lesion that can lead to the expansion and perforation of the cortical bone, displacement and root resorption of adjacent teeth. Additionally, due to its considerable size, it may extend beyond the midline (WHO et al., 2017; Kaplan *et al.*, 2005; Kaplan *et al.*, 2008). This cyst exhibits variable dimensions unrelated to the gender or the age of the patients. Reported lesions range from small, measuring 0.5 cm, to larger ones up to 12 cm (Ficarra *et al.*, 1990; Kaplan *et al.*, 2008; Poudel *et al.*, 2020).

With regard to the cystic content, fine needle puncture has shown the presence of a waxy or watery liquid, transparent and of low viscosity, which may occasionally have a reddish-brown appearance, presumably due to the presence of blood associated with the previous surgical procedure or secondary inflammation (Koppang *et al.*, 1998; Shah *et al.*, 2016). In fact, cytological analysis of this material is suggested in order to distinguish it from the contents of other cystic lesions such as the parakeratin of the odontogenic keratocyst (Lo Muzio *et al.*, 2005). Interestingly, this aspect of cystic content was also verified during the macroscopic analysis of the present lesion, however, it is emphasized that although it is a feature that can guide diagnostic impressions, the definitive diagnosis is ultimately made on the basis of microscopic features.

Referring to the histological diversity of QOG, in 2017 the WHO in the fourth edition of the Classification of Tumours of the Head and Neck: Odontogenic and Maxillofacial Tumours; indicated that to make a confident diagnosis of QOG at least seven of the following ten specific histopathological criteria must be observed: (1) variable thickness of the lining epithelium, ranging from 2-3 layers of flattened squamous or cuboidal cells to thicker regions with a stratified squamous epithelium, and (2) a luminal layer of low cuboidal or columnar cells, sometimes called hobnail cells, which are present at least focally, (3) intraepithelial microcysts, (4) apocrine metaplasia of luminal cells, (5) clear cells in the basal and parabasal layers, (6) papillary projections in the lumina, (7) mucous cells, (8) epithelial plaques or spheres similar to those seen in the lateral periodontal cyst, which are frequently identified; (9) cilia, which are occasionally seen; and (10) multiple cystic compartments. The first two criteria are considered key as they are present in all lesions (WHO *et al.*, 2017).

Subsequently, in the fifth edition of the aforementioned classification published in 2022, the WHO states that the only feature observed in all cases is the presence of low columnar or cuboidal cells (hobnail) on the luminal surface of the epithelium (WHO, 2022). The other features are not present in all cases; however, observing a higher number of these features allows for a more confident diagnosis of GOC (WHO 2022). For these reasons, the WHO

currently indicates that essential and desirable criteria exist for the diagnosis of GOC, as described in Table I.

Regarding the differential diagnosis, GOC microscopically resembles lateral periodontal cyst (LPC), botryoid odontogenic cyst (BOC), and low-grade central mucoepidermoid carcinoma (CME) (Bravo-Calderón et al., 2012; Ferreira et al., 2019; López et al., 2009; Senthilmurugan et al., 2021).

Specifically, LPC is a developmental odontogenic cyst lined by a thin non-keratinized epithelium, also exhibiting focal epithelial thickenings and glycogen-rich epithelial cells, similar to those observed in GOC. BOC is the multilocular and polycystic variant of LPC (WHO, 2022). However, most LPC and BOC are smaller than 1 cm, while GOC tends to have larger dimensions. Histologically, ciliated cells and spaces resembling ducts with mucous cells are identified in the epithelial lining of GOC (Koppang et al., 1998; de Sousa, et al., 1997; WHO, 2022).

The most important microscopic differential diagnosis is with low-grade mucoepidermoid Carcinoma (MEC) since this malignant neoplasm exhibits various cystic structures lined by an epithelium of variable thickness, primarily composed of mucous cells and, to a lesser extent, epidermoid and intermediate cells (Kaplan et al., 2008). However, the epidermoid component of MEC typically shows exophytic growth towards the periphery of cystic spaces, not as epithelial plaques or whorls protruding into the lumen, which is characteristic of GOC (Kaplan et al., 2008; Senthilmughan et al., 2021). Additionally, microscopic visualization of "hobnail" or eosinophilic cuboidal cells on the surface of the cystic lining and intraepithelial microcysts also supports the diagnosis of GOC (Kaplan et al., 2008).

Various molecules have been evaluated as potential biomarkers for the differential diagnosis between GOC and MEC. For example, the immunohistochemical expression of cytokeratin 19 (CK19) has been widely confirmed in the epithelial lining of GOC (de Souza et al., 1997; Mascitti et al., 2014; Pires et al., 2004; Sembra et al., 1994; Shen et al., 2006). However, there are no substantial differences in the expression of this protein in central MEC, as demonstrated by Pires et al. in 2004, who observed that 50% of central MECs also express CK19 (Pires et al., 2004).

Another studied molecule is the cell proliferation marker Ki67, whose immunoreactivity was confirmed in both lesions. However, it was significantly higher in GOC than in low-grade central MEC, which is consistent with the indolent biological behavior of the neoplasm (Kaplan et al., 2005). Similarly, in the epithelial component of both lesions, the immunohistochemical staining of MASPIN (mammary serine protease inhibitor) was also confirmed, with differences

in expression in mucous cells. Mucous cells were widely positive in central MEC, while only a small proportion of them were immunoreactive in GOC (Vered et al., 2010).

Interestingly, MAML2 genetic rearrangements have been considered the primary molecular tool for differential diagnosis. Fluorescence in situ hybridization (FISH) analyses demonstrated that central MECs are positive for these rearrangements in both solid and cystic areas, while GOCs were negative (Bishop et al., 2014). However, more recently, MAML2 rearrangements have also been found in recurrent lesions histologically meeting GOC criteria. This raises the possibility that some central MECs may develop from GOC, particularly those with aggressive and recurrent biological behavior (Greer et al., 2017). These heterogeneous findings underscore the need for further studies on MAML2 rearrangements, especially comparing large series of lesions.

The recurrence potential of GOC has been linked to the clinical and biological characteristics of the lesion and the type of treatment employed (Kaplan et al., 2005; Urs et al., 2017). Specifically, recurrence of GOC has been more frequently observed in cysts with a multilocular appearance, thinning or perforation of cortical bone, and in lesions considered large, occupying an area of bone larger than the space occupied by two teeth (Kaplan et al., 2005).

Regarding the treatment of GOC, various methods have been proposed, ranging from a conservative management to segmental resection. It is suggested that therapeutic planning take into consideration the characteristics of extension, multilocularity, and involvement of bone cortical (Ficarra et al., 1990; Kaplan et al., 2005; Shen et al., 200; Urs et al., 2017). In particular, Kaplan et al. in 2005 found that treatment with minor procedures such as enucleation alone or curettage is associated with a high risk of recurrence, especially in large and multilocular lesions. The risk is significantly reduced with major surgical procedures such as peripheral osteotomy or marginal resection (Kaplan et al., 2005).

Furthermore, other therapeutic options such as marsupialization, the use of Carnoy's solution, and cryotherapy as adjuvants in the treatment of the bone cavity have been proposed. However, the small number of cases treated with these modalities makes it difficult to obtain conclusive evidence about their effectiveness in reducing the risk of disease recurrence (Ficarra et al., 1990; Kaplan et al., 2005; Urs et al., 2017). Particularly, according to the characteristics of the present case, the patient underwent treatment by resection of the affected bone segment with safety margins. However, the patient's personal decision was for a more conservative method, so curettage with adjuvant cryotherapy was performed. As of now, no recurrence has been observed, only periodontal involvement of the adjoining

premolars, which are under treatment and strict follow-up. Additionally, regardless of the method used for lesion removal, it is recommended to follow up for a minimum of three years and preferably up to seven years (Kaplan et al., 2008).

Conclusion

In conclusion, the glandular odontogenic cyst (GOC) is a cystic odontogenic lesion that, despite being rare, deserves consideration in the differential diagnosis of maxillary radiolucent lesions with a high potential for growth and recurrence. It should be accurately differentiated from low-grade MEC (Mucoepidermoid Carcinoma) based on its histopathological characteristics. Preferably, treatment should involve aggressive procedures such as peripheral osteotomy or marginal resection, especially in cases of large multilocular lesions with thinning or perforation of the bone corticals.

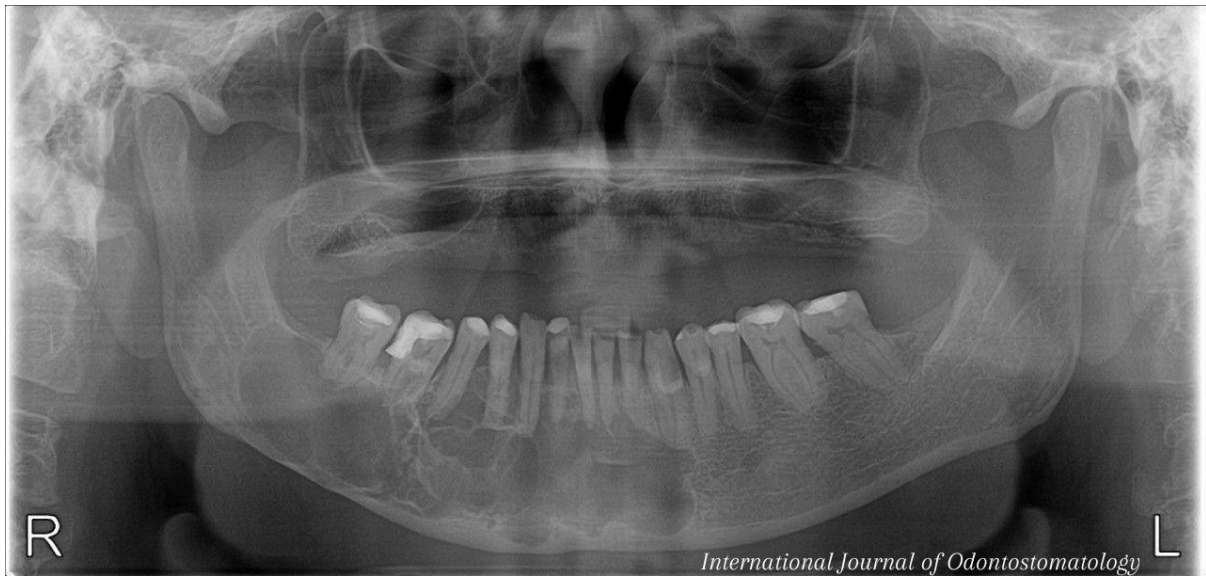


Figure 1.

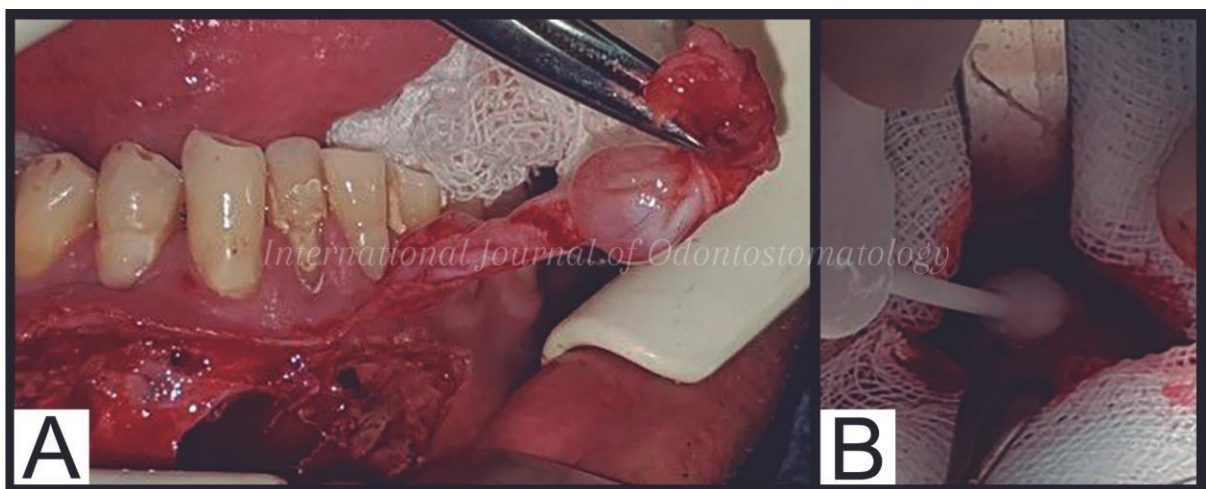


Figure 2



Figure 3

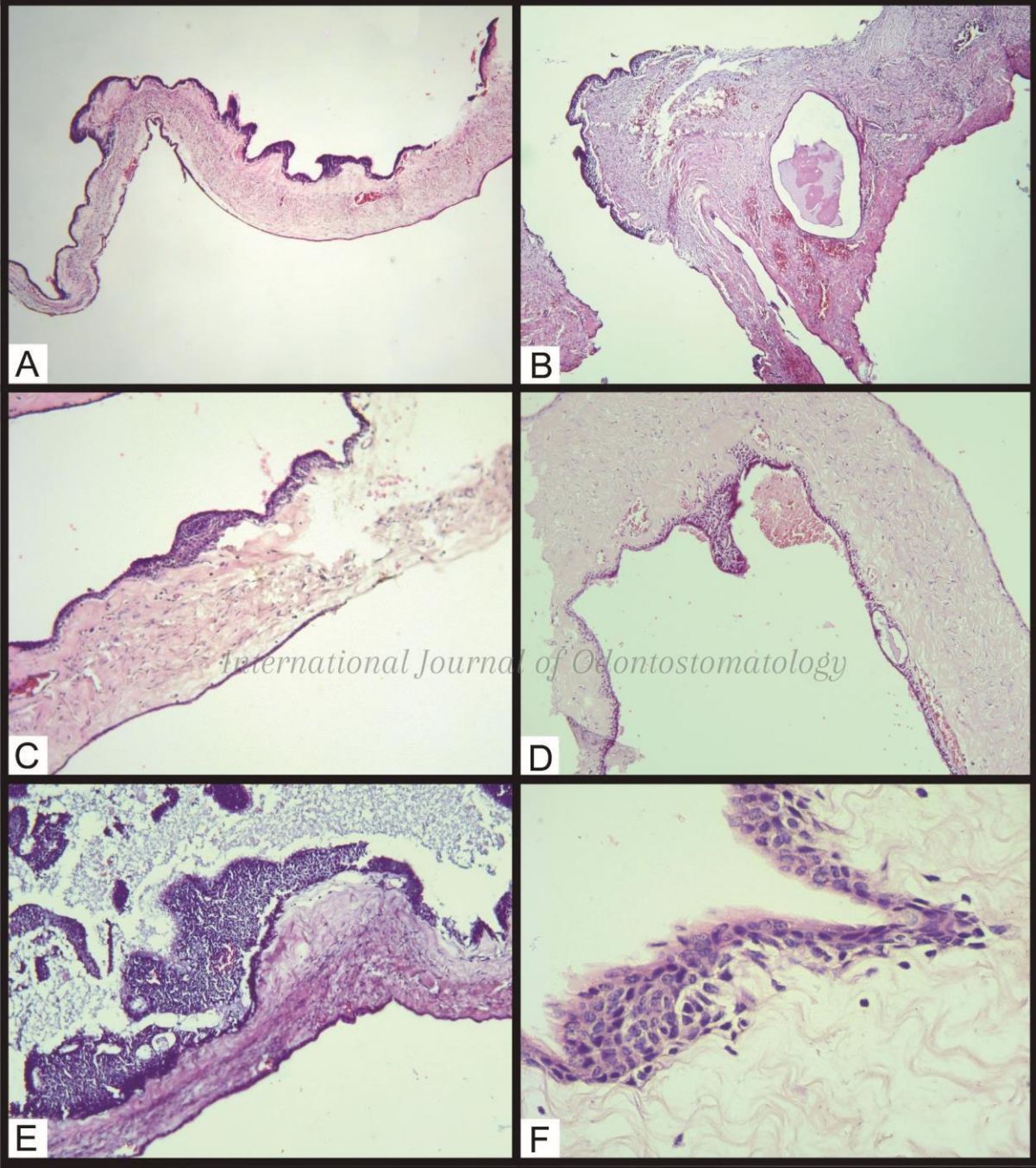


Figure 4



Figure 5

Table I. Criteria for the anatomopathological diagnosis of odontogenic glandular cyst, according to the 2022 Classification of Tumours of the Head and Neck: Odontogenic and Maxillofacial Tumours (OMS, 2022).

Essential and desirable diagnostic criteria of QOG	
Essentials	Desirable
Radiolucent cystic lesion of tooth-bearing area of the jaw. Often multilocular.	Lining of variable thickness with epithelial thickenings, plaques or papillary projections. Luminal columnar or cuboidal ("hobnail") cells Microcysts or duct-like structures Mucous or clear cells

Referencias

- Bishop, J.; Yonescu, R.; Batista, D.; Warnock, G. & Westra, W. Glandular odontogenic cysts (GOCs) lack MAML2 rearrangements: a finding to discredit the putative nature of GOC as a precursor to central mucoepidermoid carcinoma. *Head Neck Pathol*, 8(3):287-90, 2014.
- Bravo-Calderón, D.; Oliveira, D. & Martins, W. Bilateral osteoporotic bone marrow defects of the mandible: a case report. *Head Face Med.*, 8:22, 2012.
- De Sousa S.; Cabezas, N.; de Oliveira, P. & de Araújo, V. Glandular odontogenic cyst: report of a case with cytokeratin expression. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.*, 83(4):478-83, 1997.
- Ferreira, J.; Vêncio, E.; de Sá, R. & Gasperini, G. Glandular Odontogenic Cyst in Dentigerous Relationship: An Uncommon Case Report. *Case Rep Dent.*, 158-67., 2019.
- Ficarra, G.; Chou, L. & Panzoni, E. Glandular odontogenic cyst (sialo- odontogenic cyst). A case report. *Int. J. Oral Maxillofac. Surg.*, 19: 331-33, 1990.
- Gardner, D.; Kessler, H.; Morency, R. & Schaffner D. The glandular odontogenic cyst: an apparent entity. *Int. J Oral Pathol.*, 17(8): 359-66., 1988.
- Greer, R.; Eskendri, J.; Freedman, P.; Ahmadian, M.; Murakami-Walter, A. & Varella-Garcia, M. Assessment of biologically aggressive, recurrent glandular odontogenic cysts for mastermind-like 2 (MAML2) rearrangements: histopathologic and fluorescent in situ hybridization (FISH) findings in 11 cases. *J Oral Pathol Med.*, 47(2):192-197, 2018.
- Grossmann, S.; Machado, V.; Xavier, G.; Moura, M.; Gomez, R.; Aguiar, M., et al. Demographic profile of odontogenic and selected nonodontogenic cysts in a Brazilian population. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.*, 104(6): e35-41, 2007.
- Kaplan, I.; Anavi, Y. & Hirshberg, A. Glandular odontogenic cyst: a challenge in diagnosis and treatment. *Oral Dis.*, 14(7):575-81. 2008.
- Kaplan, I.; Anavi, Y.; Manor, R.; Sulkes, J. & Calderon, S. The use of molecular markers as an aid in the diagnosis of glandular odontogenic cyst. *Oral Oncol.*, 41(9):895-902, 2005.
- Kaplan, I.; Gal, G.; Anavi, Y.; Manor, R. & Calderon, S. Glandular odontogenic cyst: treatment and recurrence. *Int. J Oral Maxillofac Surg.*, 63(4):435-41, 2005.
- Koppang, H.; Johannessen, S.; Haugen, L.; Haanaes, H.; Solheim, T. & Donath, K. Glandular odontogenic cyst (sialo-odontogenic cyst): report of two cases and literature review of 45 previously reported cases. *J Oral Pathol Med.*, 27(9):455-62, 1998.

Lo Muzio, L.; Santarelli, A.; Caltabiano, R.; Rubini, C.; Pieramici, T.; Fior, A.; Trevisiol, L.; Carinci, F.; Leonardi, R.; Bufo, P.; Lanzafame, S. & Piattelli, A. p63 expression in odontogenic cysts. *International Journal of Oral and Maxillofacial Surgery*, 34(6): 668-673, 2005.

López, D.; Infante, P.; Acosta, M.; Hernández, J.; García, P.; García, A. & Gutiérrez, J. Quiste odontogénico glandular: diagnóstico diferencial y manejo de lesiones quísticas maxilares. *Rev Esp Cirug Oral y Maxilofac.*, 31(1): 57-62, 2009.

Mascitti, M.; Santarelli, A.; Sabatucci, A.; Procaccini, M.; Lo Muzio, L.; Zizzi, A., et al. Glandular odontogenic cyst: review of literature and report of a new case with cytokeratin-19 expression. *Open Dent J.*, 8:1-12, .2014.

Padayachee A & Van Wyk C. Two eystie lesions with features of both the botryoid odontogenic cyst and the central irruoepidermoid tumour: sialodontogenic cyst. *J Oral Pathol*, 16:499-04, 1987.

Pires, F.; Chen, S.; da Cruz, D.; de Almeida, O. & Kowalski, L. Cytokeratin expression in central mucoepidermoid carcinoma and glandular odontogenic cyst. *Oral Oncol.*, 40(5):545-51, 2004.

Poudel, P.; Srii, R.; Chaurasia N. & Upadhyaya, C. Glandular odontogenic cyst- Report of a rare case. *Clin Case Rep.*, 8(2):351-54, 2020.

Sadeghi, E.; Weldon, L.; Kwon, P. & Sampson, E. Mucoepidermoid odontogenic cyst. *J. Oral Maxillofac. Surg.* 20: 142-43, 1991.

Semba, I.; Kitano, M.; Mimura, T.; Sonoda, S. & Miyawaki, A. Glandular odontogenic cyst: analysis of eytokeratin expression and clinieopathological features. *J Oral Pathol Med.*, 23: 377-82, 1994.

Senthilmurugan, M.; Periasamy, S.; Kumar, S., et al. Quiste odontogénico glandular: Un dilema de diagnóstico y manejo. *Cureus*, 13(12): e207-01, 2021.

Shah, A.; Sangle, A.; Bussari, S. & Koshy, A. Glandular odontogenic cyst: A diagnostic dilemma. *Indian J Dent.*, 7(1):38-43, 2016.

Shen, J.; Fan, M.; Chen, X.; Wang, S.; Wang, L. & Li, Y. Glandular odontogenic cyst in China: report of 12 cases and immunohistochemical study. *J Oral Pathol Med.*, 35(3):175-82, 2006.

Urs, A.; Kumar, P.; Augustine, J. & Malhotra, R. Glandular odontogenic cyst: Series of five cases. *J Oral Maxillofac Pathol*, 21:239-43, 2017.

[Vered, M.; Allon, I.; Buchner, A. & Dayan, D. Is maspin immunolocalization a tool to](#)

differentiate central low-grade mucoepidermoid carcinoma from glandular odontogenic cyst?
Acta Histochem., 112(2):161-8, 2010.

WHO. Classification of Head and Neck Tumours Editorial Board. 4th ed. Lyon (France), International Agency of Research on Cancer, 2017.

WHO. Classification of Head and Neck Tumours Editorial Board. 5th ed. Lyon (France): International Agency for Research on Cancer, 2022.