

Glandular Odontogenic Cyst and Low-Grade Central Mucoepidermoid Carcinoma – A Report on 2 Cases and their Comparison

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ABSTRACT

Background: Glandular Odontogenic cyst (GOC) is an uncommon developmental cyst of the jaws of odontogenic origin which presents with overlapping histopathological features of Central Mucoepidermoid Carcinoma of low grade (LGCMEC), a rare and well-known salivary neoplasm developing within the jaw bones. Herein, 2 cases - GOC and LGCMEC are reported and their clinical, radiographical and histopathological features are compared since their treatment differ.

Case Presentation: A 52-year-old male patient with a cystic lesion in the mandibular anterior region with pain was given a diagnosis of GOC after radiographic and surgical intervention. Later, a 39-year-old female patient with an ulcero-proliferative intraoral lesion in left retromolar region with minimal cortical expansion and palpable ipsilateral submandibular lymph node was confirmed as a case of CMEC - LG with minimal atypia. Special stains demonstrated intracellular mucin in both the cases.

Management and Prognosis: The GOC was surgically enucleated and peripheral osteotomy with chemical cauterization was done whereas the LGCMEC case underwent segmental mandibulectomy along with neck dissection and surgical reconstruction.

Conclusion: The overlapping microscopic features of glandular epithelium with mucous cells in GOC and LGCMEC can make the diagnosis difficult in the absence of special stains and immunomarkers.

Keywords: Central Mucoepidermoid Carcinoma; Glandular Odontogenic Cyst; Low-grade MEC; MAML2 gene rearrangements.

INTRODUCTION

The odontogenic and salivary gland epithelia share a common origin, namely, the epithelium of the stomatodeum which develops as a thickening during weeks 5 to 6 of gestation.¹ In spite of the development into entirely different organs namely the tooth and the salivary glands, the neoplastic cells arising from both odontogenic and salivary gland epithelia can display common cytomorphological features, such as basaloid, columnar-to-cuboidal cells with palisading appearance, clear cells, and epithelial-mucous secreting cells.²

Mucoepidermoid carcinoma (MEC) was initially described as an entity by Steward et al (1945) and it constitutes 5–10% of all salivary gland tumors. Mucin-producing cells, epithelial cells, and intermediate cells are the three main cell types that define it histologically.³ Lepp (1939) was the first to report an intraosseous mucoepidermoid carcinoma located in the mandible of a 66-year-old woman.⁴ Glandular Odontogenic cyst (GOC) belongs to developmental cyst group with odontogenic origin and it was reported in the literature as Sialo-odontogenic cyst in 1987 by Padayachee and VanWyk. The name GOC was coined by Gardner in 1988. It was accepted as a separate entity by WHO since 1992.⁵ Central Low Grade MEC (LGCMEC) of the jawbones shares histological characteristics with GOC and is structurally identical to its salivary gland counterpart. The two cases

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presented here, and their diagnostic approach were a challenge for the pathologist because of their overlapping histopathological features.

Case 1: Glandular Odontogenic Cyst

In June 2018, a 52-year-old male patient reported to our Outpatient Department with the chief complaint of a swelling in lower front tooth region since past 1 year. Diffuse, dull, continuous aching pain was reportedly aggravated by mastication and relieved by medications. There was history of pus discharge in relation to the lower anterior teeth since

past 1 month but with no history of trauma or any relevant dental history. Clinical extra-oral examination revealed a diffuse swelling in the chin, bony hard on palpation with no rise of local temperature and a maximum mouth opening of 41 mm. Right and left submandibular lymph nodes were palpable, soft, mobile but non-tender. Intra-oral examination revealed generalized stains and calculus with missing 16,17,26. Other hard tissue findings were fractured 11,21 (Incisal edge), discoloured 31,41 and attrited 31,32,41,42,43. Pulp vitality tests revealed non-vital 44,43,42, 41,31,32 and 33.

Radiographic examination (Orthopantomogram - OPG) showed a well-defined, unilocular lesion extending from 34 till 45 (Figure 1.1). Intentional RCTs were done in relation to 44,43,42,41,31,32,33. The lesion was subjected to surgical enucleation with peripheral osteotomy and chemical cauterization, and the specimen was sent for histopathological examination. Microscopically, the tissue specimen revealed a cyst wall with epithelial lining of variable thickness and tufting or papillary projections into its lumen (Figure 1.2). The presence of "Hobnail cells" which are surface eosinophilic cells and it's pinching off into the cyst lumen, multiple intraepithelial microcysts lined by numerous mucous goblet cells and presence of epithelial spheres or plaque-like thickenings led to the confirmatory diagnosis of GOC (Figure 1.3) (Table 2). The intra-epithelial mucous cells were confirmed using special stains like PAS, Mucicarmine and Alcian Blue.

Case 2: Low Grade Central Mucoepidermoid Carcinoma of the Mandible

In November 2019, a 39-year-old female patient reported to our Outpatient Department with a chief complaint of sensitivity and pain in left lower back tooth region since past 1 month associated with difficulty in opening her mouth. There was no history of any discharge intraorally from that region or any fever or any significant medical history. Her dental history revealed extraction in the site of chief complaint 12 years ago. Clinical extra-oral examination revealed lower 1/3rd of left mandible showing a mild, diffuse swelling over ramus region approximately with mild facial asymmetry; ill-defined, non-tender and soft in consistency on palpation. Left submandibular, upper jugular lymph nodes and right submandibular lymph nodes were palpable, soft, and tender. Intra-orally, an ulcero-proliferative growth of 3.6 x 3.5 cm, friable to touch was seen in the left retromolar area (Figure 2.1). Adjacent 37 was tender on percussion, 38 clinically missing. Buccal cortical plate expansion of left posterior mandible was evident. Trismus was present with mouth opening of 19 mm (~2 finger breadth).

OPG revealed 2 large, well-defined radiolucencies with extensions from the distal root apices of 37 anteriorly and almost entire left ramus except 10 mm from its posterior border, sparing condylar, coronoid process and angle of left



Fig. 1.1: Preoperative OPG showed well-defined unilocular lesion extending from 34 till 45

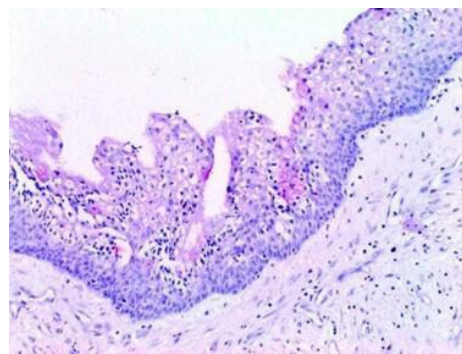


Fig. 1.2. Haematoxylin and Eosin 10X showing epithelial papillary projections or "Tufting" into the cystic lumen.

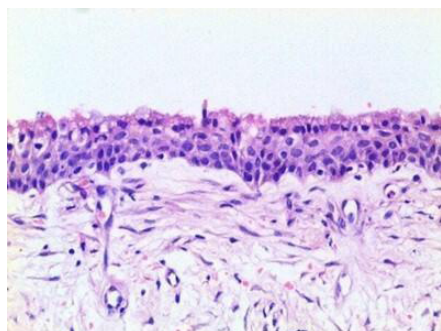


Fig. 1.3: Haematoxylin and Eosin 20X showing thin epithelium with surface eosinophilic cuboidal "Hob-nail cells"

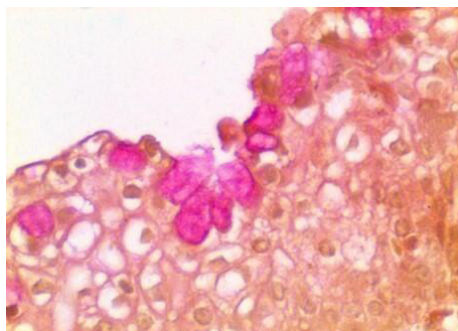


Fig. 1.4: Mucicarmine-positive goblet or mucous cells – 40x

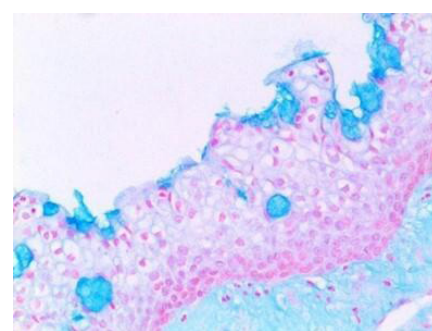


Fig. 1.5: Alcian Blue-positive goblet or mucous cells–20x

mandible with no sclerotic rim or calcifications seen. Plain (Figure 2.2) and contrast-enhanced Computed Tomographic axial images - CE-CT Head and Neck revealed soft tissue mass in left retromolar trigone, multiple sites of bony erosion on left body of mandible extending up to outer surface and extension of lesion into soft tissue of left cheek with few enlarged lymph nodes at left submandibular, upper jugular and right submandibular regions.

MANAGEMENT AND PROGNOSIS

Incisional biopsy of the lesion showed microscopically, sheets of neoplastic tissue composed predominantly of cystic spaces and an epidermoid component (in nests and Strands) in a fibrous stroma; The cystic spaces were lined by mucous secreting cells with vacuolated cytoplasm and oval nuclei, and the mucous cells were PAS, Mucicarmin and Alcian Blue positive. Few cells of intermediate type were seen. The epidermoid cells showed pleomorphism with increased Nucleus-Cytoplasmic ratio. Thus, the histopathological impression of mucoepidermoid carcinoma was given. The patient was then operated under general anesthesia for segmental resection of left posterior mandible and Supra-omohyoid Modified Neck Dissection (SOMND) with reconstruction using recon plate and screws. Intraoperative frozen sections of resected mandible margins were negative for tumor. The resected lymph nodes were positive for metastatic

deposits and the excisional biopsy showed the confirmatory of mucoepidermoid carcinoma. The grading was given as low since there was a predominant cystic component, minimal cellular atypia and a relatively high proportion of mucous cells as compared to epidermoid cells and intermediate cells (Figure 2.3).

CLINICAL IMPLICATIONS

Accounting for 0.012–1.3% of all jaw cysts, GOC is a rare developmental odontogenic cyst with an aggressive behaviour, larger size and probability of recurrence. Currently, WHO (2017, 4th Ed. Odontogenic Lesions) mentioned that a minimum seven out of 10 microscopic criteria needed to be present to confirm it. The 5th edition of the same (WHO, 2022) made no changes to its diagnostic criteria except in that the varying thickness of lining epithelium was considered as an essential criterion and presence of “Hob nail cells” were considered the most characteristic feature present in almost all cases.⁶ Some literature suggested that GOC and CMEC of the jaws might be a spectrum of one disease.

The 52-year-old male patient who reported with anterior mandible swelling was treated with surgical enucleation, peripheral osteotomy and chemical cauterization using modified carnoy's solution.

The diagnosis of GOC is difficult because it shares histopathological similarities with other lesions such as lateral



Fig. 2.1: Intraoral ulcero-proliferative growth



Fig. 2.2: Preoperative Computed Tomographic Images – Axial plane reveals cortical bone erosion/perforation in relation to ramus of left mandible.

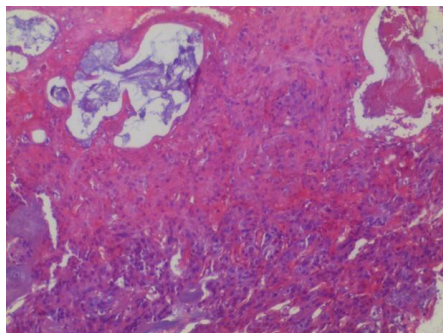


Fig. 2.3: Haematoxylin and Eosin sections –10x showing cystic spaces lined by mucous cells and epidermoid and intermediate cells.

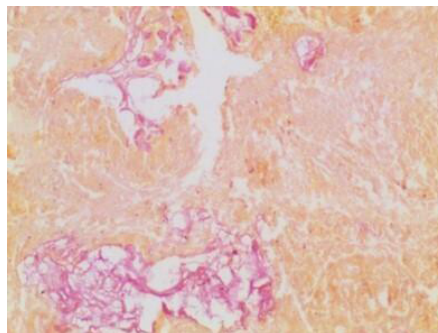


Fig. 2.4: Mucicarmin-positive mucous cells secreting into cystic spaces – 10x

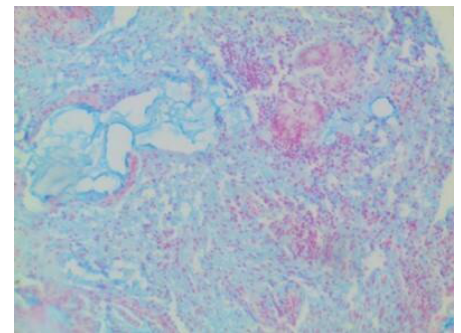


Fig. 2.5: Alcian Blue-positive mucous cells and mucin– 10x

Table 1: A comparison of clinical findings of the 2 cases

CASE1 -GOC	CASE2-LG-CMEC
M52, Anterior mandible crossing midline	F39, Posterior mandible ramus area
Radiographic features: Large unilocular radiolucency, osteosclerotic border	Large unilocular radiolucency, well-defined osteosclerotic border
Clinical findings: Slow-growing, painless, minimal cortical expansion	Large lesion with cortical expansion, pain
Differential Diagnosis: Odontogenic Keratocyst, Ameloblastoma, Central Giant cell granuloma, Botryoid Odontogenic cyst	Ameloblastoma, Oral Squamous Cell Carcinoma

periodontal cyst (LPC), botryoid odontogenic cysts (BOC), residual cysts with mucous metaplasia, and in particular low-grade mucoepidermoid cancer.⁷ GOC has an aggressive biological potential, a higher rate of cortical perforation, and a relatively high rate of recurrence, particularly in cases treated with conservative methods. Therefore, the correct diagnosis is vital for its management. Thin proliferative lining epithelium, multilocularity and the cell kinetics forming epithelial plaques and papillary projections were attributed to recurrence in GOC cases.⁵

The 39-year-old female patient with diffuse swelling in posterior mandible with perforation underwent incisional biopsy to reveal LG-CMEC. According to Brookestone and Huvos (1992)⁴ classification of central salivary gland tumors of maxilla and mandible, this case came under stage III disease with rupture of cortical plates or presence of regional metastasis (Table 3). Thus, the patient underwent segmental resection of posterior mandible with neck dissection surgery in which metastatic lymph nodes were also removed.

From histopathological findings with detectable intracellular

Table 2: Microscopic Features Of Glandular Odontogenic Cyst (GOC)

WHO 2017: 4 th Edition (Opondo et al) ⁹	Microscopic Criteria (Kaplan et al) ⁸	Fowler's Parameters ⁸
Features that must be present in all cases:	Major and Minor Criteria	
Variable thickness of epithelium lining the cyst; 2-3 cell layers of squamous or cuboidal cells to thick stratified squamous epithelium	Non-keratinized squamous epithelial lining with flat interface (Major)	Variable thickness of epithelial lining
A luminal layer of cuboidal to low columnar cells ("Hobnail Cells") present at least focally	Epithelial lining exhibits surface cuboidal cells or "Hobnail Cells" (Major)	Eosinophilic cuboidal cells ("Hobnail Cells")
Features present in most cases:		
Intra-epithelial microcysts	Intra-epithelial glandular, microcystic or duct-like (Pseudo-glandular) structures (Major)	Microcysts
Apocrine metaplasia of luminal cells		Apocrine "snouting"
Clear cells in basal and parabasal layers	Clear or vacuolated cells in basal or spinous layers (Minor)	Clear or vacuolated cells
Papillary projections ("Tufting") into the lumen	Papillary proliferations (Minor)	"Tufting" or Papillary Projections
Mucous cells	Mucous/goblet cells with intra-epithelial mucus pools with or without crypts lined by mucous producing cells (Major)	Mucous cells
Other additional microscopic features:		
Epithelial spheres similar to those seen in LPCs (Lateral Periodontal Cysts)	Presence of Spherules/Knobs or whorls or focal luminal proliferations (Major)	Epithelial Spheres
Presence of cilia	Ciliated cells (Minor)	Cilia
Multiple Cystic Compartments	Multi-cystic or multi-luminal architecture (Minor)	Multiple Compartments

WHO 2022: 5th Edition (John M. Wright and Soluk-Tekkesin)⁶:

At least 7 out of 10 criteria for microscopic features; Essential Criterion: Lining epithelium with varying thickness, Presence of "Hobnail Cells" in almost all cases as the most characteristic feature.



Table 3: Brookestone and Huvos 1992 - Clinical Staging of Central Salivary Gland Tumor including Central Mucoepidermoid Carcinoma⁴

Stages	Condition of overlying bone
Stage I	Without bony expansion and rupture of cortical plate
Stage II	Rupture of cortical plate with bony expansion
Stage III	Rupture of cortical plate or nodal involvement

Table 4: GOC and LGCMEC - Pointers to diagnosis

GOC	LGCMEC
Unilocular cystic space with thin lining	Multiple small cystic spaces
Histopathology: presence of swirling spherical aggregates or epithelial plaques	3 types of cells–Epidermoid, Mucous, Intermediate
Absence of cellular atypia	Cellular atypia
CK19 strong positive in all layers (odontogenic origin), Ki67– higher expression, p63 (5-50% basal and parabasal epithelial cells) ¹⁰ , CK13(Maruyama et al. 2021) ¹²	MUC4β (surrogate marker for LGMEC), ^{11, 13} p63 ^{10,13} (strong diffuse nuclear positivity in intermediate, squamous, and clear cells while mucous cells were negative) and MMP-2(Matrixmetalloproteinase-2) (P.R. Sawant et al. 2019) ¹³ , MASPIN (Mammary Serine protease inhibitor) ^{2,10} and Molecular/MAML2 (Mastermind-like) gene rearrangements (through Fluorescent in situ Hybridisation - FISH) ¹⁵
Special stains: Mucicarmine, Periodic Acid Schiff (PAS) stain, Alcian Blue-positive	Mucicarmine, Periodic Acid Schiff (PAS)Stain, Alcian Blue-positive

mucin (Mucicarmine and Alcian blue positive), the diagnosis was confirmed as Central MEC of Lower-grade according to Katabi grading system (2020)¹⁴ of qualitative assessment with predominant cystic architecture, lower mitoses or atypia, and a high number of mucous cells. MECs including the central ones were tumors with variable grading and a low tumor grade was generally associated with better prognosis¹⁵. Post operative period was uneventful with adequate healing and the patient is kept under regular follow-up till date.

Traditionally, GOC showed predilection in adult males in anterior mandible and CMEC (LG) in females in the posterior mandible, as in our cases. Clinically and radiographically, both lesions shared features as in Table 1.

Microscopic criteria by Kaplan (2005)⁸, Fowler (2011)⁸, WHO (2017)⁹ and WHO (2022)⁶ were applied for histopathological diagnosis and comparison (Table 2). Special stains – Mucicarmine, Alcian Blue and Periodic Acid Schiff (PAS) stains were used to demonstrate mucous cells. The ready availability of special stains made them useful in diagnosis.

In literature, the different immunomarkers of GOCs and LGMECs indicate that both are two different entities and may not represent spectrum of same pathology (Table 4). Studies have stated that MECs including intraosseous type harbour mastermind-like 2 (MAML2) gene rearrangements

characterized by translocation at t (11;19) (q2; p13) and gene fusion¹⁶.

Due to the aggressive biologic behaviour and propensity for recurrence in GOC, marginal resection with peripheral osteotomy and long-term follow-up (till 10 years) was considered. Surgical management of CMEC included segmental resection with neck dissection since it had metastasized to regional lymph nodes.

CONCLUSION

Differentiation between LGCMEC and GOC bears both treatment and prognostic implications. Both are rare intra-osseous lesions of the jaw and their histopathology confirms their diagnosis. In the advent of numerous immunomarkers to distinguish them, special stains still hold their value in diagnosis.

REFERENCES

1. Ten Cate AR, Nanci A. Structure of the oral tissues. Oral Histology-Development, Structure, and Function.2003;5:1-9.
2. 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 histochemica.2010 Mar 1;112(2):161-8.
3. Khataniar H, Senthil S, Deep SS, Ramesh R, Y K I. Intraosseous Mucoepidermoid Carcinoma of the Anterior Mandible: A Case



- Report.Cureus.2022May16;14(5): e25036.
4. Singh H, Yadav AK, Chand S, Singh A, Shukla B. Central mucoepidermoid carcinoma: Case report with review of literature. *National Journal of Maxillofacial Surgery*. 2019Jan;10(1):109.
 5. Shah AA, Sangle A, Bussari S, Koshy AV. Glandular odontogenic cyst: A diagnostic dilemma. *Indian Journal of Dentistry*. 2016 Jan;7(1):38.
 6. Soluk Tekkesin M, Wright JM. The World Health Organization Classification of Odontogenic Lesions: A Summary of the Changes of the 2022 (5th) Edition. *TurkPatolojiDerg*.2022;38(2):168-184. doi:10.5146/tjpath.2022.01573. PMID:35578902; PMCID: PMC9999699.
 7. Poudel P, Srii R, Chaurasia N, Upadhyaya C. Glandular odontogenic cyst—Report of a rare case. *Clinical case reports*. 2020 Feb;8(2):351-4.
 8. Vichare SN, Natarajan S, Baviskar PS, Ahuja SA, Vathare PP. Glandular odontogenic cyst mimickers: A review and report of two cases. *J Mahatma Gandhi Inst Med Sci*2021; 26:124-8.
 9. Opondo F, Shaik S, Opperman J, Nortjé CJ. Glandular odontogenic cyst: case series and summary of the literature. *South African Dental Journal*. 2019Oct;74(9):502-7
 10. Mascitti M, Santarelli A, Sabatucci A, Procaccini M, Lo Muzio L, Zizzi A, Rubini C. Glandular odontogenic cyst: review of literature and report of a new case with cytokeratin-19 expression. *Open Dent J*. 2014 Feb 7; 8: 1-12. doi:10.2174/1874210601408010001. PMID: 24624237; PMCID: PMC3950754.
 11. Namboodiripad PC. A review: Immunological markers for malignant salivary gland tumors. *J Oral Biol Craniofac Res*.2014 May-Aug; 4(2): 127-34. doi:10.1016/j.jobcr.2014.05.003. Epub 2014 Aug 28. PMID: 25737930; PMCID: PMC4252643.
 12. Maruyama S, Mori T, Yamazaki M, Abé T, Ryo E, Kano H, Hasegawa G, Tanuma JI. Central mucoepidermoid carcinoma arising directly from a glandular odontogenic cyst of the mandible: a case report. *DiagnosticPathology*. 2021Dec; 16:1-7.
 13. Sawant PR, Spadigam A, Dhupar A, Syed S, Carvalho K. Assessing the prognostic significance of MUC4β in mucoepidermoid carcinoma of the salivary glands: An immunohistochemical study. *Heliyon*.2019Nov 14; 5(11): e02753. doi:10.1016/j.heliyon.2019.e02753. PMID: 31844699; PMCID: PMC6895766.
 14. Folpe, A.L.; Dei Tos, A.P.; Pedetour, F.; Marino-Enriquez, A. Dedifferentiated Liposarcoma. In *WHO Classification of Tumours; Soft Tissue and Bone Tumours; WHO Classification of Tumours Editorial Board, Ed.; IARC: Lyon, France, 2022*.
 15. Nishida H, Kusaba T, Kawamura K, Oyama Y, Daa T. Histopathological Aspects of the Prognostic Factors for Salivary Gland Cancers. *Cancers* [Internet]. 2023 Feb 15;15(4):1236. Available from: <http://dx.doi.org/10.3390/cancers15041236>
 16. Greer RO, Eskendri J, Freedman P, Ahmadian M, Murakami-Walter A, Varela-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*.2018Feb;47(2): 192-197. doi:10.1111/jop.12658. Epub 2017 Nov 27. PMID: 29121421; PMCID: PMC6157737.