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Cytokeratins in Glandular Odontogenic Cyst – An Immunohistochemical Study of 4 Cases

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ABSTRACT:
Introduction: Glandular odontogenic cyst (GOC) is a relatively rare cystic lesion of the jaws, which poses a diagnostic challenge as well as a challenge in treatment. This study was conducted to evaluate the expression of cytokeratins in GOC and also to evaluate if cytokeratins be used as a diagnostic tool for GOC?
Materials and Methods: 4 cases were taken from archives of Department of Oral & Maxillofacial Pathology which were diagnosed as GOC histopathologically & Immunohistochemistry was done with 5 markers for each of 4 cases that are CK 7, CK 13, CK 14, CK 19 and CK8/18.
Results: The microscopic features which aid in its differentiation included presence of variable thickness of the lining epithelium, epithelial plaques and whorls, hobnail cells, ciliated cells, clear cells and goblet cells. Immunohistochemistry showed that epithelium of GOCs stained for CK 7, CK 13, CK 14, CK 19 with slight changes in their patterns, and no reaction to and CK8/18
Conclusion: Although GOC is relatively rare, correct diagnosis is of major clinical importance, since GOC has an aggressive potential, a high incidence of cortical perforation & a relatively high rate of recurrence, especially in cases treated with a conservative approach is observed.
Key words: cytokeratin, Glandular odontogenic cyst, Immunohistochemistry,

INTRODUCTION:

Glandular odontogenic cyst is defined as "a cyst arising in the tooth bearing areas of the jaws and is characterized by an epithelial lining with cuboidal or columnar cells, both at the surface and lining, with crypts or cystlike spaces within the thickness of the epithelium."[1]
Glandular Odontogenic cyst is an uncommon cystic lesion arising in tooth bearing areas of jaws. In 1987 it was documented as "Sialo-odontogenic Cyst" by Padayachee A and Van Wyk CW.[2] In 1988 it was termed as "glandular odontogenic cyst" by Gardener DG et al since its histological features are highly suggestive of an odontogenic origin.[3,4]
GOC generally occurs in males over 40 years of age with a predilection for the anterior region of the mandible. Radiographically, it presents as either a unilocular or multilocular well-defined radiolucent lesion. The clinical and radiographic features are nonspecific, and it can mimic any other destructive lesion of the jaw.[5]
A total of 20 different cytokeratins have so far been identified in human tissues. In epithelial cells cytokeratrin expression patterns differ according to cell type, developmental stage, differentiation status, anatomical site and degree of complexity, and have been regarded as a

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useful tool in identifying different epithelial types and origins.[6]
The present study was done to evaluate the expression of cytokeratins in GOC and also to evaluate if cytokeratins can be used as a diagnostic tool for GOC?

MATERIALS & METHODS: 4 cases were taken from archives of Department of Oral & Maxillofacial Pathology which were diagnosed as GOC histopathologically & Immunohistochemistry done. The cases were retrieved with complete relevant clinical, radiographic and histopathological data. Clinical features such as age, sex, site of lesion and presenting features were analyzed. The GOC cases were diagnosed based on the classic criteria described by Gardner DG et al[3] and WHO[7] regarding histologic typing of odontogenic cysts and tumors. All tissue specimens were fixed in 10% neutral buffered formalin (18–48 h) and routinely processed and embedded in paraffin, including decalcification in 25% formic acid for 48–72 h if necessary. Histopathologic diagnosis was confirmed by two experiential pathologists on hematoxylin and eosin-stained section for each case, and periodic-acid Schiff (PAS) and Alcian Blue-stained slides were also used. Immunostaining for CK 7, CK 13, CK 14, CK 19 and CK8/18 was performed using a standard biotinstreptavidin immunoperoxidase technique on paraffin sections.
Tissue sections of oral mucosal epithelium and salivary gland were stained as positive controls.
Immunohistochemical reactivity for CKs was detected in the cytoplasm of the epithelial cells of GOC. Cytokeratin (CK) immunostaining was semi quantitatively analyzed in the epithelial lining of the cysts as: **+ = Weakly Positive**, **++ =moderately Positive**, **+++ = strongly Positive** and - = **Negative**

RESULTS:

Table 1: **Clinical and radiographic details of the cases**

CASES	**AGE**	**SEX**	**LOCATION**	**R/F**
Case 1	24 yrs	Male	Mandibular anterior region	Unilocular
Case 2	55 yrs	Female	Extending from 11 to18	Unilocular
Case 3	19 yrs	Female	Extending from 12 to 16	Unilocular
Case 4	32 yrs	Male	Extending from 31 to 36	Unilocular

Table 2: Cytokeratin (CK) immunostaining

CASES	**CK 7**	**CK 13**	**CK 14**	**CK 19**	**CK 8/18**
Case 1	+++	+++	+++	++	_
Case 2	++	+++	+++	+++	_
Case 3	+++	+++	++	+++	_
Case 4	++	+++	++	+++	_

Table 3: Histopathologic features:

	Squamous epithelial lining with flat interface	Intraluminal papillary projections	Epithelial plaques	Hobnail cells	Goblet cells	Micro cysts	Ciliated Cells	Clear cells
Case 1	Present	Present	Present	Present	Present	Present	Absent	Present
Case 2	Present	Absent	Present	Present	Present	Absent	Present	Present
Case 3	Present	Present	Present	Absent	Present	Absent	Present	Present

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Case 4	Present	Present	Present	Present	Present	Present	Absent	Present

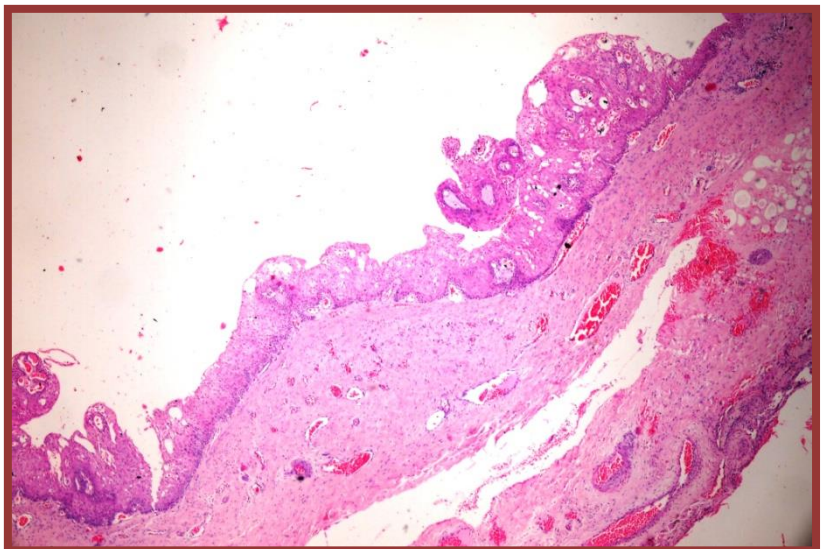

Figure 1 H&E staining showing GOC

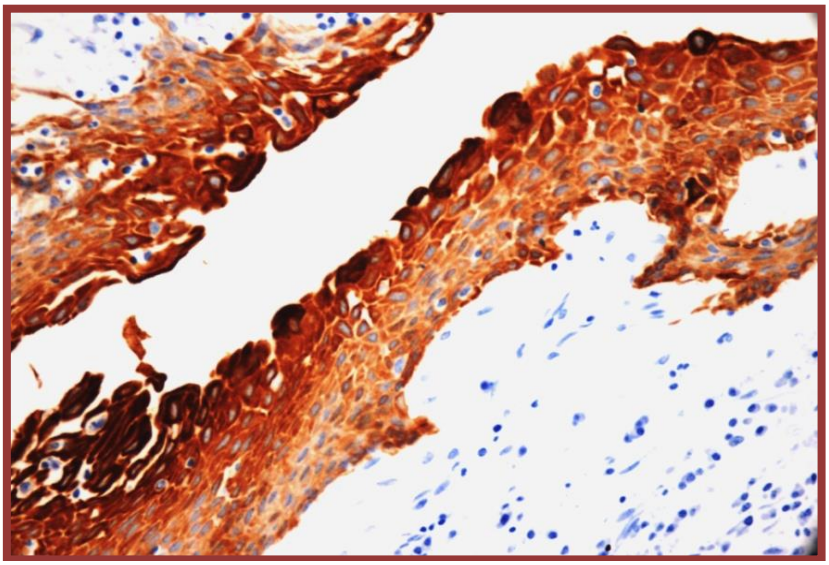

Figure 2 Immunohistochemical staining in GOC

Discussion: GOC is an uncommon developmental cyst with a frequency of 0.012%–1.3% of all the jaw cysts and its prevalence is 0.17%.[8] The current case series is a step further to correlate CK expression with origin of GOC and if cytokeratins can be used as a diagnostic tool for GOC?

According to de Sousa SO et al[9], GOC express CKs7, 13, 14 & 19 but not CKs 8 & 18. Negative CK 8 & 18 differentiates GOC from Low grade Mucoepidermoid Carcinoma.

In present study, CK 7 is moderately to strongly positive all cases. This shows that CK 7 can be used as a specific marker for knowing odontogenic origin. It is especially expressed in cells of HERS & Stellate Reticulum and can be found in several simple epithelia or occasional basal/ suprabasal cells of stratified epithelium.[10]

In present study, CK 13 is strongly positive in all cases indicating odontogenic origin of GOC. CK 13 is predominantly present in Dental Lamina and is Restricted to suprabasal layers of squamous stratified epithelium. It is also found positive in epithelial islands with metaplastic squamous cells, some inner stellate cells & flattened cells lining cystic

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structures.[11]

In this study, CK 14 is moderately to strongly positive indicating odontogenic epithelium. It is the main intermediate filament of Odontogenic epithelium and observed in Dental Lamina, in Reduced Enamel Epithelium & in almost all cells of Enamel Organ. It is expressed intensely positive in basal cell layer & plaque like areas, less intensely in suprabasal layer of cystic epithelium.[12]

In this study, CK 19 is showing positive results in all cases of GOCs. This supports Odontogenic origin of GOC. Its Positive detection in preameloblasts & secretory ameloblasts shows its association with secretory differentiation and can be used as a marker of odontogenic differentiation.**[11]**

In present study, CK 8/18 shows negative results. This supports odontogenic origin & differentiates GOCs from Mucoepidermoid Carcinoma. CK 8/18 is Not seen in epithelia of Odontogenic Neoplasms. It is Positive in Salivary gland tumors and helps to differentiate odontogenic epithelium from Salivary glands.[13]

According to Pires FB et al all GOCs expressed CK 5, CK 7, CK 8, CK 13, CK 14 & CK 19. All Odontogenic cysts expressed CK 5, CK 13 & CK 14. 91% also expressed CK 19. Only 7% of Odontogenic lesions expressed CK 18, which was expressed by all Mucoepidermoid Carcinomas of Central & Salivary gland types.

Histopathologically, it may prove to be a diagnostic dilemma due to its close resemblance to lateral periodontal cyst, Botryoid odontogenic cyst, dentigerous cyst and most importantly Central mucoepidermoid carcinoma. It is mandatory to differentiate GOC from the much more aggressive lesions like Central mucoepidermoid carcinoma, and we recommend the use of CK 7, CK 13, CK 14 and CK 19 antibody to establish odontogenic origin when in doubt.

Conclusion: Although GOC is relatively rare, correct diagnosis is of major clinical importance, since GOC has an aggressive potential, a high incidence of cortical perforation & a relatively high rate of recurrence, especially in cases treated with a conservative approach is observed.

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