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Insights Of Dentinogenic Ghost Cell Tumor -A Complete Review

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ABSTRACT : The Calcifying Odontogenic Cyst (COC), Dentinogenic Ghost Cell Tumors (DGCT), Ghost Cell Odontogenic Carcinoma (GCOC) represents a group of odontogenic ghost cell lesions of the jaw.The Calcifying Odontogenic Cyst (COC) was first described by Gorlin and his collegues.Two organizing principles of classification of COC's are Monoistic and Dualistic concept.Based on the dualistic concept the current WHO classification termed Calcifying Odontogenic Cyst for the cystic variant and Dentinogenic Ghost Cell Tumor for the neoplastic entity.The presence of ghost cells and dentinoid formation is the most characteristic feature of the dentinogenic ghost cell tumor. Recurrent DGCT have shown to exhibit malignant characteristics that has been diagnosed as Ghost Cell Odontogenic Carcinoma (GCOC)

KEYWORDS: Calcifying Odontogenic Cyst (COC), Monoistic and Dualistic concept, Dentinogenic Ghost Cell Tumors (DGCT), Ghost cells, Ghost Cell Odontogenic Carcinoma (GCOC)

INTRODUCTION:

Odontogenic Tumors are lesions derived from epithelial, ectomesenchymal or both the elements that have been part of the tooth forming apparatus [1,2,3]. **Odontogenic cysts** are the most common type of cysts occurring within the jaws. They arise as a result of proliferation and cystic degeneration of odontogenic epithetlial rests [1,4].

The WHO (2022) classification of odontogenic tumors and cysts of the jaws: [5]

ODONTOGENIC TUMORS:

Benign Epithelial Odontogenic Tumor:

Adenomatoid Odontogenic Tumor

Squamous Odontogenic Tumor

Calcifying Epithelial Odontogenic Tumor

Ameloblastoma- Unicystic

Ameloblastoma- Extraosseous / Peripheral

Ameloblastoma- Conventional

Adenoid Ameloblastoma

Metastasizing Ameloblastoma

Benign Mixed Epithelial and Mesenchymal Odontogenic Tumors:

Odontoma

Primordial Odontogenic Tumor

Ameloblastic Fibroma

Dentinigenic Ghost Cell Tumor

Benign Mesenchymal Odontogenic Tumors:

Odontogenic Fibroma

Cementoblastoma

Cemento – Ossifying Fibroma

Odontogenic Myxoma

Malignant Odontogenic Tumors:

Sclerosing Odontogenic Carcinoma

Ameloblastic Carcinoma

Clear Cell Odontogenic Carcinoma

Ghost Cell Odontogenic Carcinoma

Primary Intraosseous Carcinoma

Odontogenic Carcinosarcoma

Odontogenic Sarcomas

CYSTS OF THE JAWS:

Radicular Cyst

Inflammatory Collateral Cysts

Surgical Ciliated Cyst

Nasopalatine Duct Cyst

Gingival Cyst

Dentigerous Cyst

Orthokeratinized Odontogenic Cyst

Lateral Periodontal Cyst

Botryoid Odontogenic Cyst

Calcifying Odontogenic Cyst

Glandular Odontogenic Cyst

Odontogenic Keratocyst

HISTORY AND CLASSIFICATION :

The Calcifying Odontogenic Cyst (COC), Dentinogenic Ghost Cell Tumors (DGCT), Ghost Cell Odontogenic Carcinoma (GCOC) represents a group of odontogenic ghost cell lesions of the jaw.[6,7]

The Calcifying Odontogenic Cyst (COC) was first described by Gorlin and his colleagues in 1962 as a entity of odontogenic origin.[8,9] He was the first person to describe Calcifying Ghost Cell Odontogenic Cyst (CGCOC) under the term Calcifying Odontogenic Cyst[10,11,12,13]as the cystic variant comprises majority of CGCOC (85%) The term COC has been most predominantly used and it still conquers in some literature.[10,14,15]

Two organizing principles of classification of COC's have been put forward : **Monoistic** and **Dualistic** Concept.[8,13] The **monoistic** concept, best exemplified by the World Health Organization classification[16] postulates that all COC's are neoplastic in nature, even though the majority are cystic in architecture and appear to be non-neoplastic. In contrast the **dualistic** concept favoured by most of the researchers[17,18,19] proposes that COC's contain two different entities, a cyst and a neoplasm. The cystic lesion are termed as "**Calcifying Cystic Odontogenic Tumor**" and the neoplastic entity as "**Dentinogenic Ghost Cell Tumor**"[8,9]

Based on the dualistic concept the current WHO classification termed Calcifying Odontogenic Cyst for the cystic variant and Dentinogenic Ghost Cell Tumor for the neoplastic entity.[20]

The benign or the cystic form is most frequently seen (80%-98%).The neoplastic or the solid mass variant contributes for about 11.5% of the cases.[20,21]

In 1991, Buchner classified COC majorly on clinical grounds namely- Peripheral COC and Central COC, further subclassifying each of them into cystic and neoplastic variants and he further included the rare malignant counterpart of COC in the classification.[10,13]

TYPE	DESCRIPTION
A	PERIPHERAL
	• CYSTIC
	• NEOPLASTIC
B	CENTRAL
	• CYSTIC
	1. Associated with Odontoma
	2. Associated with Odontogenic Tumors
	3. Clear Cell or Pigmented Variant
	• NEOPLASTIC
	• MALIGNANT

CLINICAL CLASSIFICATION OF CALCIFYING ODONTOGENIC CYST :

The **Central** or **intraosseous** lesions frequently exhibit an asymptomatic, expansile bony hard jaw swelling. The **Peripheral** or **extraosseous** lesions manifests as an asymptomatic, well defined smooth surface nodular mass of size of 0.5 -3.0 cm on the alveolar mucosa or gingiva.[20,22,23,24]

DENTINOGENIC GHOST CELL TUMOR :

The WHO panel of experts on Odontogenic Tumors has defined DGCT as **"locally invasive neoplasm characterized by ameloblastoma like islands of epithelial cells in a mature connective tissue stroma with aberrant Keratinization which may be found in the form of ghost cells in association with varying amounts of dysplastic dentin"[25,26]**

CLINICAL TYPES :

It is an extremely rare odontogenic tumor and exits both as a central and a peripheral type.

The Peripheral or the extraosseous lesions exhibit limited growth potential and usually occurs in Sixth decade of life, with an average age range of 10-92 years whereas the Central or the intraosseous lesions are locally invasive and age ranges from 12 to 75 years of age with the peak incidence in Fourth decade of life.[6,27]

ETIOLOGY AND CLINICAL FEATURES :

The etiology of this lesion is still unknown , but it has been suggested that the missense mutation in the beta catenin in the wingless integrated pathways plays a crucial role in the development.[25,28]

Extraosseous lesions appear as firm, painless nodules on gingival or alveolar mucosa with a preference for anterior locations whereas intraosseous lesions manifest as painless bone swelling in canine to first molar region with distinct facial symmetry due to expansion of the jaw and occasionally accompanied by pus discharge, tooth displacement or mobility.[6,29,30,31]

The lesions are predominantly seen in males with equal distribution between maxilla and mandible.[6,19]

RADIOGRAPHIC FEATURES :

DGCT appears as radiolucent, radiopaque or mixed lesion depending on the amount of calcifications. It can occur in a multilocular or unilocular manner, with either well-defined or poorly-defined edges.The presence of impacted teeth, displacement or root resorption of adjacent teeth has been reported in some cases.[6,32] Occlusal radiographs shows a bicortical expansion.[8,33,34]

HISTOPATHOLOGIC FEATURES :

Histopathologically, both the intraosseous and extraosseous variants of DGCT are characterized by the presence of sheets and islands of odontogenic epithelium with ameloblastic differentiation that occasionally undergoes cystic degeneration in a mature connective tissue stroma.Few cells namely Ghost cells are scattered among the odontogenic epithelium.[6]

Thoma and Goldman in 1946 coined the term "**Ghost Cells**".[25]

Swollen ellipsoidal keratinized epithelial cells that have lost their nuclei, leaving only a faint imprint of the original nucleus, are the appearance of these ghost cells.[35,4]

They are known to have resistant to resorption and have the potential to calcify.They are presumed to be derived either from the transformation of epithelial cells, metaplastic transformation of odontogenic epithelium, squamous metaplasia with secondary calcification due to degeneration of epithelial cells, ischaemia or as a result of apoptotic process.[25,32]

Production of dysplastic dentin or dentinoid material which appears as amorphous masses of eosinophilic material containing widely separated cell bodies may be seen in association with the tumor of epithelium.[6,36] The rationale for the formation of dentinoid material has been considered to represent an inflammatory response of the body tissue towards masses of ghost cells or masses of ghost cells induce granulation tissue to lay down juxtaepithelial osteoid which may may calcify. On the contrary some researchers hypothesized that the formation of dentinoid might be an inductive phenomenon or a metaplastic change in the connective tissue.[6,37]

Praetorius et al suggested that the dentinoid material is of mesodermal origin based on the following findings:[25,26]

- Connective tissue stains like Van Gieson, Heidenhain, Goldner, and Masson will stain dentinoid.
- Luminal proliferations typically do not contain it unless the basement membrane disintegrates and connective tissue grows between epithelial ghost cells.

According to WHO the proportion of ghost cells (>1% -2%) and dentinoid is vital for the diagnosis of DGCT.[6,16]

TREATMENT :

The treatment for both the variants of DGCT are different due to the difference in their recurrence rate and malignant potential.[6,30]

The treatment most commonly recommended for peripheral DGCT is local excision and is not thought to recur. Central DGCT's are aggressive neoplasms that show locally invasive behavior and recurrence rates upto 71% and some recurrence cases are reported not only following local excisional enucleation but also 1-5 years after segmental mandibular resection and partial maxillectomy.[6,38]

MALIGNANT POTENTIAL :

DGCT can either be benign or malignant depending on the histopathological features.[8,18,39] Recurrent DGCT have shown to exhibit malignant characteristics that has been diagnosed as **Ghost Cell Odontogenic Carcinoma (GCOC)** It is a particular rare malignant counterpart of DGCT. About 32.5% of GCOC are derived from DGCT or COC.[6,40]

The guidelines that are followed for the diagnosis of GCOC as well as to rule out DGCT includes : groups of ghost cells, necrosis, prominent mitosis, infiltrative growth pattern and aggressive behavior.[41]

IMMUNOHISTOCHEMISTRY OF GCOC :

The immunohistochemical analysis of GCOC's was first described by Scott and Wood proving the epithelial origin by a positive anti-cytokeratin expression.[42]

Folpe et al. conducted a thorough investigation into the tumor's immunohistochemical expression and found that it exhibited squamoid differentiation and epithelial features. Their study found that GCOC had no immune histochemical evidence of p53 expression, low immunoreactivity for proliferating cell nuclear antigen, mild reactivity for vimentin, high reactivity for high and low molecular weight cytokeratin, and carcinoembryonic antigen.[43,44]

CONCLUSION :

GCOC being a rare and unpredictable malignant odontogenic tumor, long term surveillance of patients is mandatory as metastasis to distant sites has been reported.[44]

Reviews of some other literature has shown that there has been three cases of metastatic odontogenic ghost cell carcinoma has been reported which includes metastasis to lung in one case, metastasis to skin, lung and brain in the other and metastasis in the cranium the third case.[45]

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