Disorganized histomorphology: Dentinogenic ghost cell tumor

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INTRODUCTION

The World Health Organization (WHO) panel of experts on odontogenic tumors has defined dentinogenic ghost cell tumor (DGCT) as “locally invasive neoplasm characterized by ameloblastoma, like islands of epithelial cells in a mature connective tissue stroma. Aberrant keratinization may be found in the form of ghost cells in association with varying amounts of dysplastic dentin.” It occurs in an average age of 50 years with a slight male predilection and equal frequency of involvement of maxilla and mandible in canine to first molar region as a predominant site. Calcification, root resorption and association of impacted tooth are observed radiographically.

The etiology of this rare lesion is still unknown, but it has been suggested that missense mutation in β-catenin in wingless integrated (Wnt) pathway plays a crucial role in the development of DGCT. The treatment is conservative enucleation, but local reoccurrence was noted. In this article, the authors present a case of an 80-year-old female diagnosed with DGCT, a neoplastic form of calcifying odontogenic cyst (COC), due to its characteristic histologic features, numerous ghost cells and dentinoid material.

CASE REPORT

A female patient aged 80 years had a chief complaint of slow-growing swelling in the right side of the face since 1 year. Extraoral examination showed asymmetry with diffuse swelling. Intraorally, the swelling was hard, nontendered and nonulcerated, involving the right maxillary alveolar ridge. Obliteration of buccal vestibule and missing regional teeth were noticed [Figure 1].

Radiographic examination revealed the presence of a radiolucent resorptive lesion involving right maxillary residual ridge and maxillary antrum admixed with areas of radio-opacities [Figure 2]. The lesion was provisionally diagnosed as ameloblastoma and was excised under general anesthesia. The excised tumor was sent for histopathological examination.

Microscopically, sheets and rounded islands of odontogenic epithelium lined with tall columnar ameloblast-like cells and loose stellate reticulum type cells with mature connective tissue were observed. Active formation of dysplastic dentin in connective tissue stroma and prominent eosinophilic transformation of anucleated epithelial cell called “ghost cell” in epithelium and connective tissue resulting in multinucleated foreign body giant cell reaction were also present [Figure 3]. Van Gieson stain showed positivity for ghost cell and dysplastic dentin, whereas pan-cytokeratin positivity was observed in the odontogenic epithelial islands [Figures 4-7].

**DISCUSSION**

COC constitutes 1%–2% of all odontogenic lesions occurring in oral cavity. Out of this, 88% of COC shows cystic nature, whereas 12% are solid in nature. In 2005, the WHO has renamed COC based on its proliferative qualities as calcifying cystic odontogenic tumor (CCOT) to the cystic type of COC and neoplastic variant as DGCT to the solid form of COC.[3,4]

DGCT is a neoplastic counterpart of COC described by Praetorius et al. in the year 1981.[5] It affects both the jaws with slightly higher ratio in the anterior region. Clinically, the lesion is asymptomatic but causes noticeable swelling with asymmetry of face, which in turn depends on the size of the lesion. Mixed features of radiolucent destruction and
The histopathology shows a cystic lining of odontogenic epithelium surrounded by numerous ghost cells and formation of dentinoid-like material juxtaposed to epithelial lining. The ghost cells are altered cells undergoing aberrant keratinization arranged singly or in sheets with defined cell outline but devoid of nucleus. It is believed to arise from the different layers of epithelium with a tendency to infiltrate into connective tissue where they evoke foreign body reactions with the formation of giant cells. The classical feature is the presence of dentinoid-like material which is thought to be an inductive phenomenon, whereas Howel in 1968 suggested that dentinoid-like material is due to the inflammatory response of the body to the ghost cells. The histopathology of the present case showed the nests of odontogenic epithelium with tall columnar and stellate reticulum-like cells with no inflammatory response in or around the dentinoid-like area.

The pathogenesis behind DGCT is still controversial and has created a way for researchers to intrude into the molecular level of genes. The complex process of odontogenesis is tightly regulated by growth molecules and transcription factors. The Wnt and sonic hedgehog play a crucial role in tooth initiation, morphogenesis and differentiation. The plethora of molecules and their intricacy of interaction during tooth formation may lead to homeostatic errors which in turn result in abnormal or no formation of the tooth and other related disorders.

It has been suggested that Wnt/β-catenin signaling promotes tooth neogenesis, but mutation in Wnt/β-catenin pathway can result in the formation of smaller tooth or misshapen tooth and ectopic eruption of tooth. β-catenin is a coactivator of lymphoid enhancer factor (Lef), which is a cell type-specific transcription factor that mediates Wnt signaling during odontogenesis. Lef initiates histodifferentiation by mediating the epithelial–mesenchymal interaction through Wnt signaling and fibroblast growth factor signaling. Therefore, loss or alteration of these factors can cause arrested tooth development at late bud stage. The molecular mechanism/genetic aberration confirmed the potent role of β-catenin in the formation of abnormal dysplastic dentin in DGCT.

The immunohistochemistry assessment by Piattelli et al. showed positivity for cytokeratin characterizing the presence of an odontogenic epithelium whereas the calcified bodies and ghost cells were devoid of immunoreactivity. The negative immunoreaction represented their derivation either
from metaplastic transformation of odontogenic epithelium or a product of coagulative necrosis of the odontogenic epithelium. The present case also showed strong positivity of odontogenic epithelium with pan-cytokeratin whereas ghost cells and the dentinoid-like material showed bright red/magenta color with van Gieson stain.\[7\]

The treatment modalities for DGCT were enucleation until the local recurrence was noted. A more radical approach is accepted considering the biological behavior and neoplastic nature of DGCT. The present case was also treated with en bloc resection followed by uneventful healing. The patient is under follow-up since 6 months, and no recurrence is observed till date.

**CONCLUSION**

DGCT remains rare and controversial counterpart of COC due to the characteristic ghost cell, dentinoid, and its common resemblance to the benign ameloblastoma. Here, we presented a case of DGCT which is unique due to multivariate age and histological presentation.

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**REFERENCES**