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Calcifying Odontogenic Cyst with Odontome: A Case Report and Recent Updates in the Pathogenesis

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Abstract

Calcifying odontogenic cyst (COC), also known as "Gorlin cyst, "is a rare developmental odontogenic lesion first described by Gorlin in 1962. COC appears in both cystic and solid forms. COC mimics other odontogenic cysts clinically and radio graphically, and only histology may provide a definitive diagnosis. The fact that beta-catenin is the only gene that has been found to be mutated in COC lends credence to the idea that this mutation alters the Wnt signaling system, which is the cornerstone of the development of tumors. The current article describes a case of a 17-year-old male patient who came with swelling in the anterior maxilla with mixed radiolucent and opaque, concluding in a provisional diagnosis of a developmental cyst with odontome.

Keywords: Beta catenin, Dentinoid, Ghost cells, Gorlin cyst, Wnt pathway.

Introduction

Since its first description, it has become clear that the calcifying odontogenic cyst (COC) may present in a variety of forms, some of which resemble benign odontogenic tumors. The WHO categorized this as an odontogenic tumor in 1992 and 2005 [1]. In the most recent classification, which was done in 2017, COC has been classified as a developing cyst. With a prevalence among individuals in their third decade, COC is a relatively rare lesion that makes up 0.1 percent of all records and 1.3 percent of all odontogenic cysts [2,3].

Here, we discuss a case of a calcifying odontogenic cyst with an odontome in an adolescent patient's anterior maxilla.

Case Report

A 17-year-old male patient reported swelling in the upper front teeth to the outpatient department. The patient had a history of trauma from a road traffic accident a year ago. Extraoral examination reveals a 2x1.5cm swelling in the anterior maxilla that is firm to cystic in nature and non-tender when palpated. **(Figure 1).**

Intraoral examination revealed an expansion of the buccal cortical plate extending from the distal aspect of 11 to the distal aspect of 23. Palatally, there is a displacement of 22.

A 1.5x1.5 cm mixed radiolucent radio-opaque lesion extending from the level of interdental bone to the floor of the nasal cavity was found in the interdental area of 21,22. (Figure 2a). There are several calcified formations to be seen. Loss of lamina dura of 21 and displacement of 22 is noted.

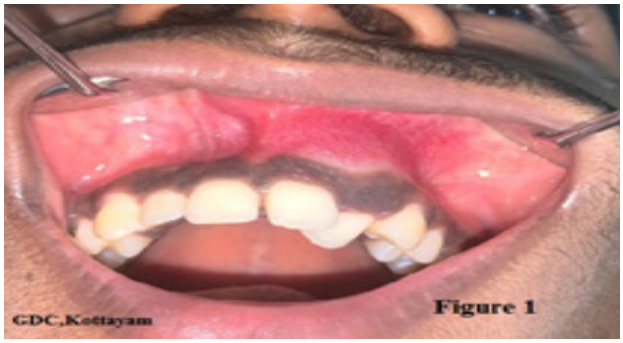


Figure 1: Intra Oral Examination Shows 2 X1.5 Cm Swelling in The Anterior Maxilla

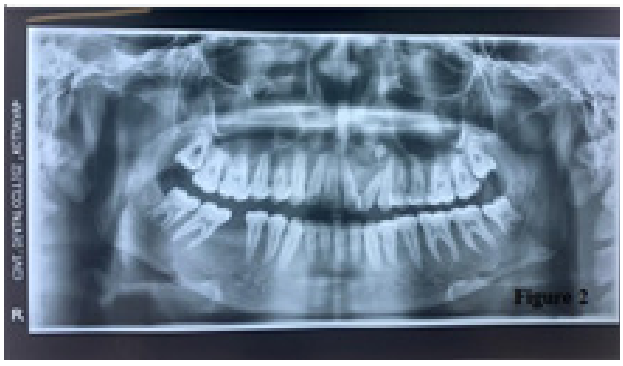
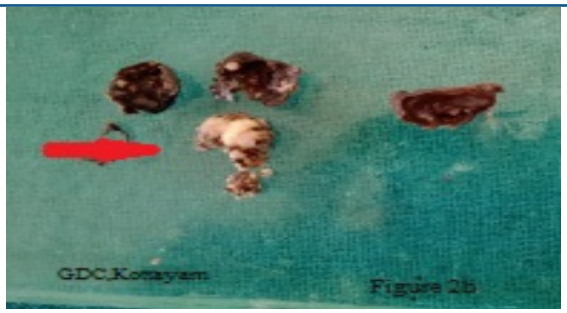


Figure 2a: Opg Showing Well Defined Radiolucent Area with Radioopaque Calcified Material in Inter Radicular Area of 22, 23.

Based on the clinical and radiographical features a provisional diagnosis of developmental odontogenic cyst associated with odontome probably COC was given. The differential diagnosis includes benign odontogenic tumours associated with odontome such as Adenomatoid odontogenic tumour. Cyst enucleation was done from the anterior maxilla 21,22,23 region and was sent for histopathological examination.

The single formalin-fixed soft tissue bit received measured 1.5x1.0x0.9cm, was black in colour, and had a firm consistency. A longitudinally cut section reveals a cystic lumen with hard tissue that resembles an odontome. **(Figure 2b and 2c)**



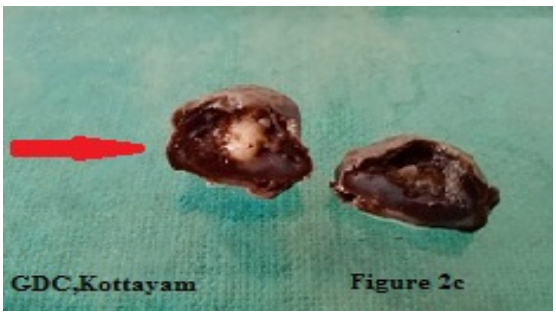
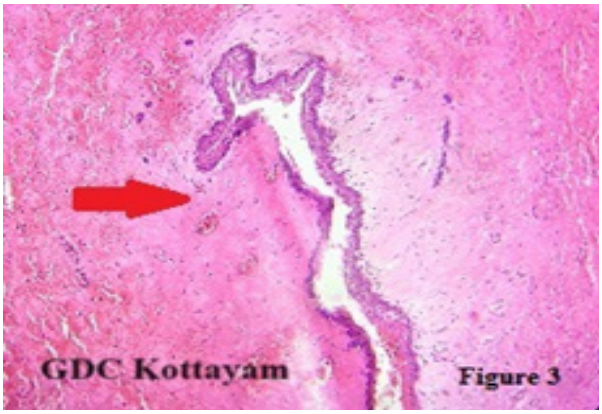


Figure 2b and 2c: Longitudinally Cut Section Showing Cystic Lumen with Structures Resembling Odontoma.

Histopathology revealed a densely collagenous cyst wall lined by an odontogenic epithelium of 2–5 cell layer thickness and low columnar basal cells with hyper chromatic nuclei. Within the epithelium, there were numerous pale eosinophilic, ballooned, ellipsoid epithelial cells with indistinct outlines suggesting ghost cells. The stroma showed eosinophilic dentinoid-like material and calcification. Stroma has a few islands, nests, and cords of inactive odontogenic rests. In the stroma, there were a few active ameloblastomatous follicles with peripheral low columnar cells. **(Figure 3,4,5).** Mild diffuse collection of chronic inflammatory cells predominantly lymphocytes and intense vascularity were noted. These findings were consistent with those of a Calcifying Odontogenic Cyst with Odontome**.**



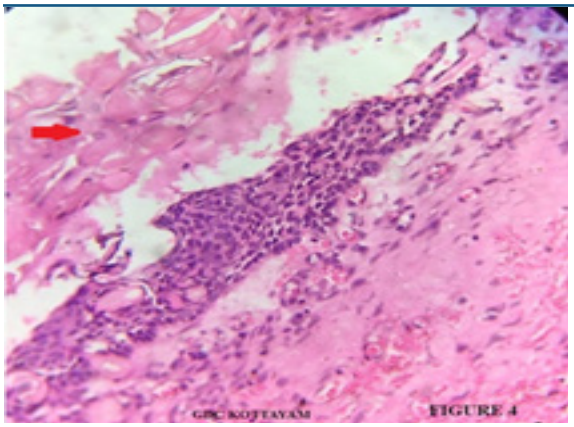
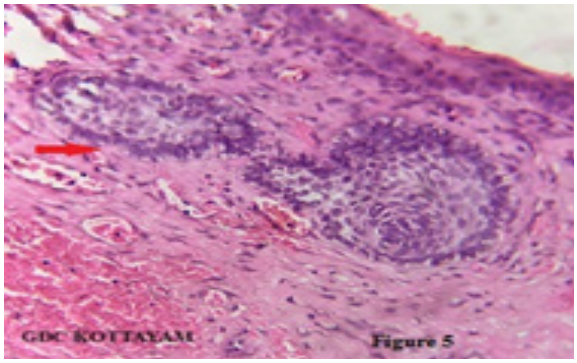


Figure 3: **Collagenous Cyst Wall Lined by Odontogenic Epithelium and Inactive Odontogenic Rests. (h&e 10x magnification). Figure 4**: **Pale Eosinophilic Ellipsoid Cells with Indistinct Outline Resembling Ghost Cells. (H&E 10x magnification)**



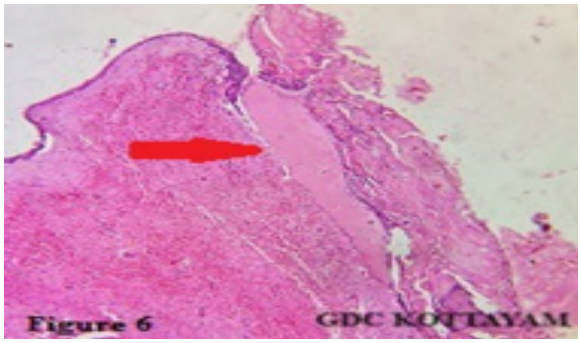


Figure 5: Ameloblastomatous Islands with Peripheral Low Columnar Cells (H&E 40xmagnification). **Figure 6: Eosinophilic Dentinoid Like Material Subjacent to Epithelium and Ghost Cells Supra Epithelially (H&E 10x magnification)**

Discussion

The COC is a rare entity with an enigmatic pathophysiology; the most important symptoms are histological in nature rather than clinical or radiological. The clinical, histological, and biochemical aspects of COCs are extremely different. This cystic lesion presents as a unilocular radiolucent lesion with radiopacity on radiographic examination. However, it can also develop in non-osseous areas such as the gingiva, which accounts for 15 to 25% of all COC instances that have been reported [4].

Preatorius et al. classified COC into two distinct types based on the dualistic approach: cystic and neoplastic. The cystic lesion is a calcifying cystic odontogenic tumor, and the neoplastic form is a dentinogenic ghost cell tumor. All COCs are calcifying cystic odontogenic tumors (CCOT), as defined by the WHO in 2005. In 2017, WHO categorized CCOT as cystic or neoplastic according to their behavior as non-neoplastic lesions [2].

The peripheral gingival form was generated from the dental lamina ("of Serres") or primitive oral epithelium, whereas COCs were developed from the reduced enamel organ, remnants of odontogenic epithelium within the tooth follicle, or remnants of odontogenic epithelium. While molecular changes in odontogenesis have been attributed to the development of distinct odontogenic pathological entities, odontogenic lesions histologically resemble stages of embryonic tooth development [5,6].

The epithelial lining exhibits odontogenic characteristics, including a prominent basal layer composed of palisaded columnar or cuboidal cells and hyperchromatic nuclei polarized away from the basement membrane. The most significant characteristic of COC is the presence of ghost cells. Most of the time, it is unclear how ghost cells develop. The majority of researchers believe that they represent an unusual or abnormal type of cellular keratinization called "ghost cell keratinization [7].

Particularly in the thicker areas of the epithelial lining, collections of ghost cells are seen. They are eosinophilic, and although their cell outlines are often distinct, they can occasionally become blurry, giving the appearance that clusters of them have fused together. The remnants of the original nucleus may still be visible in a few ghost cells, but most of them have lost their chromatin and are in various stages of degeneration, leaving just a faint outline. The ghost cells are a calcification-prone, abnormal kind of keratinization. Sapp and Gardner noted that calcification may take place in some ghost cells, first as small spherical entities and eventually as fine, powdery, or coarse basophilic granules [8-10].

The correlation between the stimulation of the Wnt/Beta-catenin pathway, the development of GCs, and their calcified characteristics has been demonstrated in numerous studies [11]. Genetic modifications have an impact on Wnt activation. This pathway has been linked to the development of cysts and odontogenic tumors. The discovery that beta-catenin is the only gene altered in COC supports the theory that this mutation leads to a change in the Wnt signaling system, which is the basis for tumor development. Therefore, the odontogenic epithelium's aberrant signaling, which is controlled by beta-catenin, contributes to the pathogenesis of COC [12].

It is plausible to suggest that an abnormal stimulus to the primitive lamina's cellular remnants (the rest of Serres) establishes the development of ameloblastoid cells through genetic modification of the WNT pathway and abnormal beta-catenin activity. This contributed to the growth of a less aggressive and more differentiated ameloblastoma form of tumor. This concept will also account for the existence of dysplastic calcification and the similarities between the COC epithelium and an ameloblastoma [13].

The lining epithelium may induce the formation of a dentinoid or an odontome in the cyst wall. Odontogenic tissue produces dentin and enamel as a result of the active interactions between the odontogenic mesenchyme and epithelium. Because of this, aberrant calcifications like enameloid, dentinoid, or cementum-like material may emerge when odontogenic epithelial remnants develop without differentiating [6]. The various phases of the COC's calcified material deposition in diseased tissues have not yet been identified. It could be a short and transient phase. The tissue that is produced may change and lose its enameloid-like properties [10].

Examined the ghost cells' reactivity to antibodies against amelogenin, enamelin, enamelysin (MMP20), and sheathlin (prism sheath protein) to determine what the ghost cells were made of. They noticed that the ghost cells in COCs have immunolocalized enamel-related proteins in their cytoplasm. In order to assess the localization of amelogenin in human odontogenic tumors immunohistochemically, confirmed that specific ghost cells in the linings of COCs were heavily stained [14].

Amelogenin protein has been found by Yoshida et al. in the epithelial linings of five of the specimens as well as in the cytoplasm of ghost cells in all 16 of their instances. They demonstrated that the nuclei of epithelial lining cells only occasionally had Ki67-positive responses. They came to the conclusion that COCs with various histological characteristics have the potential to become malignant and might not even be distinct entities [15].

For COC, simple enucleation and curettage are the recommended treatments. Recurrences after 8 years after enucleation have been observed; therefore, long-term follow-up is advised. It should be noticed that recurrence includes the risk of becoming transformed into a malignant lesion. This pathological entity must therefore be managed with a long follow-up [16].

Conclusion

Uncommon tumors like COCs are frequently asymptomatic. Numerous studies have shown a connection between activating the Wnt/Beta-catenin pathway, the growth of GCs, and their calcified features. Therefore, the pathogenesis of COC is influenced by the aberrant signalling of the odontogenic epithelium, which is regulated by beta-catenin. The composition of the ghost cells was determined by their reaction to antibodies against amelogenin, enamelin, enamelysin (MMP20), and sheathlin (prism sheath protein). They discovered that the immunolocalized proteins relevant to enamel are present in the cytoplasm of the ghost cells in COCs.A pathological investigation is necessary since the diagnosis is based on radio-clinical and histological indications. A lengthy radiological follow-up is typically necessary because of the possibility of COC recurrence, especially in the case of a histology diagnosis different from COC.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/ her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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