

## INVITED REVIEW

### Dentigerous Cyst Involving Multiple Teeth in Non Syndromic Patients and Cholesterol Granuloma - A Review.

Gayathri Ramesh, Aparna Dave, Kanwar Deep Singh, Ramesh Nagarajappa

#### Abstract

Dentigerous cysts are the most common developmental odontogenic cysts of the jaw, arising from impacted mandibular third molars, less frequently with impacted maxillary canines or other teeth. Although mostly solitary, multiple cysts occur in association with syndromes such as Mucopolysaccharidosis type VI, Cleidocranial dysplasia, basal cell nevus syndrome, Maroteaux - Lamy syndrome and Gardner's syndrome. Multiple cysts in non-syndromic patients are extremely rare, occurring almost exclusively in the mandible. We hereby review solitary dentigerous cyst involving multiple teeth and on cholesterol granuloma.

**Key words:** Dentigerous cyst; multiple teeth; anterior; mandible; midline; cholesterol granuloma.

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#### Introduction

Developmental cysts of the oral and maxillofacial region are usually asymptomatic, but have the potential to become extremely large and cause cortical expansion and erosion.<sup>1</sup> A dentigerous cyst (DC) is one such type of developmental cyst, that encloses the crown of the unerupted tooth and is attached to the neck.<sup>2</sup> The exact pathogenesis of DC's remains unknown; however most authors favor a developmental origin from a tooth follicle.<sup>3</sup> It is of worth to mention that DC cannot be diagnosed using radiographic evidence only but must be based on both macroscopic and microscopic examination of the specimen, because various other lesions, such as unicystic ameloblastoma and odontogenic keratocyst can occur in the same position.<sup>4,5</sup> Most often they develop in association with impacted mandibular third molars, less frequently with impacted maxillary canines or other teeth. There are also cases being reported of dentigerous cysts associated with supernumerary teeth and odontomas.<sup>6</sup> DC's are usually solitary, but are known to be multiple in patients with certain syndromes, such as mucopolysaccharidosis type VI and basal cell nevus syndrome, Gardner's syndrome and Cleidocranial dysplasia.<sup>7,8</sup> There are limited cases of multiple cysts occurring in non-syndromic patients. Multiple cysts in non-syndromic patients are extremely rare, occurring almost exclusively in the mandible.<sup>9</sup> There are no reports of solitary DC involving multiple teeth with detailed description of gross specimen. This paper

gives a review on the same and cholesterol granuloma.

#### Discussion

DC is a type of odontogenic cyst formed from the epithelium associated with the development of dental apparatus. It has been estimated that 10% of impacted teeth have formed this cyst and frequency in general population being 1.44 in every 100 unerupted teeth.<sup>10</sup> Most often they develop in association with impacted mandibular third molars, less frequently with impacted maxillary canines or other teeth and also sometimes associated with supernumerary teeth and odontomas.<sup>6</sup> DC's are most commonly seen during 2<sup>nd</sup> and 3<sup>rd</sup> decade of life which is usually solitary, but are known to be multiple in patients with certain syndromes, such as mucopolysaccharidosis type VI, basal cell nevus syndrome, Gardner's syndrome and Cleidocranial dysplasia.<sup>7,8</sup> Multiple cysts in non-syndromic patients are extremely rare, occurring almost exclusively in the mandible.<sup>9</sup> The earliest case of multiple DC would appear to be that recorded by Glaswald, in 1844.<sup>11</sup>

The epidemiological studies of DC have shown the prevalence rate among various populations as being 18.1% in cases collected over a 30-year period in UK population, 24.08% in South African series collected over a 46-year period<sup>12,13</sup> and a similar frequency of cases were reported among Canadian series amongst all odontogenic cysts.<sup>14</sup> DC's are more common in males than females, in majority of cases. The reason for this sex difference is

unknown. However, Daley and Wysocki suggested that it may be related to smaller jaw size in female patients and a greater tendency for prophylactic extraction of third molar.<sup>15</sup>

The literal meaning of dentigerous is 'tooth bearing' and seems most appropriate for this cyst. Although DC's are common lesions, their precise origin is uncertain. It has been suggested that dentigerous cysts may develop by fluid accumulation either between the reduced enamel epithelium and the enamel, or alternatively between individual layers of the reduced enamel epithelium.<sup>11</sup> The pressure exerted by an erupting tooth on the surrounding connective tissue follicle has been suggested as obstructing the venous outflow to increase transudation of fluid across the capillary wall, so that the increased hydrostatic pressure of this fluid separates the follicle from the crown with or without the epithelium. It has also been argued that over time, the capillary permeability is altered and protein-rich exudates accumulate within this newly formed space, which causes more fluid accumulation by osmosis and enlargement of the cyst.<sup>16,12</sup>

An inflammatory etiology has also been proposed in the pathogenesis of some DC's. It has been suggested that the crowns of permanent teeth may erupt into radicular cysts or other periapical inflammatory lesions at the apices of its deciduous predecessors. This theory is supported by clinical and radiographic evidence of inflammation of deciduous teeth in cases with histologically confirmed DC's associated with permanent successors. Such lesions have been described as "inflammatory follicular cysts" distinguishing them from the more common lesions not associated with primary precursors.

Radiographically, a hyperplastic dental follicle can be confused with a small DC. Most authorities believe that a pericoronal radiolucency of more than 4mm is suggestive of a small dentigerous cyst.<sup>14,12</sup> It is accepted that the final diagnosis of DC depends on the combined radiographic, intra-operative and histological findings.

The majority of DC's is asymptomatic and is often found on radiographic examination when patients present with a missing tooth or failure of tooth eruption. DC's associated with unerupted teeth in edentulous patients, may present with as slowly enlarging, painless jaw swellings. When these become infected, may also present with pain.<sup>12</sup>

DC's commonly present as unilocular radiolucency associated with the crowns of unerupted teeth and often has well-defined sclerotic borders. In the English literature search there are only few reports of solitary DC involving multiple teeth. The oldest case was by Robert H. Ivy reported involving two teeth in one cyst in a 14 year old patient with impacted mandibular left second and third molars and another case in the same article of female patient aged 10 years under radiograph showing two DC's, connected with the unerupted left mandibular canine and first premolar.<sup>17</sup> A case of a 9-year-old girl showed a large expansile radiolucent region from the mandibular left second molar tooth to the mandibular right canine tooth germ under radiographic examination. The mandibular left 32, 33, 34 and 35 teeth were displaced to the inferior border.<sup>18</sup> This is the only case reported with mid line crossing in the mandible associated with multiple teeth. Although there is one case in the maxillary anterior region involving two impacted supernumerary teeth lying vertically and inverted within the lesion, having cone shaped crowns and one short root each apical to maxillary central incisor in a 14 year old female patient.<sup>19</sup> Another case affected a 43 year old male patient in the mandible as a large radiolucent lesion extending from the left lateral incisor to the left third molar area along with displaced 33, 34 & 35 to the inferior border resulting in paresthesia of inferior alveolar nerve.<sup>20</sup> But none of the above mentioned reports explain the gross features of the excised specimen regarding association of single cystic lining with multiple teeth.

Gross examination of enucleated DC lining; usually reveal attachment to the cemento-enamel junction of associated teeth. Microscopically, the epithelial linings of DC's resemble the reduced enamel epithelium and consist of flat or cuboidal cells of 2 to 4 cell layers thick. Localized proliferation of the epithelial lining has been reported in areas of inflammation. The epithelium may also contain mucous producing or ciliated cells representing metaplastic change. DC's usually having a thin fibrous capsule with widely separated fibroblasts and stroma. The stroma is often loose in places, with accumulation of glycosaminoglycans, while isolated cords and islands of inactive odontogenic epithelium are also often seen in the cyst walls. The stroma is usually not inflamed, although inflammation is seen when DC's become infected.<sup>21</sup>

Inflamed DC walls occasionally contain cholesterol crystals, haemosiderin pigments and Rushton's hyaline bodies similar to those reported in radicular cysts.<sup>12</sup> Notably, once cholesterol crystals have been deposited in the cysts wall, they behave as foreign bodies and elicit a foreign body giant cell reaction.<sup>22</sup> According to J H Lee et al first reported a case of cholesterol granuloma within a mandibular odontogenic cyst.<sup>23</sup> The clinical significance of cholesterol clefts in odontogenic cysts is yet to be determined. The incidence of cholesterol crystals is reported as highest in inflammatory cysts, particularly in radicular cysts, while the lowest incidence is reported for cysts of non-inflammatory origin such as odontogenic keratocysts.<sup>24</sup> While in Md. Firoz Iqbal's study proportionately more cases with cholesterol clefts was elicited amongst DC's as compared with radicular cysts and odontogenic keratocysts.<sup>22</sup> However Yeo et al reported Cholesterol crystals in the epithelial lining and lumen in 16.8% cases, while 12.6% of cases in the cyst wall.<sup>25</sup> This suggests that the inflammatory process plays an important role in the pathogenesis of cholesterol crystals.

Few authors suggest that cholesterol crystals accumulate in the tissues as a result of degeneration and disintegration of epithelial cells.<sup>26</sup> While others on the other hand, suggested circulating plasma lipids as a more likely source, because cholesterol crystals are common in atherosclerotic plaques and circulating lipids have been identified as the origin of cholesterol in atherosclerosis.<sup>12</sup> In Browne's study, cholesterol clefts were more prevalent in cases where there was haemosiderin pigment.<sup>24</sup> He postulated that the main source of cholesterol crystals was disintegrating erythrocytes. Since erythrocytes have no internal membranes and the plasma membrane is the only possible source of erythrocyte cholesterol, it is difficult to see how the large volume of cholesterol crystals seen in odontogenic cysts could be derived from erythrocyte membranes alone.<sup>27</sup> In another study by Yamazaki et al. suggests that perlecan (a basement membrane heparan sulfate proteoglycan) which is present abundantly in the cyst wall of immature granulation tissue might be related to the development of cholesterol granuloma.<sup>28</sup>

Md. Firoz Iqbal in his study has found what is not mentioned earlier in any studies, is the correlation between the presence of foamy macrophages and

cholesterol crystals, intracellular cholesterol crystals has been described in odontogenic cysts, that is recorded similar to intracellular crystals in atherosclerosis and Similarly, a further novel aspect of his study, is that there is correlation between the presence of foamy macrophages and haemosiderin in odontogenic cysts. He also concludes in his study as, since it is also possible that both of these deposits arise independent of one another in response to inflammation, it would be interesting to further probe the chemical nature of lipid deposits in cholesterol crystals and foamy macrophages in odontogenic cysts using frozen sections as described by others.<sup>22</sup>

Similarly, it would be interesting to characterize the distribution of LDL, oxidized LDL and lipoprotein lipase in such sections by immunohistochemistry, as well as by Western blot analysis. It is strongly suggested that, such further study would reveal an origin for these lipid deposits from plasma components, similar to atherosclerosis.<sup>22</sup>

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