Case Report

Enucleation of a Rare Hybrid Odontogenic Lesion in the Anterior Maxilla of a 10-Year-Old Boy

Amanda Gruza, DMD1,2, Jason Choi, DDS, FRCDC1, Curtis Chen, DDS, PhD, Diplomat ABOMR3 and Catherine F. Poh, DDS, PhD, FRCDC and Diplomat ABOMP1*

1Faculty of Dentistry, University of British Columbia, Vancouver, BC, Canada
2College of Dentistry, University of Saskatchewan, Saskatoon, SK, Canada
3Faculty of Dentistry, University of Washington, Seattle, WA, USA

Abstract

Hybrid odontogenic lesions are a well-recognized phenomenon. They most often show features of various odontogenic neoplasms arising within cyst-like structures. The etiopathogenesis of hybrid odontogenic lesions is not well defined, however, the presence of numerous, closely approximated sources of pluripotent epithelial cells in the developing jaws is likely associated with their development. This case highlights an interesting mixed radiolucent and radiopaque, expansile cystic lesion with a follicular relationship to an unerupted tooth in a young child. Histologically, the lesion showed a combination of dentigerous cyst, calcifying odontogenic cyst and adenomatoid odontogenic tumor. Close radiographic proximity of the hybrid odontogenic lesion to a focal expansion of the gubernacular canal suggests that the adenomatoid odontogenic tumor portion of the hybrid lesion may have arisen directly from this structure, resulting in delayed eruption of the adjacent tooth and subsequent development of a dentigerous cyst with foci of calcifying odontogenic cyst. Complete enucleation of the cystic structure with retention of the associated tooth was performed, with a 6-month follow-up showing complete healing of the surgical site and no evidence of recurrence of the cystic lesion. To date, there have been only six reported cases of lesions with features of both calcifying odontogenic cyst and adenomatoid odontogenic tumor. The current case represents the first documented case of a dentigerous cyst with foci of both calcifying odontogenic cyst and adenomatoid odontogenic tumor. Given the variable nature and biological behavior of the odontogenic entities that compose hybrid odontogenic lesions, unusual clinical presentations and unexpected progression are possible. Further documentation of such hybrid lesions is necessary to fully elucidate how these entities behave clinically, radiographically and pathologically.

Keywords

Hybrid odontogenic tumor, Hybrid odontogenic cyst, Hybrid odontogenic neoplasm, Dentigerous cyst, Calcifying odontogenic cyst

Introduction

Recently, there have been several publications of so-called “hybrid odontogenic tumors” [1-14] including those with features of various odontogenic neoplasms arising within cyst-like structures [9-14]. The hybrid odontogenic lesions arise most commonly in the first two decades of life and appear to affect males and females equally [1-20]. The etiopathogenesis of these hybrid odontogenic lesions has not been fully elucidated. Odontogenic cysts and tumors are known to arise from the various sources of pluripotent epithelial cells within the oral cavity, including the dental lamina, gubernacular cord, odontogenic epithelial rests and reduced enamel epithelium [21-23]. In the early mixed dentition, developing tooth buds are often in close proximity to many of these sources of pluripotent epithelial cells. It is thus conceivable, that the tooth buds and early odontogenic cysts and tumors arising from these sources could influence one another in their respective development. It is also possible, given their close proximity, that these structures could eventually merge resulting in the formation of hybrid odontogenic lesions with diverse histological features. This case report presents radiographic and histologic evidence...

*Corresponding author: Dr. Catherine F. Poh, Faculty of Dentistry, University of British Columbia, 2199 Wesbrook Mall, Vancouver, BC, V6T1Z3, Canada, Tel: 604-675-8000 ext 7072, Fax: 604-675-8263
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supportive of this theory. We present a cyst-like lesion with a follicular relationship to an unerupted tooth and close proximity to a gubernacular cord, histologically consistent with a hybrid odontogenic lesion composed of a dentigerous cyst (DC) with foci of calcifying odontogenic cyst (COC) and adenomatoid odontogenic tumor (AOT).

Case Report

A 10-year-old otherwise healthy Asian boy presented to his family dentist with delayed eruption of his right permanent maxillary central incisor. Upon clinical examination, a large, asymptomatic swelling was observed in the right anterior maxilla. The patient was subsequently referred to an oral and maxillofacial surgeon for further evaluation. Extra-oral examination showed age appropriate development with no gross facial asymmetry, no submandibular or cervical lymphadenopathy, and no cranial nerve deficits. Intra-oral examination revealed a swelling in the right anterior maxilla adjacent the roots of the right central and lateral incisors (Figure 1). The lesion was non-mobile and non-tender on palpation. Buccal bony expansion was apparent, without evidence of palatal expansion. The overlying mucosa was intact and showed an area of faint blue discoloration. There was no associated paresthesia, nor anesthesia. Dental development was within normal limits, with the exception of an unerupted permanent maxillary central incisor and associated retained primary maxillary central incisor. All erupted teeth were noted to be periodontally sound and non-curious. There was no mobility of the teeth adjacent the lesion, and vitality tests were within normal limits.

Panoramic imaging showed a well-defined, unilocular, cystic radiolucency in the right anterior maxilla associated with a superiorly displaced permanent right central incisor and distally displaced root of the permanent right lateral incisor. Conebeam computed tomography (CBCT) confirmed the presence of a well-defined, unilocular, cystic, hypodense lesion associated with the impacted right central incisor within the anterior maxilla. The cystic lesion extended from the maxillary right canine to the left central incisor. Hyperdense entities were noted within the cystic lumen (thin blue arrow, Figure 2). The lesion appeared attached to the unerupted central incisor at the cementoenamel junction (CEJ), with displacement of the tooth superiorly where it approximated the nasal floor. A gubernacular canal was noted to extend inferiorly from the cystic lesion through the alveolar bone (thick blue arrowhead). Faint hyperdense entities are present in the posterior aspect of the cystic lumen (thin blue arrow).

Informed consent was obtained from the patient and his parents, and surgical excision of the lesion was completed under general anesthesia. A full thickness flap was elevated and the lesion was aspirated with an 18-gauge needle on a 10 cc syringe. The aspirate revealed a yellow fluid mixed with blood. Microscopic examination showed a cystic cavity lined, almost entirely, by thin, non-keratinized stratified

**Figure 1:** Clinical photo showing an expansile lesion in the right anterior maxilla extending from the mesial aspect of the right canine to the mesial aspect of the left central incisor with associated buccal expansion.

**Figure 2:** A) Pre-operative panoramic image showing a cystic structure associated with the crown of an impacted right central incisor; B) Pre-operative cone beam computed tomography showing a hypodense cystic structure associated with the crown of an impacted right central incisor and corresponding gubernacular canal (thick blue arrowhead); faint hyperdense entities are present in the posterior aspect of the cystic lumen (thin blue arrow).
Discussion

Based on the clinical examination and radiographic presence of a mixed hypo- and hyper-dense lesion with a follicular relationship to an impacted tooth, the clinical differential diagnosis included conventional dentigerous cyst (DC) with dystrophic calcification, adenomatoid odontogenic tumor (AOT), calcifying odontogenic cyst (COC), and calcifying epithelial odontogenic tumor (CEOT) [24].

The DC is a developmental odontogenic cyst which originates from a separation of the follicle from an unerupted tooth with subsequent accumulation of fluid between the odontogenic epithelium and the crown. It is the most common odontogenic cyst. The most commonly associated impacted tooth is the mandibular third molar. Maxillary third molars, maxillary canines, and mandibular second premolars are also commonly associated with DCs. Most of these cysts remain asymptomatic, showing symptoms only in the presence of prominent bony expansion or secondary infection. Radiographically, the DC presents as a unilocular radiolucency attached to the unerupted tooth at the CEJ. The border most often appears corticated and well-defined.
Displacement of the associated unerupted tooth can occur, as can resorption of adjacent roots. Dystrophic calcification within the cyst wall can result in a mixed radiolucent and radio-opaque appearance radiographically, mimicking other odontogenic tumors [25]. Histologically, non-inflamed DCs show a thin, attenuated squamous epithelial lining with absence of keratin and rete ridge formation. Dystrophic calcification may be identified in the epithelial cyst lining.

AOTs are benign neoplasms thought to arise from odontogenic epithelium, odontogenic rests, or the gubernacular cord. The vast majority of these tumors occur in adolescence, namely the second decade of life. The AOT is found primarily in the anterior maxilla, associated with an unerupted canine. A female predilection is noted. Most AOTs are asymptomatic and are discovered following investigation of an unerupted permanent tooth. Rare cases have been associated with enlargement of the adjacent bone. Radiographically, the AOT presents as a unilocular radiolucency with small radio-opacities, representing internal calcifications, surrounding the crown of an unerupted tooth. The border is most often corticated and well-defined. Compared to the DC, the cystic attachment point of an AOT is often located along the root, apical to the CEJ. The AOT, which has been documented to occur in combination with COCs [16,17,19-21,26], CEOTs [21] and odontomas [21], is known to present with a variety of histologic patterns characteristically showing formation of duct-like or rosette-like structures [21,27].

COCs have been categorized as cysts, neoplasms, and hamartomas [28]. This uncertainty results from the numerous clinical, histopathological, and behavioural variations this lesion may present with. Clinically, the most common presentation is that of an asymptomatic bony expansion in the anterior maxilla or mandible. Radiographically, COCs appear most often as unilocular radiolucencies, although multi-locularity can be seen. The border is well-defined and in one third of cases encompasses an unerupted tooth. The most commonly associated tooth is the maxillary or mandibular canine. COCs are often associated with radiopacities within the cystic structure. Displacement or resorption of adjacent roots is often present. Since it was first described [29], the COC has been reported to have substantial histopathologic variability. Reports of cystic, solid, and hybrid variants have been described extensively in the published literature [15,28,30,31]. The most common presentation is that of a benign cystic neoplasm, characterized by an ameloblastoma-like epithelium with ghost cells which may calcify [32]. In addition to the variable histologic presentations, calcifying odontogenic cysts also occur in conjunction with other known odontogenic tumors such as ameloblastoma [33], ameloblastic fibroma [33], previously classified ameloblastic fibro-odontoma [31,33], odontoma [15,29,34], and AOT [15-20]. These rare hybrid odontogenic neoplasms appear to retain separate and distinct histopathological features while existing within a single neoplastic entity.

The present case highlights an interesting mixed radiolucent and radiopaque, expansile cystic lesion with a follicular relationship to an unerupted tooth in a young child which histologically showed a combination of DC, COC, and AOT. To date, there have been only six reported cases of lesions with features of both COC and AOT [15-20] published in the English language literature, all reviewed in detail by Soares, et al. [19] and summarized in Table 1. The current case represents the first documented case of a DC with foci of both COC and AOT.

It has been suggested that the gubernacular cord, a remnant of the dental lamina [30], is the site of origin of AOTs [35,36]. It is plausible, that the small focus of AOT found in the present case arose directly from the gubernacular cord, suggested radiographically, by the focal expansion of the gubernacular canal (Figure 2).

According to the intra-follicular theory of DC formation, an erupting tooth exerts pressure on the dental follicle leading to obstruction of venous outflow [37]. This results in serum transudation, increased hydrostatic pressure, and separation of the follicle from the crown. It is thus conceivable, that in the current case, pressure was exerted on the dental follicle by both the erupting tooth and the obstructing AOT, resulting in the development of a DC. Hong, et al. described a similar process for the development of COC as a result of a proximate odontoma [28], suggesting that the foci of COC present in the current case may have resulted through the same process responsible for formation of the DC. The concurrent existence, and abrupt transition between a COC within a DC has also previously been described by Praetorious, et al. [31].
Table 1: Summary of all hybrid lesions containing foci of both COC and AOT published in the English language literature.

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Sex</th>
<th>Age (Year)</th>
<th>Site</th>
<th>Clinical Appearance</th>
<th>Radiographic Appearance</th>
<th>Radiographic Features</th>
<th>Clinical Diagnosis</th>
<th>Treatment</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Freedman, et al. [15]</td>
<td>F</td>
<td>15</td>
<td>Posterior mandible</td>
<td>Soft, painless, fluctuant swelling on lingual of mandibular molar region</td>
<td>Well-circumscribed unilocular radiolucency showing irregular resorption of distal root of first molar</td>
<td>Extracapsular</td>
<td>COC</td>
<td>Enucleation with curettage</td>
<td>None by 3 years after treatment</td>
</tr>
<tr>
<td>2</td>
<td>Zeitoun, et al. [16]</td>
<td>M</td>
<td>35</td>
<td>Anterior mandible</td>
<td>Painless swelling of anterior mandible with buccolingual expansion; no anesthesia, associated incisors were mobile and had reduced vitality</td>
<td>Well-demarcated radiolucency with patchy areas of calcification; involved teeth showed root resorption and lesion scalloped between the roots</td>
<td>Extracapsular</td>
<td>Yes</td>
<td>Enucleation with extraction and apicectomy of adjacent teeth</td>
<td>None by 18 months after treatment</td>
</tr>
<tr>
<td>3</td>
<td>Buch, et al. [17]</td>
<td>F</td>
<td>11</td>
<td>Posterior mandible</td>
<td>Expanded vestibular cortical bone in right mandibular premolar region</td>
<td>Typical follicular cystic lesion; however, the imaging reveals that the attachment site is apical to the CEJ</td>
<td>Follicular</td>
<td>No</td>
<td>Enucleation with removal of associated tooth</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>Ledesma-Montes, et al. [18]</td>
<td>M</td>
<td>19</td>
<td>Posterior maxilla</td>
<td>Radiolucent, unilocular, ill-defined limits</td>
<td>Radiolucent, unilocular, ill-defined limits</td>
<td>Follicular</td>
<td>No</td>
<td>N/A</td>
<td>None by 44 months after treatment</td>
</tr>
<tr>
<td>5</td>
<td>Soares, et al. [19]</td>
<td>F</td>
<td>2</td>
<td>Anterior maxilla</td>
<td>Slow-growing, non-tender hard bугe over the right anterior maxilla; involved maxilla; involved teeth were non-mobile with normal vitality</td>
<td>Large unilocular radiolucency with multiple radiopaque clusters and a well-demarcated radiopaque border; unerupted central incisor within lesion</td>
<td>Extracapsular</td>
<td>Yes</td>
<td>Enucleation</td>
<td>None by 1 months after treatment</td>
</tr>
<tr>
<td>6</td>
<td>Balaji, et al. [20]</td>
<td>M</td>
<td>43</td>
<td>Anterior maxilla</td>
<td>Indistinct, non-tender, hard bulge over the right anterior maxilla; involved maxilla; involved teeth were non-mobile with normal vitality</td>
<td>Oval, radiolucent lesion in the right anterior maxilla; involved maxilla; involved teeth were non-mobile with normal vitality</td>
<td>Extracapsular</td>
<td>N/A</td>
<td>None</td>
<td>None by 6 months after treatment</td>
</tr>
</tbody>
</table>
Other possible hypotheses for the development of a DC with features of AOT and COC include confluence of the dental follicle and gubernacular cord, or development of a hybrid odontogenic tumor with histologic features of multiple entities arising from a single source of multi-potential pluripotent cells. In this case report, the close proximity between developing tooth buds and sources of pluripotent epithelial cells, such as the gubernacular cord, may be responsible for the development of hybrid odontogenic lesions. Developing odontogenic cysts and tumors have the potential to influence the closely approximated tooth buds both physically and biochemically. It is therefore feasible, that one structure may influence or merge with the other, resulting in the formation of various types of hybrid odontogenic lesions with diverse histological features. Given the variable nature and biological behavior of the various odontogenic cysts and tumors composing these hybrid odontogenic lesions, there is potential for unexpected progression and behavior [26].

Based on the published cases of hybrid odontogenic lesions containing foci of COC and AOT, it appears that surgical enucleation, with or without curettage, is an effective treatment [29,31-33,36,37]. To date, none of these cases have been associated with lesion recurrence, nor malignant transformation.

**Conclusion**

We have presented a rare hybrid odontogenic lesion with DC, AOT, and COC in the anterior maxilla of a 10-year-old boy. Simple enucleation seems to be reasonable treatment with no recurrence at 6-month follow-up. The pathogenesis of the present hybrid lesion may be attributed to development of an AOT from a gubernacular canal, with subsequent obstruction of the developing permanent right central incisor and resultant formation of a DC with an associated COC component. Further documentation of such hybrid tumors is necessary to fully elucidate the etiopathogenesis of these entities as well as how these entities behave clinically, radiographically and pathologically. Information regarding the long-term follow-up of these lesions will also allow for the determination of the most appropriate treatment strategies and more accurate prognoses.

**Conflict of Interest Statement**

Amanda Gruza, Jason Choi, Curtis Chen and Catherine Poh declare that they have no conflicts of interest.

**Ethical Approval**

This article does not contain any studies with human or animal subjects performed by any of the authors. The review and report of radiographic and pathologic information is under the institutional ethical approval (UBC/BCCA H16-00611). All reporting procedures performed were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments.

**References**


