Archegonous Cystic Odontoma Is Not Necessarily Primordial

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To the Editors,

Regarding the recent article by Argyris et al. [1] on archegonous cystic odontoma (ACO), also descriptively termed “primordial odontogenic cyst (POC) with induction phenomenon (zonal fibroblastic hypercellularity) and dentinoid material,” we would like to make some conceptual comments and discuss our own observations of the microscopic features of a dentigerous cyst (DC) with hamartomatous tissue alterations in the wall and mural deposits of dentinoid in unrelated DCs.

A 39-year-old woman appeared for treatment with an asymptomatic cystic lesion in the left mandible. A well-corticated, unilocular radiolucency on the distal aspect of an unerupted third molar was consistent with a DC of the lateral type (Fig. 1a). The lesion was extirpated and has shown no recurrence during the 2 years after surgery. The enucleated cyst measured 14 × 8 × 8 mm and partially surrounded the crown. The majority of the cyst lining was non-keratinized, simple (consisting of flat or cuboidal cells; DC-type) to stratified squamous (containing clear cells; lateral periodontal cyst-type) epithelium (Fig. 1b–d). The unicystic ameloblastoma (UA)-like lining had a focus of intraluminal growth (Fig. 1d, e), but was negative for calretinin and Ki-67. In small areas, cord-like epithelial extensions were apparent (Fig. 1c). The fibromyxoid wall was largely uninfamed and showed focal deposits of irregular dentin, strongly basophilic, laminated, enamel-like material [2] (Fig. 2a), and dentinoid with clear

epithelial rests (Fig. 2b). No evidence of unequivocal enamel or ameloblast-type epithelium was seen in any of the sections. At the deeper border, there were numerous small droplets of calcified or eosinophilic material, products commonly associated with follicular hamartoma or multiple calcifying hyperplastic dental follicles [3] (Figs. 1c, 2c, d). Other focal mural components resembled odontogenic fibroma (Fig. 2e) and ameloblastic fibroma (Fig. 2f). Ghost cells and amyloid were absent. A diagnosis of DC with mural hamartoma was made.

The originality of ACO described by Argyris et al. [1] results from its location at the site of a congenitally missing tooth and its histopathology, exhibiting both cystic proliferation of fibroblastic and ameloblastic fibroma-like tissues and mural deposits of dentinoid, which convinced the authors that it was a true POC associated with an aborted tooth (cystic aborted odontoma). They performed a thorough job in reviewing the literature on POC and placed great emphasis on the origin rather than the product. However, the present case would seem to provide evidence that the so-called ACO is not restricted to POC but also forms part of DC.

Analogous observations have been reported in the literature under various bizarre terminologies [4–9]. The most important problem in attempting to categorize ACO is “What is the basic pathological process, cyst or cystic neoplasm?” Although the presence of immature dental tissues in cysts other than calcifying odontogenic cyst has generated controversy, ACO apparently has features that overlap both cyst and hamartoma. With epithelial proliferation and mesenchymal induction, the overgrowth of tooth elements may occur in the cyst wall. An alternative explanation is the possibility of a cyst arising in a developing odontoma with no or only minimal hard tissue formation (soft tissue odontoma) [10, 11]. It is also probable

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Fig. 1 **a** Unilocular radiolucency distal to the mandibular third molar. **b** Cystic lumen lined by epithelium of variable thickness is surrounded by fibrous wall. **c** Fibromyxoid wall lined by epithelium with basal cell extensions. *Arrow* indicates a deep-seated, whorled structure. **d** The lining epithelium is simple (*upper*), stratified (*middle*), and ameloblastomatous (below). Clear cells are scattered. **e** Intraluminal nodule containing globoid bodies of lightly basophilic material surrounded by a hyaline ring. H&E, original magnification $\times 40$ (**b**), $\times 100$ (**c**, **e**), $\times 200$ (**d**)

that a primordial lesion might simply represent failed tooth development with a secondary cystic dilatation in an aborted enamel organ.

Theoretically, hamartomatous cysts form a spectrum ranging from immature to mature dental tissues in which differentiation may progress to the dentin and/or enamel formation stage. Probably prompted by the underlying odontogenic mesenchyme, ameloblastic differentiation, although subtle, may occur in the odontogenic epithelial lining, creating a UA-like histology. The overlying ameloblastic epithelium reciprocally stimulates the proliferation and differentiation of mural immature fibroblasts into dental papilla-like and dentinoid-producing cells, resulting in a basic ACO morphology. Many different combinations of rudimentary odontogenesis can be seen: immature (dentinoid and dental papilla-like tissue) [1], intermediate (irregular dentin and pulp-like tissue) [5], and mature (irregular dentin, a poorly formed enamel matrix, an inactive ameloblastic epithelium and/or pulp-like tissue) [6, 8, 9] patterns. The case we have described represents an intermediate form containing enamel-like material.

The nature of dentinoid is still poorly understood; it seems likely a pathological product of inductive interaction between odontogenic epithelial and mesenchymal tissues [12]. Dentinoid deposition is unspecific and has been identified in a wide variety of lesions [1, 12], such as odontogenic keratocyst [13, 14], glandular odontogenic

cyst [15], ameloblastoma including UA [12, 16, 17], odontogenic carcinoma [12], and so on. As shown in Fig. 3, some DCs also contained dentinoid or osteodentin that can undergo calcification, but neither enamel nor enamel matrix was formed. Many of the previously reported cases of the so-called cystic odontoma lacking ghost cell masses probably represent this process [18].

The lining epithelium of ACO is suggestive of UA. Interestingly, two reported cases of UA have shown distinct nodules of ameloblastic fibroma-like tissue in the fibrous capsule [19, 20], and two further examples of adenomatoid odontogenic tumor featured a cemento-ossifying fibromatous reaction at the lesion periphery [21, 22]. It is worth noting that odontogenic fibroma-like and ameloblastic fibroma-like proliferations, both evident in our present lesion, developed just beneath the epithelial lining of DC [23], POC [24], and inflammatory cyst [25]. Therefore, the cyst epithelium, although non-neoplastic, may be programmed to induce fibromatous transformation of mural odontogenic mesenchyme.

In summary, ACO described by Argyris et al. [1] appears to form one end of a histological spectrum, which at its other end- includes the lesions described by Gomez et al. [6] and Costa et al. [9] and also, possibly, our present case. In our opinion, there may be some resistance to use the term “odontoma” for ACO. Even at an immature or developing stage, odontoma would be expected to show

Fig. 2 **a** Irregular dentin and laminated enamel-like material (*arrowhead*) are formed at the luminal surface. Clusters of detached lining epithelium are floating within the cavity. *Arrow* indicates epithelial rests. **b** Fibrillar dentinoid and droplet calcifications in close proximity to clear epithelial rests (*arrow*). **c** High-power view of Fig. 1c (*arrow*) showing groups of calcified droplets and eosinophilic

globules. *Arrow* indicates epithelial rests. **d** Small basophilic bodies identical to those seen in Fig. 1e become incorporated into an eosinophilic material. *Arrow* indicates epithelial rests. **e** Odontogenic fibroma-like proliferation. **f** Ameloblastic fibroma-like nodule. H&E, original magnification $\times 100$ (**a**, **f**), $\times 200$ (**b–e**)

some evidence of organization into incipient tooth germs or bear some resemblance to a “normal” stage of odontogenesis [10]. Although ACO actually represents some form of hamartoma (cystic tumor-like malformation of odontogenic soft and hard tissues), it does not contain a vestigial enamel organ component diagnostic of odontoma. Accordingly, a more appropriate designation for this

unique entity may be “complex odontogenic cyst with mural hamartoma.” Alternative descriptive appellations might include cystic odontogenic hamartoma, cystic hamartoma with rudimentary odontogenesis or with immature odontogenic tissue and odontogenic cyst of undetermined origin with hamartomatous components: you choose!

Fig. 3 a, b Mural deposits of osteodentin with calcification in unrelated dentigerous cysts. Arrow indicates mucous cells (**b**). H&E, original magnification $\times 200$ (**a, b**)

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