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LETTER TO THE EDITOR

Calcifying Odontogenic Cyst Showing a Varied Epithelial Lining: An Additional Case with Implications for the Divergent Differentiation Capacity of the Cyst Epithelium

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To the Editors,

Argyris and Koutlas [1] have described a single cystic lesion of orthokeratinized odontogenic cyst (OOC) and odontogenic keratocyst (OKC) with focal ghost cell keratinization/calcification in a patient with Gardner syndrome. They speculated that two distinct types of keratinizing OCs occurred simultaneously as separate foci within the same lesion under the common molecular (Wnt/β-catenin) pathway, since examination of multiple sections revealed that at no point were the two cysts in continuity. This is an interesting contribution demonstrating the morphological diversity that OCs may show [2–4]. Here we add an unusual case of calcifying odontogenic cyst (COC) in which the unicystic epithelium combined areas resembling dentigerous cyst (DC), OOC and OKC, with a minor component of mucous cells and duct-like structures. The COC lining also showed occasional granular parakeratosis (GP).

The patient, a 33-year-old man, presented with a painless facial swelling. The left maxilla was occupied by a well demarcated, unilocular cystic lesion measuring 4 cm in largest dimension. It contained the crown of an impacted canine and showed a 1-cm radiopaque mass within the basal portion of the lesion. Radiographic follow-up at 5 years showed no recurrence. Histologically, the enucleated cyst had a single cavity with a small luminal nodule (Fig. 1). This polypoid proliferation resembled plexiform ameloblastoma, but contained ghost cells, calcification or dentinoid (COC). Considerable variation in the morphology of the epithelial lining was found; it was mostly simple, non-keratinized thin or hyperplastic squamous (DC-type) epithelium, but parakeratinized (OKC-type) and orthokeratinized (OOC-type) areas were also seen (Fig. 2). Another part of the cyst epithelium had mucous cells and duct-like structures (microcysts), and such foci were in part indistinguishable from glandular odontogenic cyst (GOC) (Fig. 2). In addition to ghost cells, the COC-type epithelium contained a few ameloblast-like cells housing small fine to large coarse keratohyaline granules (GP) (Fig. 3). The diagnosis of COC with focal para/orthokeratinization and mucous cell differentiation was made.

In most cases, it is possible to classify OCs readily into one of the existing entities. There remains a small group of complex lesions in which different types of OC are combined. Various combinations and proportions of histological components have been reported in these polymorphous OCs, and no two cysts have looked precisely the same: COC with OOC [5], COC with OKC [6], OOC with OKC and ghost cell keratinization/calcification [1], GOC with DC [7], GOC with OKC and OOC [8], GOC with squamous differentiation [9–11], GOC with para- or orthokeratinization [12, 13] and GOC with ghost cell keratinization [14]. Although the literature is replete with observations of the respiratory epithelium in OCs including OKC [2–4, 15, 16], neither intraepithelial mucous cell nor duct-like structure has been recognized as part of the morphological spectrum of COC and OOC. The occurrence of mucous secreting cells in the present maxillary OC may be the result of metaplasia or prosoplasia because of no sinonasal involvement [4]. In view of the fact that mucin-laden goblet cell is known as an example of single-cell gland, it is possible that additional

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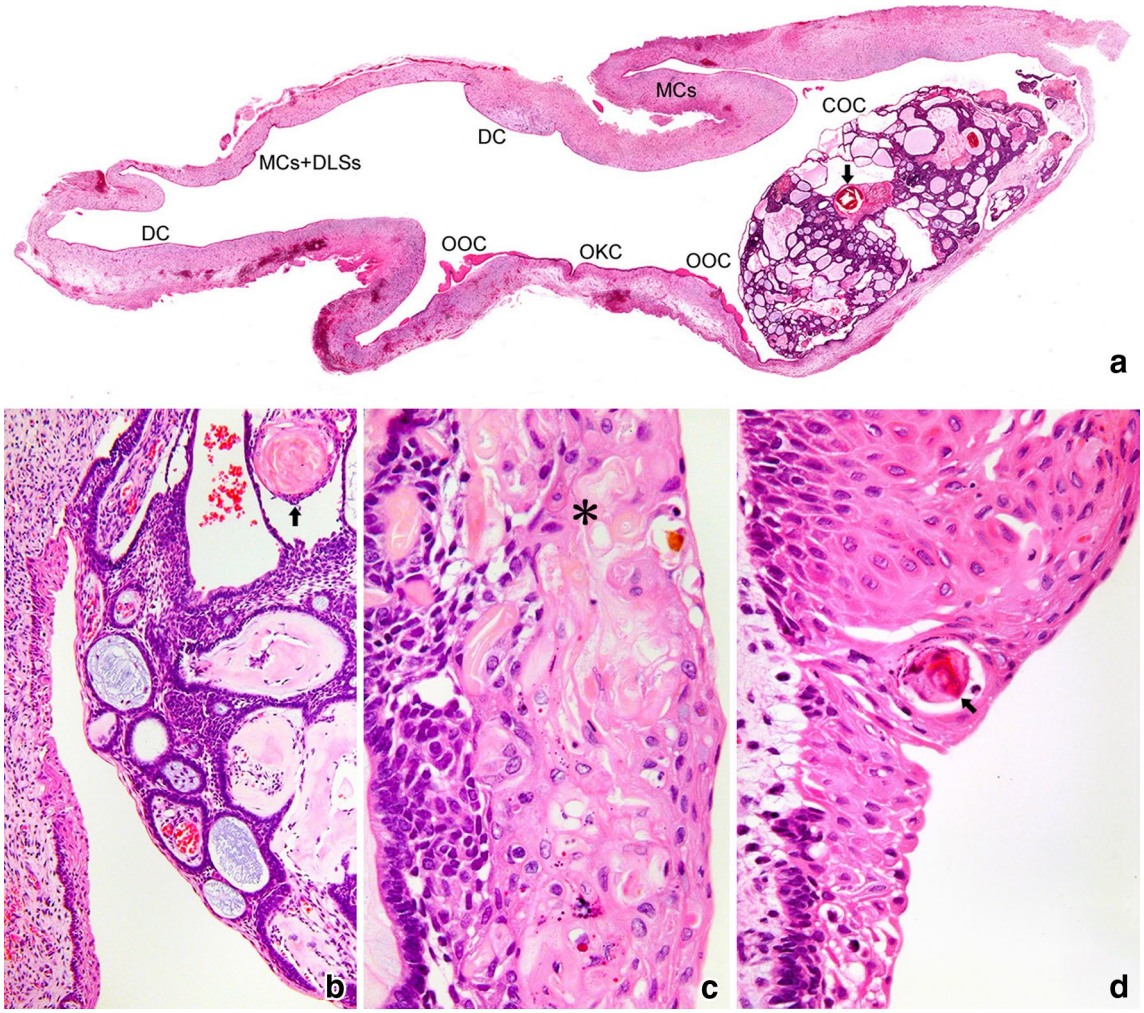

Fig. 1 **a** Unilocular cyst with a luminal nodule; *COC* calcifying odontogenic cyst, *OOC* orthokeratinized odontogenic cyst, *OKC* odontogenic keratocyst, *DC* dentigerous cyst, *MCs* mucous cells, *DLSs* duct-like structures. Arrow indicates calcification. **b** Ghost cell mass (arrow) and dentinoid in COC. **c** Ghost cells (asterisk) in COC. **d** Granular parakeratosis (arrow) in the non-keratinized hyperplastic squamous lining

glandular differentiation may take place in the "composite" cyst epithelium described here.

GP is an acquired disorder of keratinization (arrest of keratinocyte differentiation), now defined as an incidental microscopic pattern resulting from failure to degrade keratohyaline granules due to basic defect in converting profilaggrin to filaggrin [17, 18]. Histologically, it represents abnormally retained keratohyaline granules within parakeratotic squamous cells. Although GP has been reported in association with various dermatoses, inflammatory conditions and neoplastic processes of the skin [17, 18], this is the first description of such a feature in an odontogenic lesion. In our case, GP was focally seen in the ameloblastoma-like lining of COC and showed no relationship with ghost cells, which represent hard keratinization without keratohyaline granules [19].

In summary, the present COC is a single cystic process characterized principally by a remarkable admixture of DC, OOC and OKC components. There are also areas mimicking GOC. It has long been recognized that OCs frequently show the divergent differentiation and the various forms of metaplasia or prosoplasia [2–4]. A complex combination of two or more architectural or cellular peculiarities within one cyst suggests that with a subsequent interval of dormancy, the postembryonic odontogenic epithelium can proliferate at any time to form ameloblastic [20, 21], squamous, keratotic, ghost, ciliated/mucous and sebaceous cells in pathologic states [2–4]. In purely pragmatic terms, the existence of "composite" OCs underscores the limitations of diagnosis based on small (marsupialized) biopsies. Considering significant differences in clinical behavior of developmental OCs (i.e., DC, OKC,

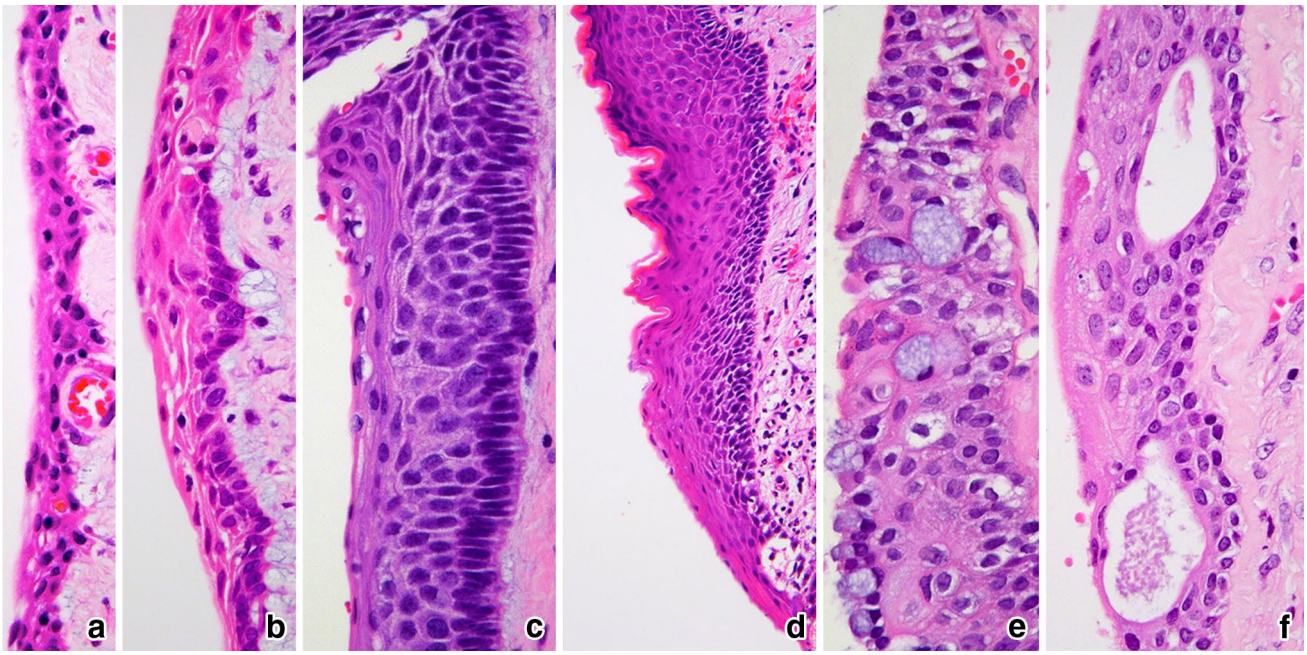

Fig. 2 Variability of the lining epithelium; simple (**a**) or non-keratinized (**b**) DC-type, parakeratinized OKC-type (**c**) and orthokeratinized OOC-type (**d**) linings. Mucous cells (**e**) and duct-like structures (**f**) in the cyst epithelium

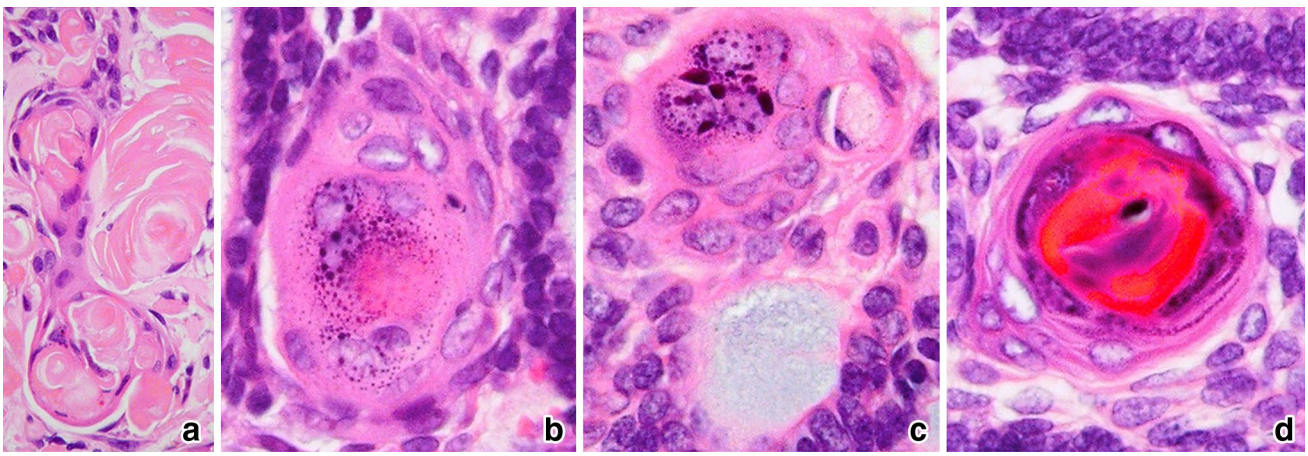

Fig. 3 COC component. **a** Ghost cells; **b**, **c** Granular parakeratosis in ameloblast-like cells; **d** Granular parakeratosis

OOC, GOC and COC), extensive sampling of the entire cyst is important.

Compliance with Ethical Standards

Conflict of interest The authors declare no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained.

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