J Oral Pathol Med (2004) 33: 125–8

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CASE REPORT

Solid variant of odontogenic keratocyst

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A case of an unusual lesion from the maxilla is presented. Macroscopically, the lesion was solid and histologically consisted of 'multiple separate keratocysts' of varying size that infiltrated into the surrounding bone and soft tissues. Panoramic image and CT scans showed a multilocular honeycomb ill-defined radiolucency with infiltration into the maxillary sinus and floor of orbit. This lesion should be differentiated from similar odontogenic lesions, such as keratoameloblastoma and papilliferous keratoameloblastoma. As there was no evidence of follicles, islands of ameloblastoma, or papilliferous structures in the entire specimen, the lesion could not be diagnosed as either a keratoameloblastoma or a papilliferous keratoameloblastoma. The invasive and destructive growth behavior, the histopathological features, and the histochemical pattern of the collagen stroma imply that this solid lesion is a neoplasia. It is suggested that the proper term for this lesion is solid variant of odontogenic keratocyst.
J Oral Pathol Med (2004) **33**: 125–8

Keywords: neoplasm; odontogenic keratocyst; solid variant

Keratocyst is a distinctive developmental odontogenic cyst with specific histologic features and clinical behavior (1). The histologic features consist of an epithelial lining of uniform thickness and a parakeratinized surface. The basal cells are palisaded columnar or cuboidal and display reverse polarity of the nuclei. Occasionally, basal budding and small satellite cysts are present in the fibrous wall, adjacent to the main cystic lumen.

Keratocysts differ from other odontogenic cysts in that they have a biologically aggressive behavior because of a high-proliferative activity of the lining epithelium, a tendency to extend along bony cancellous spaces, and a considerably high rate of recurrence (1–3). Radiologically, most keratocysts are unilocular radiolucencies. Multiloculation is more common in large lesions. The borders are smooth or scalloped and corticated (1).

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Accepted for publication April 29, 2003

Recently, an unusual lesion in the maxilla, which macroscopically was solid and histologically consisted of numerous microcysts that resembled keratocysts, was examined. Radiologically, it manifested as a honeycomb radiolucency.

The aim of this study is to present the histopathologic features of this unusual lesion, to compare and differentiate it from similar odontogenic lesions, such as keratoameloblastoma, and to suggest that the proper term for this lesion is solid variant of odontogenic keratocyst.

Case report

In October 2000, a 72-year-old Caucasian man was referred to the Department of Oral and Maxillofacial Surgery, Poriya Hospital, Tiberias, for evaluation of a swelling in the right maxilla of several months duration. Extraoral examination revealed no signs of swelling and the overlying skin was of normal color and texture and freely mobile. There was no restriction in jaw movements and sensation was intact. No cervical lymph nodes were palpable. Intraoral examination revealed a buccal tender, firm swelling in the right maxilla, extending from the premolar region to the tuberosity. Overlying mucosa was intact.

Panoramic image showed a multilocular ill-defined radiolucent lesion, 4.0 cm × 3.0 cm, with a honeycomb appearance, extending from the right maxillary premolar region to the tuberosity, superiorly to the floor of the orbit and medially to the nasal cavity and right maxillary sinus (Fig. 1). No other pathologic radiolucencies were found in either jaw. CT scans with contrast medium showed partial infiltration of the lesion into the right maxillary sinus and floor of orbit and a consistency of soft tissue with foci of radiopaque calcifications (Fig. 2).

An incisional biopsy from the buccal vestibule was performed and revealed the presence of a solid intraosseous lesion. Microscopically, the lesion consisted of numerous large and small cystic structures resembling keratocysts. The cysts were lined by parakeratinized stratified squamous epithelium with keratin-filled lumina. Several cysts contained desquamated squames and necrotic material. As there is no good diagnostic term for this lesion but there are some similarities of its histologic features to the case described by Said-Al-Naief et al. (4) as keratoameloblastoma, the tentative diagnosis of the incisional biopsy was keratoameloblastoma. A comment was made that the final diagnosis

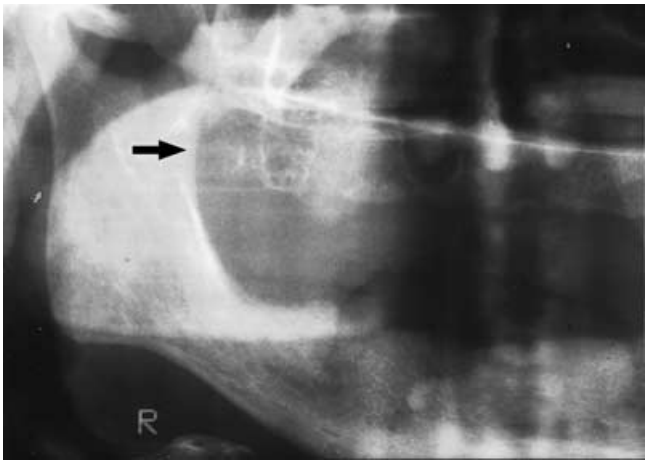

Figure 1 Panoramic radiograph showing a multilocular radiolucent lesion with ill-defined borders in the right maxilla (black arrow).

would be established only after resection of the lesion and thorough histological examination of the entire specimen. Nevoid basal cell carcinoma syndrome was excluded as common characteristic signs and symptoms (i.e. multiple basal cell carcinomas of the skin, multiple jaw cysts, and other skeletal abnormalities) were not revealed after extensive physical examination and thorough investigation of past medical history.

Under nasotracheal anesthesia, a hemimaxillectomy was performed with further extension to the floor of the orbit and zygomatic buttress. Frozen sections of the surgical margins were free of tumor. Immediate reconstruction of the floor of the orbit with free iliac crest bone graft and miniplate fixation was carried out. Postoperative course was uneventful with no recurrence after 24 months.

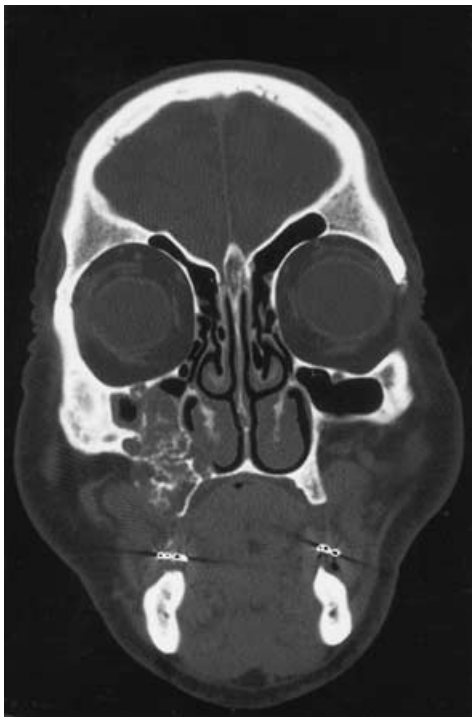

Figure 2 Coronal CT scan with contrast medium demonstrating a lesion that destroys the right maxillary alveolar ridge, the floor of the maxillary sinus, and occupies most of its space. The floor of the right orbit is also involved. Radiopaque foci are observed within the lesion.

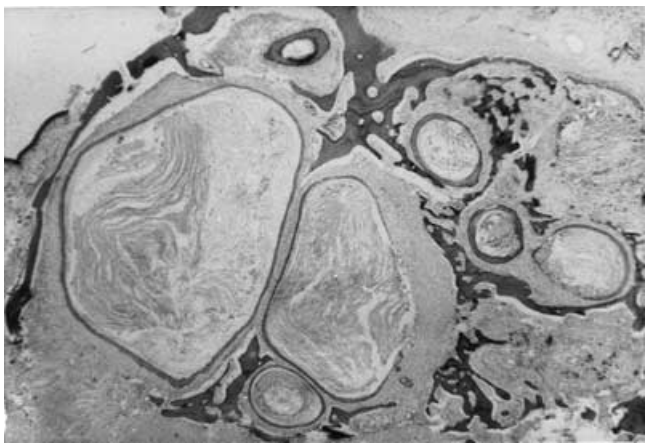

Figure 3 Low-power photomicrograph showing several cystic spaces of varying size infiltrating the cancellous bone (hematoxylin–eosin stain, original magnification ×10).

Pathological findings

Macroscopic appearance: On resection the lesion was solid with multiple small cystic spaces.

Microscopic findings: Analysis of hematoxylin and eosin sections representative of the entire specimen demonstrated a solid lesion consisting of multiple keratocysts of varying size (Fig. 3). The cysts were lined by parakeratotic stratified squamous epithelium, usually of a uniform thickness (2–10 cells thick). In some cysts, the surface epithelium was corrugated. The basal layer consisted of cuboidal and/or columnar cells with areas of palisaded, hyperchromatic nuclei that demonstrated reverse polarity (Fig. 4). The lumen of most cysts was filled with concentric layers of keratin, desquamated squames and/or necrotic material (Fig. 5). In

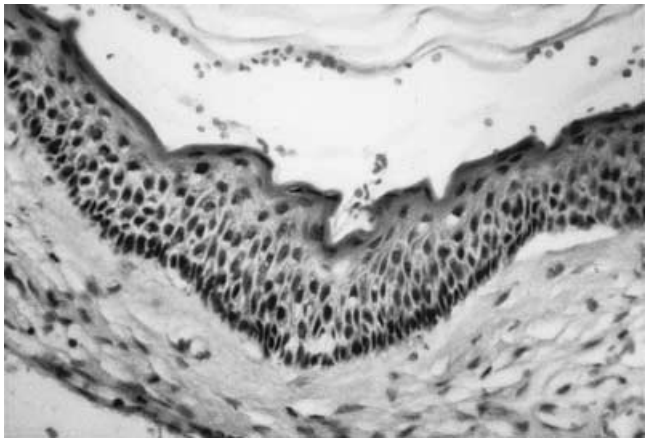

Figure 4 Photomicrograph of a wall of a microcyst lined by parakeratotic stratified squamous epithelium with corrugated surface. Basal cells are cuboidal to low columnar with hyperchromatic nuclei arranged in a palisaded pattern. (hematoxylin–eosin stain, original magnification ×200).

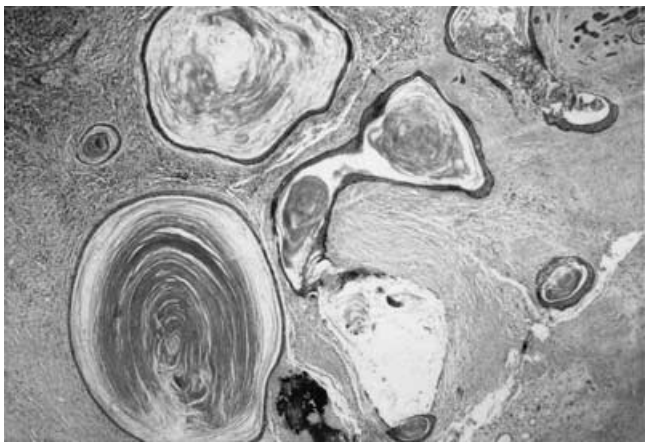

Figure 5 Photomicrograph of several microcysts. Lumina are filled with concentric layers of keratin, keratin and necrotic debris, and with desquamated squames (hematoxylin–eosin stain, original magnification ×40).

the remaining cysts the lumen was clear and the epithelial lining showed a tendency to separate from the underlying connective tissue (Fig. 6). In a number of cysts, basal proliferation and budding of the epithelium was prominent. The relatively large cysts were frequently accompanied by numerous smaller cysts and/or small solid epithelial proliferations resembling dental lamina or inert odontogenic rests.

The supporting connective tissue was cellular and well vascularized in some areas while in others it was amorphous, eosinophilic and hyalinized. Basophilic foci of calcifications were also present in the hyalinized areas. Picrosirius red staining and examination with polarizing microscopy revealed that both thin and thick collagen fibers of the supporting connective tissue demonstrated polarization colors of green to greenish-yellow range, which is a known pattern of the collagen wall of keratocyst as well as of the stroma of some odontogenic tumors (5–7). A massive chronic inflammatory reaction with giant cells was readily present adjacent to cysts that ruptured and released their keratin content into the connective tissue. The epithelial lining of these cysts loses the typical histological features of keratocyst and resembles that of an inflammatory cyst. The lesion showed infiltration into the surrounding cancellous bone and bone fragments were present between the cystic structures.

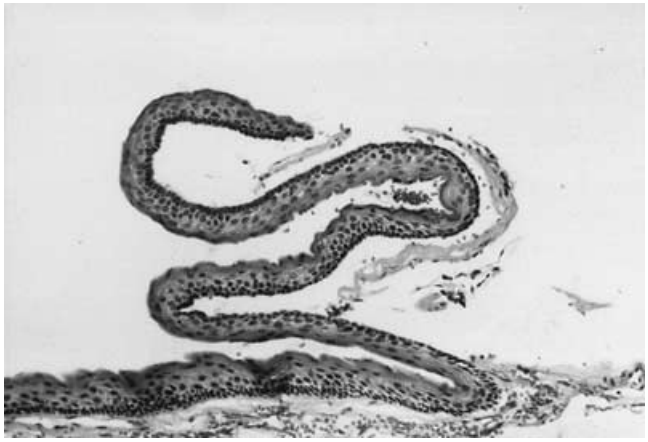

Figure 6 Photomicrograph of an area in which the lining epithelium has separated from the underlying connective tissue. The epithelium demonstrates typical features of a keratocyst (hematoxylin–eosin stain, original magnification ×100).

There was no histological evidence of microcysts with a papilliferous appearance of the lining epithelium and no evidence of follicles of conventional follicular ameloblastoma even after careful examination of the entire specimen. The final diagnosis for this unusual lesion was *solid odontogenic keratocyst*.

Discussion

Keratocyst is an important developmental odontogenic cyst because of its infiltrative mode of growth and strong tendency to recur after removal. The cyst is also considered as a distinctive entity because of its specific confirmed histological features (1–3).

The unusual lesion reported in the present article fulfills all the histological criteria for the diagnosis of a typical keratocyst, except that it was composed of *multiple separate keratocysts* rather than a typical single-lumen cyst. The clinico-pathological differential diagnosis includes odontogenic lesions with some similar histological features, such as keratoameloblastoma, papilliferous keratoameloblastoma and odontogenic keratocyst.

The WHO (8) vaguely defines keratoameloblastoma as an 'extensive keratinization in ameloblastoma', supposedly intending that this is an ameloblastoma with 'unequivocal keratinization, particularly in the centers of epithelial follicles, forming at the extent of the stellate reticulum-like cells' (9). Only four cases of keratoameloblastoma have been reported in the literature (4, 10–12). In the present case, there was no evidence of follicles or islands resembling ameloblastoma even after meticulous examination of the entire specimen, therefore a diagnosis of keratoameloblastoma could not be established.

Papilliferous keratoameloblastoma is another rare lesion that was considered. Pindborg (13) describes it as a lesion that consists of numerous microcysts, some lined by parakeratinized epithelium and contain keratin, while others have non-keratinized epithelium with a papilliferous appearance. In the present case, there were numerous microcysts of various size that were lined by parakeratinized epithelium and containing keratin. No microcysts with papilliferous lining were observed in the entire specimen. Thus, it does not fulfill the criteria of papilliferous keratoameloblastoma.

A thorough search of the English language literature revealed only one case histologically identical to the present one that was diagnosed as a 'keratocyst' (14). It also consisted of multiple separate keratocysts that invaded into adjacent soft and hard tissues; however, as it lacks a macroscopic description, there is no information whether the lesion was cystic or solid.

The present case should be diagnosed as a neoplasm and not a cyst as macroscopically it presented as a solid lesion with biologically aggressive behavior. Histologically, it consisted of multiple separate keratocysts; thus it cannot be diagnosed as a typical keratocyst, but rather as a variant of

keratocyst, and therefore a proper name for this lesion should be *solid variant of odontogenic keratocyst.* In the WHO classification of odontogenic tumors and cysts, there are other odontogenic cysts with a recognized solid neoplastic variant, i.e. the calcifying odontogenic cyst and the odontogenic/dentinogenic ghost cell tumor, respectively (15). The solid variant consists of infiltrating solid structures, some of which demonstrate cyst formation (16). On the other hand, there are also well-recognized solid odontogenic neoplasms that may present with a cystic variant. For example, the ameloblastoma may demonstrate a microscopic cystic appearance, varying from microcysts within a predominantly solid tumor to an almost complete cystic tumor (cystic ameloblastoma) (17). The present case is a solid lesion with microcystic formation that each showed characteristic histopathological features of a keratocyst. As it possessed an aggressive biologic behavior similar to that of ameloblastoma, it is possible it presents a solid neoplastic variant of keratocyst.

There is abundant body of evidence that supports the view that keratocyst is a neoplasm. At the immunohistochemical level, studies on the expression of neoplasia-associated markers, PCNA, Ki-67 and P53 in the lining epithelium of the keratocyst, have shown a more frequent and intense positivity as compared to other odontogenic cysts. At the DNA level, it has been demonstrated that in at least some keratocysts, the tumor suppressor gene *ptch* is inactivated with an ultimate loss of the control of the proliferative activity of the lining epithelium (18). In addition, the character of the collagen fibers of keratocyst and the role that they could play in its expansion have been studied by assessing the polarization colors of these fibers after picrosirius red staining (6). In the keratocyst, the green to greenish-yellow color of both thin and thick fibers imply loosely arranged fibers that differ from the tightly packed fibers seen in other odontogenic cysts but are similar to the collagen fibers in the stroma of some odontogenic tumors (5, 7). This suggests that the collagen in the keratocyst wall could be regarded as a structural support and also as part of the neoplastic behavior of the keratocyst (6). The collagen fibers in the present lesion demonstrated polarization fibers of green to greenish-yellow range similar to the pattern seen in odontogenic tumors. It is therefore possible that the present lesion completes the spectrum of histopathologic variants of the odontogenic keratocyst, with the single typical cystic lesion at one end through the single cystic lesion with multiple satellite microcysts and the solid neoplastic variant at the other end.

Accurate evaluation of the clinical spectrum, histological features, radiological characteristics and biologic behavior of solid variant of odontogenic keratocyst or neoplastic variant of keratocyst, must await the report of further studies.

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Acknowledgements

The study was supported by the Ed and Herb Stein Chair in Oral Pathology, Tel Aviv University. Grateful acknowledgments go to Dr Ibrahim Shagrawi, Department of Pathology, Poriya Hospital, Tiberias, for his kind supply of the histopathologic material. The authors would like to thank Ms Rita Lazar for editorial assistance and Mrs Nurit Chaimovichi for technical assistance.