Calcifying odontogenic cyst with ameloblastic fibroma: Report of three cases

Cheng-Chung Lin, BDS,[a] Chung-Ho Chen, BDS,[b] Li-Min Lin, MS, PhD,[c] Yuk-Kwan Chen, BDS, MS,[d] John M. Wright, DDS, MS,[e] Harvey P. Kessler, DDS, MS,[f] Yi-Shing Lisa Cheng, DDS, MS, PhD,[g] and Edward Ellis III, DDS,[h] Kaohsiung, Taiwan, and Dallas, Tex

KAOHSIUNG MEDICAL UNIVERSITY, BAYLOR COLLEGE OF DENTISTRY-TEXAS A & M UNIVERSITY HEALTH SCIENCE CENTER, UNIVERSITY OF TEXAS SOUTH-WESTERN MEDICAL CENTER

Although it is a rare event, odontogenic tumors such as ameloblastoma, ameloblastic fibroma (AF), ameloblastic fibro-odontoma, and odontoma have been reported associated with calcifying odontogenic cyst (COC). There are only four cases of COC with AF cited in the English literature. However, three of these four cases were either included in a review of a series of cases or reported as an abstract, and limited clinical and histological information was provided. We present three additional cases of COC with AF and discuss the management for this combined lesion. Because COC is known for its histologic diversity and variable clinical behavior, and the clinical significance of an association of COC with AF is still unknown, we think it is valuable to report COC with AF with detailed clinical and pathological documentation. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;98:451-60)**

The calcifying odontogenic cyst (COC) was first reported as a separate pathologic entity by Gorlin et al in 1962.[1] Because of its histological complexity and morphologic diversity, it is still debated whether COC is a cyst or a neoplasm. The WHO classified COC as a "benign neoplasm related to odontogenic apparatus" and defined it as "a cystic lesion in which the epithelial lining shows a well-defined basal layer of columnar cells, an overlying layer that is often many cells thick and that may resemble stellate reticulum, and masses of ghost epithelial cells that may be in the epithelial cyst lining or in the fibrous capsule."[2] The majority of COCs are cystic in architecture but on rare occasions they appear as solid lesions.[3-6] The epithelial lining of a COC appears to have the ability to induce the formation of dental tissues in the adjacent connective tissue wall, and the association of COC with odontoma is relatively common.[5,8,9] Other odontogenic tumors, such as ameloblastoma, adenomatoid odontogenic tumor (AOT), ameloblastic fibroma (AF), and ameloblastic fibro-odontoma may sometimes be associated with COC, but their occurrence is reported to be extremely rare.[4-6,11-15] To our knowledge, there are four cases of COC with AF in the English literature, and we report here three additional cases found in Asia and North America. We believe that the occurrence of odontogenesis and other odontogenic tumors in COC may be more frequent than what the literature implies.

[a]Professor and Head, Department of Oral Pathology, College of Dental Medicine, Kaohsiung Medical University, Taiwan.
[b]Associate Professor and Head, Department of Oral and Maxillofacial Surgery, Kaohsiung Medical University, Taiwan.
[c]Professor, Department of Oral Pathology, College of Dental Medicine, Kaohsiung Medical University, Taiwan.
[d]Assistant Professor, Department of Oral Pathology, College of Dental Medicine, Kaohsiung Medical University, Taiwan.
[e]Professor and Director of Pathology, Diagnostic Sciences, Baylor College of Dentistry-TAMUSHSC, Dallas, Tex.
[f]Associate Professor, Diagnostic Sciences, Baylor College of Dentistry-TAMUSHSC, Dallas, Tex.
[g]Assistant Professor, Diagnostic Sciences, Baylor College of Dentistry-TAMUSHSC, Dallas, Tex.
[h]Professor, Oral and Maxillofacial Surgery, University of Texas, Southwestern Medical Center, Dallas, Tex.
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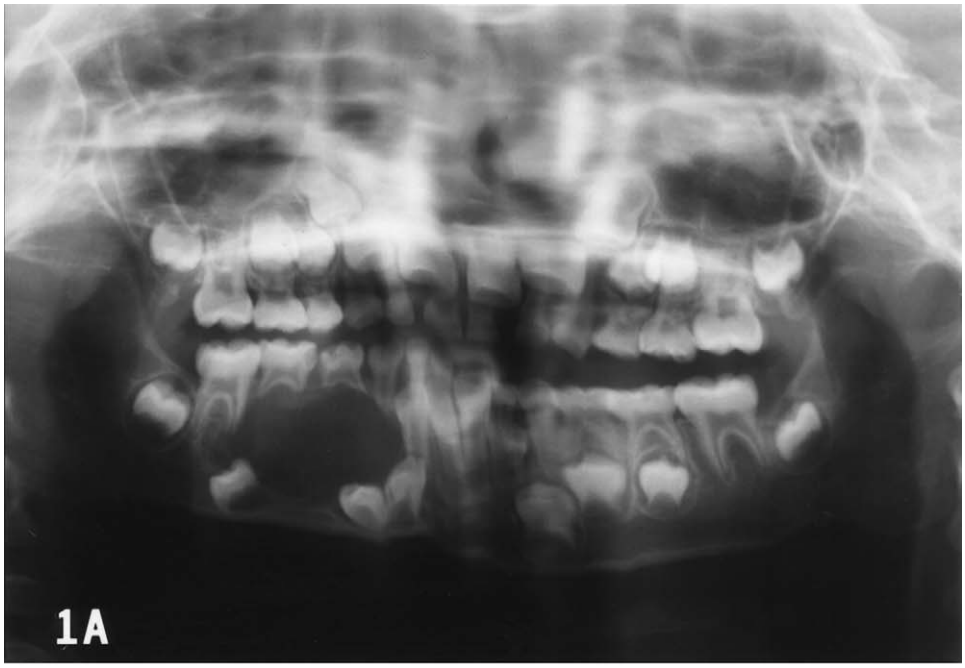
CASE REPORT

Case 1

A 6-year-old Taiwanese girl was referred by a local dentist to the dental department of Kaohsiung Medical University Hospital for treatment of a dentigerous cyst in the right mandible. Her mother noted a painless swelling in her right mandibular vestibule about 10 days previously. A panoramic radiograph revealed a 3.8 × 2.0 cm, well-defined radiolucency in the right mandibular body (Fig 1, *A*). The canine and premolars, showing no root formation, were pushed to the lower border of the mandible and with their crowns embedded in the lesion. The clinical diagnosis was a benign odontogenic tumor. An enucleation was performed and the surgical specimen showed a cystic lesion filled with blood clot. Some areas of the cystic wall were thickened and contained three nodules of white fibrous tissue measuring up to 1.3 × 0.6 cm in diameter (Fig 1, *B*, *arrows*). Microscopically, the cyst was lined by cuboidal to columnar epithelial cells with islands of ghost cells (Fig 1, *C*). Calcifications were occasionally seen. In the cyst wall, a hypercellular immature fibrous tissue with scattered odontogenic epithelial elements was found. In other areas, elongated epithelial strands with ameloblastic differentiation showing columnar cells at the periphery and stellate reticulum-like cells in the center were found distributed in the hypercellular immature fibrous tissue (Fig 1, *D*). The final



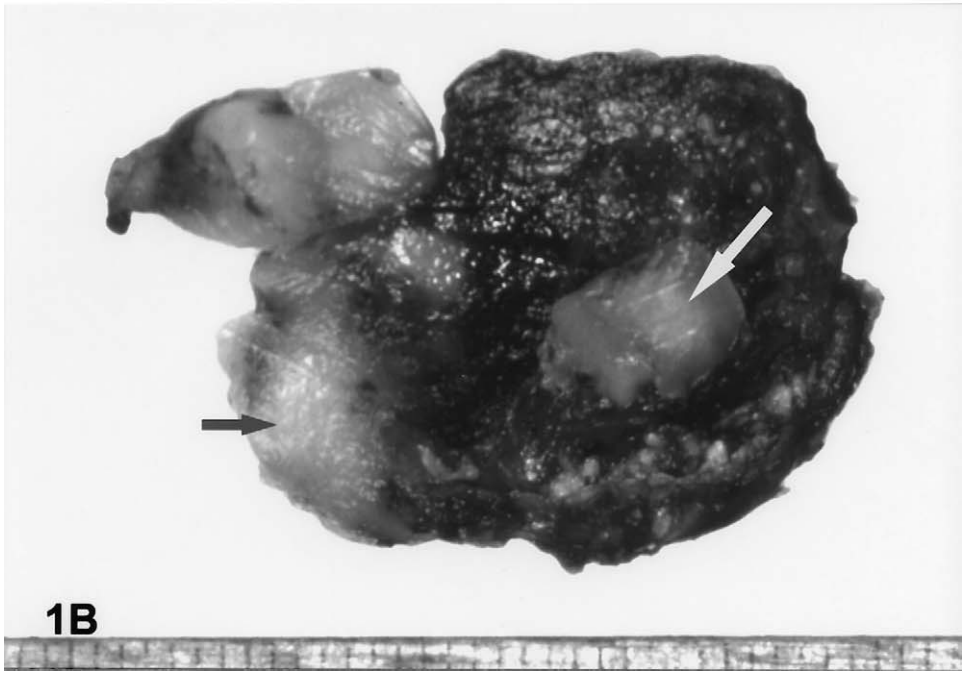


Fig 1. The clinical and histologic features of a right mandibular lesion in a 6-year-old Taiwanese girl. **A,** The panoramic radiograph showing a well-defined radiolucency in right mandibular body associated with impacted teeth #28 and #29. **B,** The surgical specimen showed a cystic lesion filled with blood clot. Some areas of the cystic wall were thickened and contained three white fibrous nodules (*arrows*). **C,** Microscopically, the cyst was lined by cuboidal to columnar epithelial cells with islands of ghost cells (hematoxylin-eosin stain; original magnification ×5). **D,** Elongated epithelial strands with ameloblastic differentiation showing columnar cells in the periphery and stellate reticulum-like cells in the center were found distributed in a hypercellular immature fibrous tissue (hematoxylin-eosin stain; original magnification ×20). **E,** The panoramic radiograph taken 20 months after operation showing bone healing, no recurrence and eruption of #28 and #29.

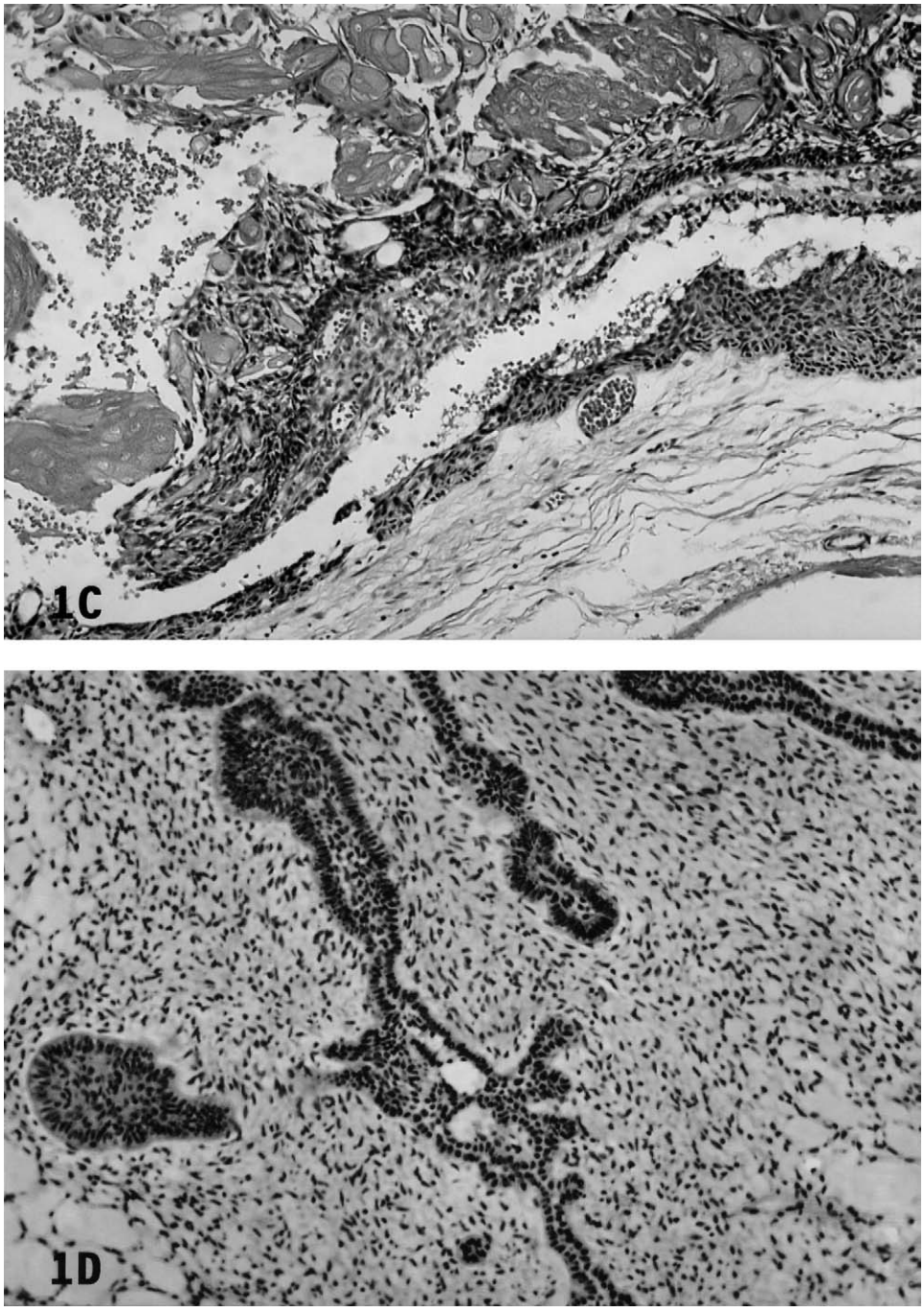


Fig 1. Continued

pathologic diagnosis was calcifying odontogenic cyst with ameloblastic fibroma. Post-operative follow-up was uneventful. The patient was last seen 20 months after the operation and a panoramic radiograph was taken (Fig 1, *E*). Teeth #28 and 29 were erupting and there was no recurrence.

Case 2

A 13-year-old African-American boy presented to the Oral and Maxillofacial Surgery Department at the University of Texas Southwestern Medical School for swelling of his left face that began three weeks earlier and had steadily been increasing in size. The swelling was associated with dull pain in the area. His past medical history was benign—he denied nausea, vomiting, weight loss, fever or chills. There was a visible swelling of the left cheek, fullness in the left maxillary buccal vestibule, and slight mobility of his left maxillary second molar. The submucosal mass was rubbery in consistency and had greatly expanded and thinned the buccal cortex.

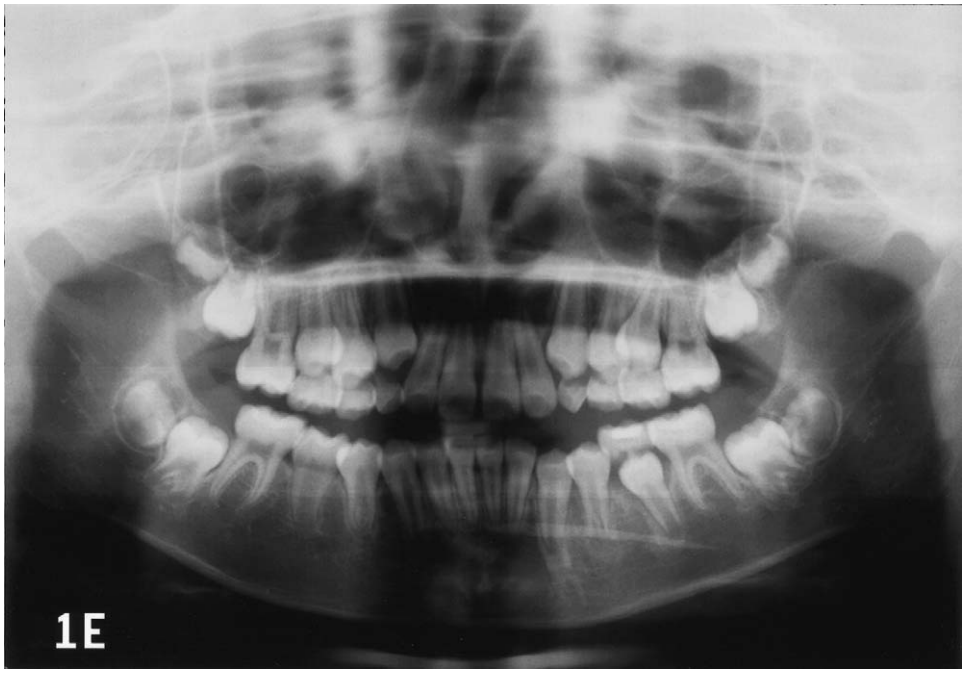


Fig 1. Continued

No sensory deficits were present, and the overlying mucosa was of normal color. A panoramic radiograph showed a large radiolucency associated with impacted tooth #16 (Fig 2, *A*). There was some evidence of root resorption of teeth #14 and 15, both of which were also associated with the lesion. Aspiration produced several milliliters of a thin dark liquid. A biopsy was obtained through a vestibular incision, and the hospital pathology department diagnosed the lesion as a cystic ameloblastoma. The specimen was subsequently reviewed by one of the authors (J.M.W.) who reclassified the lesion as a calcifying odontogenic cyst, with areas of ameloblastic fibroma. The lesion was subsequently excised through a Le Fort I osteotomy approach and macroscopically it appeared predominantly cystic (Fig 2, *B*).

On microscopic examination, the excision specimen was predominantly cystic and the luminal surface was lined by epithelium of variable morphology. In most areas it was stratified and showed proliferation into the cyst wall. The proliferating epithelium, however, remained in continuity with the luminal epithelium. The cells were predominantly basaloid but showed areas of loosening resembling stellate reticulum. Basal cells were palisaded, but reverse nuclear polarity was not prominent. Throughout the epithelial lining were numerous ghost cells and occasional calcifications (Fig 2, *C*). One area of the cyst wall was thickened and the fibroblasts showed uniform hypercellularity suspended within a fibrillar matrix. Numerous thin strands of odontogenic epithelium were suspended in this cellular connective tissue (Fig 2, *D*). A diagnosis of calcifying odontogenic cyst with ameloblastic fibroma was made. The patient failed to return for follow-up.

Case 3

A 22-year-old White male presented with a ''cyst-like'' lesion around the crown of an impacted mandibular right third molar. The impacted tooth was extracted and the lesional tissue was curetted. The submitted specimen consisted of elongated, sac-like fragments of soft tissue having the architecture of a cyst wall. Focal areas of thickening of the wall were present, producing slight nodular elevations into the lumen.

On microscopic examination, an epithelial lined cyst was present. The epithelial lining showed standard features of odontogenic epithelium, being characterized by a relatively uniform epithelial thickness with a prominent palisaded and mildly hyperchromatic basal cell layer composed of columnar cells (Fig 3, *A*). Reverse polarity of the nuclei and areas of subnuclear vacuole formation were found in the basal cell layer in many areas. The epithelium maintained a flat interface, without significant rete ridge formation, with the underlying connective tissue of the cyst wall. The areas of nodular thickening in the cyst wall seen on the gross tissue examination showed a variety of patterns. In some areas, prominent nodules of ghost cell keratinization protruded into the lumen (Fig 3, *B*). In other areas, the lining epithelium became proliferative, growing in a plexiform pattern of thin, lamina-like strands and cords of epithelium. Intermixed with this plexiform growth pattern, sheet-like areas containing whorled masses of spindle-shaped cells and occasional duct-like structures, reminiscent of adenomatoid odontogenic tumor, were also present (Fig 3, *C*). In other areas, the nodular thickening was generated by a proliferation of strands, cords, and islands of ameloblastic epithelium embedded in a loose myxoid but hypercellular stroma analogous to dental papilla (Fig 3, *D*). A diagnosis of

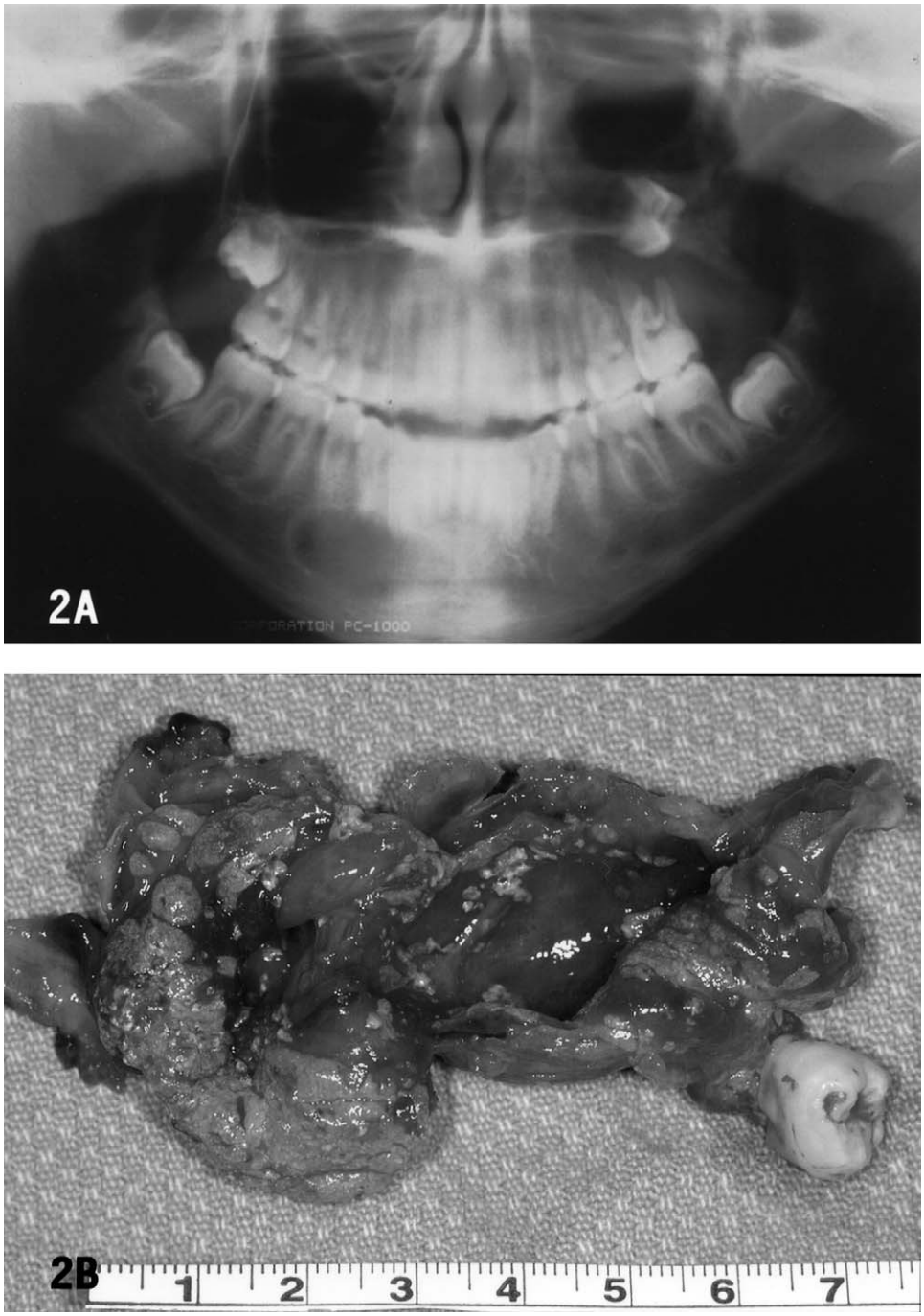


Fig 2. The clinical and histologic features of a left maxillary lesion in a 13-year-old African-American boy. **A,** The panoramic radiograph depicting a large radiolucency of left posterior maxilla with displacement of the third molar. **B,** The surgical specimen showed a predominantly cystic lesion. **C,** Photomicrograph showing the numerous ghost cells in the cyst lining epithelium (hematoxylin-eosin stain; original magnification ×10). **D,** Photomicrograph displaying thickened cyst wall with numerous thin strands of odontogenic epithelium suspended in a hypercellular fibrous stroma (hematoxylin-eosin stain; original magnification ×2).

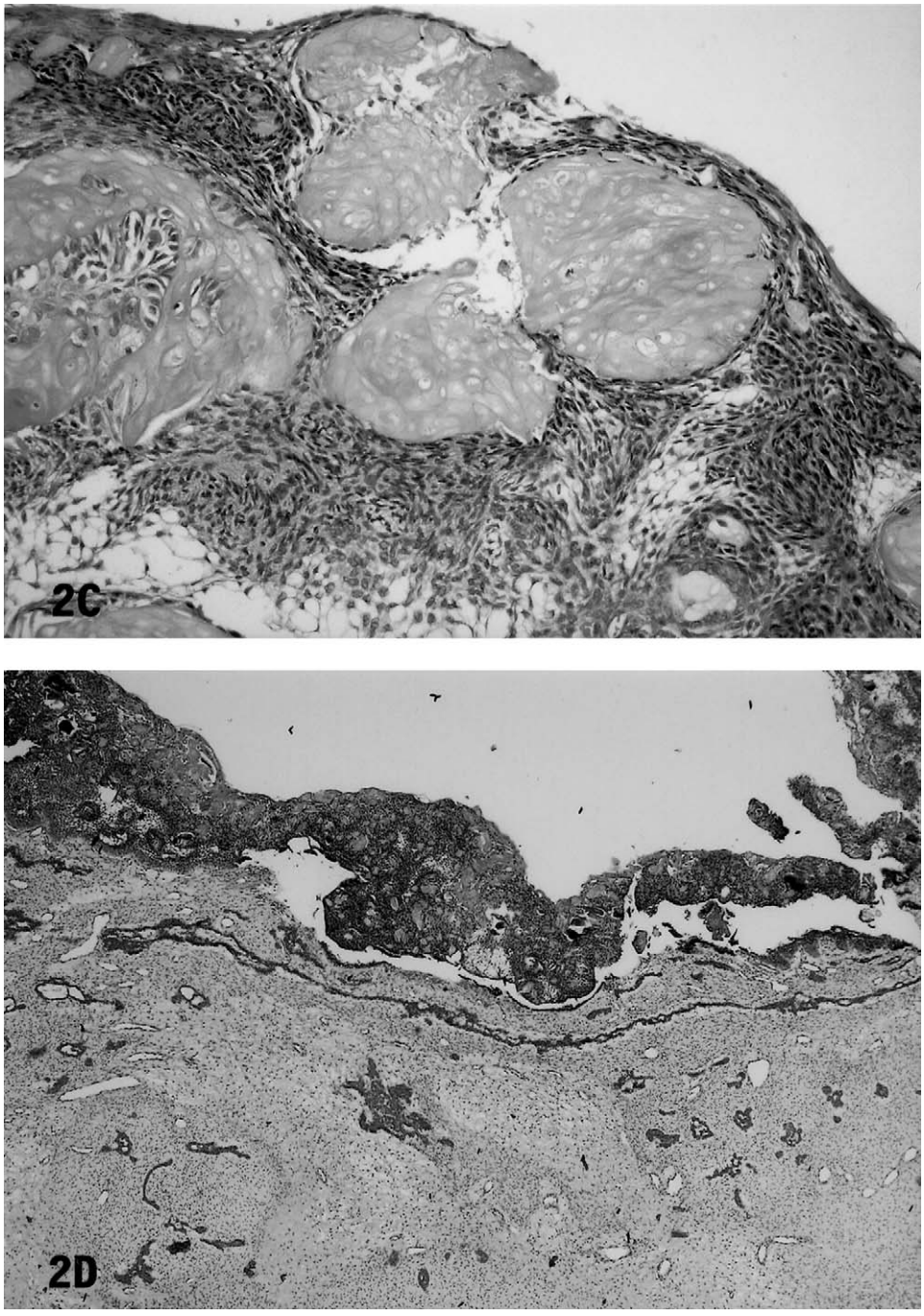


Fig 2. Continued

calcifying odontogenic cyst with ameloblastic fibroma was made. The patient did not show for follow-up.

DISCUSSION

COC was first described as a distinct entity by Gorlin et al in 1962. This lesion is uncommon and shows considerable diversity in its clinical and histopathologic features, as well as in its biologic behavior.[2-5,17-19] There are four previously mentioned cases of COC with AF in the English literature.[3,5,11,14] Shear mentioned one case of COC associated with AF in the text of a book chapter that was documented with a photomicrograph; however, no clinical or histologic description of this case was provided.[5] Farman et al[11] reported a case of COC with ameloblastic fibro-odontoma and discussed the pathogenesis of this condition. We believe Farman's case

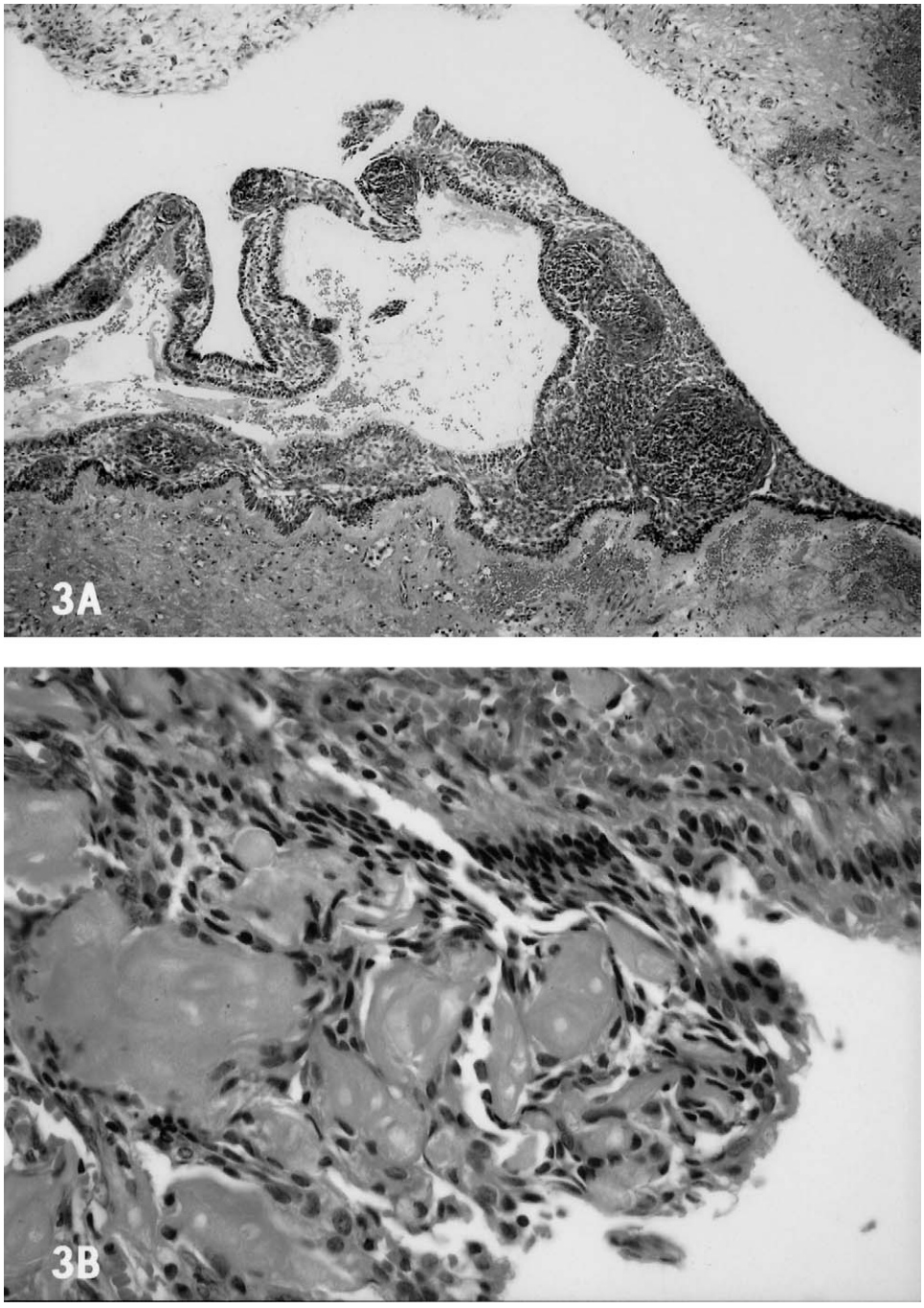


Fig 3. The histologic features of a cystic lesion in the right mandible of a 22-year-old White male. **A,** Low power view demonstrating odontogenic epithelium characterized by a relatively uniform epithelial thickness with a prominent palisaded and mildly hyperchromatic basal cell layer composed of columnar cells (hematoxylin-eosin stain; original magnification ×2). **B,** High power view showing a nodule of odontogenic epithelium undergoing ghost cell keratinization protruding into the lumen of the cyst (hematoxylin-eosin stain; original magnification ×20). **C,** High power view illustrating an area resembling adenomatoid odontogenic tumor. Arrows indicate duct-like structures (hematoxylin-eosin stain; original magnification ×20). **D,** Lower power view displaying islands of ameloblastic epithelium embedded in a loose myxoid but hypercellular stroma analogous to dental papilla (hematoxylin-eosin stain; original magnification ×5).

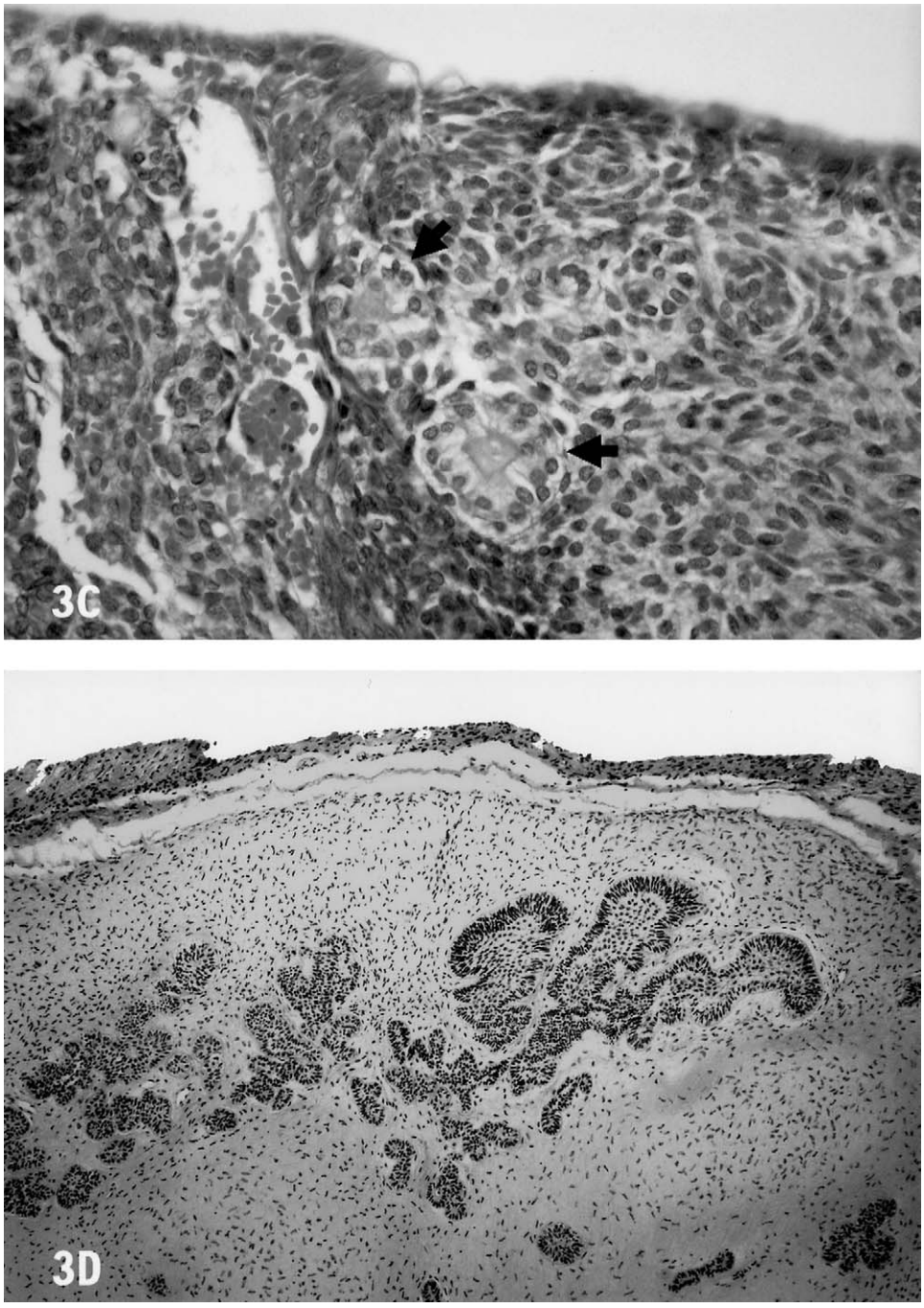


Fig 3. Continued

would be better classified as COC with AF rather than AFO because there was no calcified tooth material or enamel identified in the AF area in his case. Praetorius et al[3] reported 16 cases of COC and discussed the range, variations, and neoplastic potential of COC. In this series, a case of a 17-year-old boy (No.7) having AF in COC was included. Recently, Yoon et al[14] also reported a hybrid odontogenic tumor composed of COC and AF at the biennial meeting of the International Association of Oral Pathologists in 2002. The present report adds three cases of COC with AF. We believe that the occurrence of odontogenesis and odontogenic tumors in COC may be more frequent than what was reported in the previous literature.

Table I. The reported cases of calcifying odontogenic cyst with ameloblastic fibroma

Author	*Case #*	*Age*	*Race*	*Sex*	*Location*	*Treatment*	*Follow-up*
Shear[5]	1	-	-	-	-	-	-
Farman et al[11]	2	42	Cape color/ South Africa	F	Right mandible	Enucleation	-
Pracetorius et al[3]	3	17	-	M	Left mandible	Resection	-
Yoon et al[14]	4	22	Korean	F	Right posterior maxilla		No recurrence for 1 year
Lin et al	5	6	Taiwanese	F	Right mandible associated with impacted permanent teeth	Enucleation	No recurrence for 20 months.
	6	13	African-American	M	Left maxilla associated with impacted first molar	Excision	-
	7	22	W	M	Right mandible around impacted third molar	Curettage	-

Whether AF with COC may behave differently from AF or COC alone and the prognosis for this kind of combined lesion is still unclear. Unfortunately, this was not clarified from the reported cases so far due to limited numbers of cases and limited follow-up information (Table I). Although the treatment for COC and AF is usually conservative (enucleation for COC and excision or curettage for AF[16]), the treatment for reported AF with COC cases includes enucleation, excision, and resection (Table I). The case reported by Praetorius et al[3] was treated with resection apparently due to the authors' concept that the mural development of AF in COC required a more radical procedure. However, no evidence or follow-up information from the literature supports this point of view so far. Our case 1 showed no tendency for more aggressive biological behavior, with no recurrence of 20 months follow-up. On the other hand, a variety of other odontogenic tumors including ameloblastoma, AOT, ameloblastic fibro-odontoma, and odontoma have also been reported arising in COC.[6-10,12,13,15] With the available clinical information, the treatments for most of these lesions were also reported to be enucleation or excision.[7,8,11,13] Although most of these cases were focused on the histopathology and the follow-up information was not given,[7,8,10,15] Tajima et al[11] reported a case of ameloblastoma in COC, and Zeitoun et al[12] reported a case of AOT in COC, both without recurrence following treatment follow-up periods of 5 years and 18 months, respectively. While the clinical information may not be enough to determine the biological behavior and prognosis of this kind of combined lesion, the treatment is likely to be the same as for the associated neoplasm.[16]

Whether AF or COC arises first in cases of COC with AF is also still unknown. In the early discussion of odontogenic tumors associated with COC, Shear[5] has already pointed out this question. Altini and Farman[17] believed that the development of the COC component is a secondary event within the pre-existing odontogenic tumor. Praetorius et al[3] defined the COC with dental hard tissues in close relation to the lining epithelium as the "odontome producing type" and believed that the odontogenic tumor develops in the wall of the pre-existing COC. Takeda et al[16] investigated the histopathologic features of the satellite cysts and epithelial islands in the connective tissue wall of unilocular COC. Their results suggest that COC may arise *de novo* and is not a secondary phenomenon in pre-existing odontogenic tumors.

Although there are only four previously documented cases of COC with AF in the English literature, we report three additional cases found in Asia and North America and believe that the occurrence, although rare, may be more frequent than has been reported in the literature. Although enucleation and excision appeared to cure AF with COC, long-term follow-up data and additional cases are still needed to clarify the clinical significance of these lesions.

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Reprint requests:

Cheng-Chung Lin, BDS
Dept. of Oral Pathology
College of Dental Medicine
Kaohsiung Medical University,
100, Shih-Chuan 1st Road,
Kaohsiung City, 807, Taiwan
cclin99@hotmail.com