



Original Article

Odontogenic Fibroma: A Clinicopathological Study of 15 Cases

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Background/Purpose: Odontogenic fibroma (ODF) is a rare odontogenic tumor. It can be further divided into peripheral odontogenic fibroma (PODF) and central odontogenic fibroma (CODF). This retrospective study evaluated the clinical and histopathological features of 15 ODFs in Taiwanese patients.

Methods: Fifteen consecutive cases of ODF were collected from 1984 to 2009. The clinical data and microscopic features of these cases were reviewed and analyzed.

Results: Twelve PODFs were excised from six male and six female patients (mean age: 35 years) and three CODFs from two male and one female patients (mean age: 11 years). Eight of the 12 PODFs were found on the mandibular gingiva and four on the maxillary gingiva, with the most common site being the mandibular anterior and premolar region (5 cases). Two CODFs were located in the molar region of the mandible and one in the anterior maxilla. Two CODFs showed a mixed lesion and one a radiolucent lesion. No recurrence of the 15 ODFs was found after total excision or enucleation. Microscopically, 58.3% of the PODFs showed surface ulceration. Calcified foci composed of osteoid, cementoid, or cementicle-like materials were noted in all 15 ODFs. Nests or strands of odontogenic epithelium were found in all 15 ODFs. The stromal component was mainly fibro-collagenous in nine of the 12 PODFs, whereas two of the three CODFs contained predominantly myxomatous stroma.

Conclusion: PODFs occurred more commonly than CODFs. PODF showed an equal sex distribution and was found more frequently in patients in the third to fourth decades of life. The most commonly affected site was the mandibular gingiva, especially the anterior and premolar gingiva. Only three CODFs were found; therefore, we could not draw any conclusions about CODF in Taiwanese patients.

Key Words: central odontogenic fibroma, clinical features, histopathology, peripheral odontogenic fibroma

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Odontogenic fibroma (ODF) originates from odontogenic ectomesenchyme.¹ ODF can be further divided into central (intraosseous) odontogenic fibroma (CODF) and peripheral (extraosseous) odontogenic fibroma (PODF), according to the anatomical sites involved. ODF is defined by the World Health Organization (WHO) as, "a rare neoplasm characterized by varying amounts of inactive-looking odontogenic epithelium embedded in a mature, fibrous stroma."² In 40,000 consecutive oral biopsies from a Canadian population, there were only 25 CODFs (0.06%) and 36 PODFs (0.09%).³ Buchner et al have shown 23 PODFs (0.02%) and 16 CODFs (0.02%) among 91,178 oral lesions.⁴ Although PODF is relatively rare, it is the most common peripheral odontogenic tumor (51%, 23/45).⁵ Moreover, PODF is more common than its central counterpart by a ratio of 1.4:1.⁵

Microscopically, two histological types of ODF have been described by the WHO: epithelium-poor (or simple) and epithelium-rich (formerly complex or WHO) types.² The epithelium-poor type is characterized by a fibromyxoid stroma with scattered odontogenic epithelial islands and cords. Calcifications occur occasionally. The epithelium-rich type consists mainly of cellular, fibrous connective tissue stroma. Islands or strands of odontogenic epithelium are an integral component. Calcified foci that consist of osteoid, dentinoid, or cementum-like materials are often found. There have also been reported cases with coexistence of a giant cell granuloma-like component⁶ or the presence of granular cells in the stroma.⁷

ODF is considered to be an "elusive and controversial tumor" due to its rarity and the uncertainty of the number of distinct types.⁸ This suggests the need to add more data to elucidate further the clinicopathological features of the tumor. To the best of our knowledge, there has only been one series of 25 PODFs reported in Taiwanese patients.⁹ In the present study, we investigated the clinical and histopathological features of 15 ODFs and compared our results with those from previous studies of ODF.

Materials and Methods

The study group consisted of 15 cases of ODF, from January 1984 to December 2009, that were retrieved from the archives of the Department of Oral Pathology and Oral Diagnosis, National Taiwan University Hospital, Taipei, Taiwan. Demographic data, including the sex and age of patients, as well as the duration, location, size, clinical diagnosis, symptoms and signs, radiographic features, treatment, and recurrence of the lesions were obtained by reviewing the dental or medical charts. The upper and lower jawbones were divided into three regions: anterior (incisor/canine), premolar, and molar. The location of the lesion was determined by the region in which the major part of the lesion was located.

All surgical specimens were obtained from total excision or enucleation of the tumor. The specimens were then fixed in 10% neutral formalin for at least 24 hours, dehydrated in graded alcohol, and then embedded in paraffin. The tissue blocks were cut in serial sections of 5 μ m, and stained with hematoxylin and eosin. A review of the diagnosis and further analysis of the histopathological characteristics of the stained tissue sections was performed independently by two oral pathologists. The microscopic criteria for diagnosis of ODF included the presence of odontogenic epithelium in a fibrous or myxomatous stroma. Evidence of calcification might or might not have been discernible in the sections. Further examination and analysis of the histopathological characteristics focused on: the type and intactness of surface epithelium of PODF; the presence of epithelial down-growth of PODF; the composition of the tumor stroma (fibro-collagenous or myxomatous); inflammation (acute, chronic or mixed; mild, moderate, or severe) in the tumor stroma; the morphology (nests or strands) and distribution (sparse, less than one-third; moderate, between one- and two-thirds; abundant, more than two-thirds of the tumor section area) of odontogenic epithelium; evidence of juxta-epithelial hyalinization; type of calcified material (osteoid, cementoid, or cementicle-like); and the presence

of giant cells or granular cells in the stroma. The inter-observer reproducibility was 94%. In sections with discrepant assessments, a double-headed light microscope was used to achieve consensus.

Results

The 15 ODFs consisted of 12 PODFs and three CODFs. The mean age of the 15 patients (8 male and 7 female) was 30 years (range: 5–74 years). The demographic and clinical data of the 15 ODF patients are presented in Table 1. The histopathological features of the 12 PODFs and three CODFs are shown in Table 2.

PODF

Twelve PODFs were excised from six male and six female patients (mean age: 35 years; range: 15–74 years). PODFs were found more frequently in patients in the third to fourth decade of life (6 cases). PODFs occurred more commonly on the mandibular gingiva (8 cases) than on the maxillary gingiva (4 cases). The most common site was the mandibular anterior and premolar gingiva (5 cases), followed by the maxillary anterior gingiva (4 cases), and mandibular posterior gingiva (3 cases). The mean greatest diameter of the lesions was 1.9 cm (range: 0.8–5.5 cm).

A swelling or a mass was the only clinical presentation (Figure 1A). All PODFs showed no symptoms. The mean duration of the lesion was 18 (range, 5–48) months. None of the PODFs were correctly diagnosed at the time of initial clinical presentation. PODFs were most frequently misdiagnosed as pyogenic granulomas (7 cases). All 12 PODFs were treated by total surgical excision, and no recurrence was found.

Microscopically, the majority of the PODFs were covered by parakeratinized stratified squamous epithelium (11 cases) with focal ulceration (7 cases) and epithelial down-growth (11 cases). The stromal component of the lesion was predominantly fibro-collagenous (9 cases, Figures 1B–F) or predominantly myxomatous (3 cases). Eight

of the 12 PODFs showed a chronic inflammatory cell infiltrate and two a mixed acute and chronic inflammatory cell infiltrate in the stroma. The odontogenic epithelium was arranged in nests (12 cases, Figure 1B) or strands (11 cases, Figure 1C). Juxta-epithelial hyalinization (Figure 1B) was discernible in four PODFs. Calcifications were noted in all 12 PODFs. The mineralized components were identified as osteoid (8 cases, Figure 1D), cementoid (4 cases, Figure 1E), and/or cementicle-like (2 cases, Figure 1F) materials. No multinucleated giant cells or granular cells were found in any of the 12 PODFs.

CODF

Three CODFs were removed from two male and one female patients (mean age: 11 years; range: 5–19 years). Two CODFs were located in the mandibular posterior region and one in the maxillary anterior region. The mean greatest diameter of the lesions was 2.2 cm (range: 2–2.5 cm). The mean duration of the lesion was 12.7 months (range: 1–36 months). One CODF presented as a tumor mass, another as a painful swelling, and the other had no symptoms and signs. Radiographic features of the CODFs were either a mixed radiolucent and radiopaque lesion (2 cases) or a radiolucent lesion (1 case). One of our three CODFs (case 15) presented, by panoramic radiography, as a mixed radiolucent and radiopaque lesion with a well-defined sclerotic border in the right posterior and ascending ramus region of the mandible. It looked like a dentigerous cyst with the right lower second and third molars included within the lesion (Figure 2A). None of the CODFs were correctly diagnosed at the time of initial clinical presentation. All three lesions were treated by surgical enucleation, and no recurrence was found.

Microscopically, the stromal component was predominantly myxomatous (2 cases) or fibro-collagenous (1 case) (Figures 2B–E). The odontogenic epithelium was arranged in nests (3 cases, Figure 2B) or strands (2 cases, Figure 2C). Notably, dystrophic calcification in the nests of odontogenic epithelium was noted in one case (case 15,

Table 1. Demographic and clinical data of 15 patients with odontogenic fibroma

Peripheral odontogenic fibroma								
Case	Age (yr)/sex	Location (gingiva)	Greatest diameter (cm)	Symptoms and signs	Duration (mo)	Radiographic feature	Clinical diagnosis	Treatment
1	33/F	#13 to #15 area	3.0	Mass	6	NA	Pyogenic granuloma	Total excision
2	24/F	#46 area	1.0	Mass	48	NA	Papilloma	Total excision
3	25/F	#47 and #48 area	3.0	Mass	12	NA	Pyogenic granuloma	Total excision
4	17/M	#32 and #33 area	2.5	Swelling	5	NA	Fibroma	Total excision
5	15/F	#46 and #47 area	0.8	Swelling	24	NA	Pyogenic granuloma	Total excision
6	23/F	#11 and #12 area	0.8	Swelling	12	NA	Pyogenic granuloma	Total excision
7	40/M	#13 to #15 area	1.5	Swelling	6	NA	Pyogenic granuloma	Total excision
8	74/F	#33 to #43 area	5.5	Swelling	24	NA	Gingival fibromatosis	Total excision
9	34/M	#32 and #33 area	1.0	Swelling	24	NA	Soft tissue tumor	Total excision
10	51/M	#31 to #42 area	1.5	Swelling	12	NA	Pyogenic granuloma	Total excision
11	35/M	#33 and #34 area	1.2	Swelling	36	NA	Peripheral ossifying fibroma	Total excision
12	45/M	#23 and #24 area	1.0	Swelling	12	NA	Pyogenic granuloma	Total excision
Central odontogenic fibroma								
13	19/M	#38 area	2.0	None	1	Radiolucent	Ameloblastoma	Enucleation
14	5/F	#51 and #52 area	2.0	Mass	36	Mixed	Fibro-osseous lesion	Enucleation
15	10/M	#47 and #48 area	2.5	Painful swelling	1	Mixed	Dentigerous cyst	Enucleation

M = male; F = female; NA = not available.

Table 2. Histopathological features of 15 odontogenic fibromas

Peripheral odontogenic fibroma												
Case	Covering epithelium	Epithelial down-growth	Stroma	Inflammation	Odontogenic epithelium		Juxta-epithelial hyalinization	Calcified material		Cementicle-like		
					Nests	Strands		Osteoid	Cementoid			
1	Parakeratinized with focal ulceration	+	Myxomatous	Chronic, severe	+	+	-	+	-	-		
2	Parakeratinized	+	Fibro-collagenous	None	+	+	-	+	-	-		
3	Parakeratinized	+	Fibro-collagenous	Chronic, mild	+	+	-	-	-	-		
4	Parakeratinized with focal ulceration	-	Fibro-collagenous	Chronic, mild	+	-	-	+	+	+		
5	Parakeratinized with focal ulceration	+	Fibro-collagenous	None	+	+	+	+	-	-		
6	Parakeratinized	+	Fibro-collagenous	Acute and chronic	+	+	-	-	+	+		
7	Parakeratinized with focal ulceration	+	Myxomatous	Chronic, severe	+	+	+	-	+	-		
8	Parakeratinized	+	Fibro-collagenous	Chronic, moderate	+	+	-	+	-	-		
9	Parakeratinized	+	Myxomatous	Chronic, moderate	+	+	+	+	-	-		
10	Parakeratinized with focal ulceration	+	Fibro-collagenous	Acute and chronic	+	+	-	-	-	-		
11	Parakeratinized with focal ulceration	+	Fibro-collagenous	Chronic, mild	+	+	+	+	+	-		
12	Parakeratinized with focal ulceration	+	Fibro-collagenous	Chronic, severe	+	+	-	+	-	-		
Central odontogenic fibroma												
13	-	-	Myxomatous	None	+	+	-	-	+	-		
14	-	-	Fibro-collagenous	None	+	-	-	+	-	-		
15	-	-	Myxomatous	None	+	+	-	+	-	-		

M = male; F = female; NA = not available.

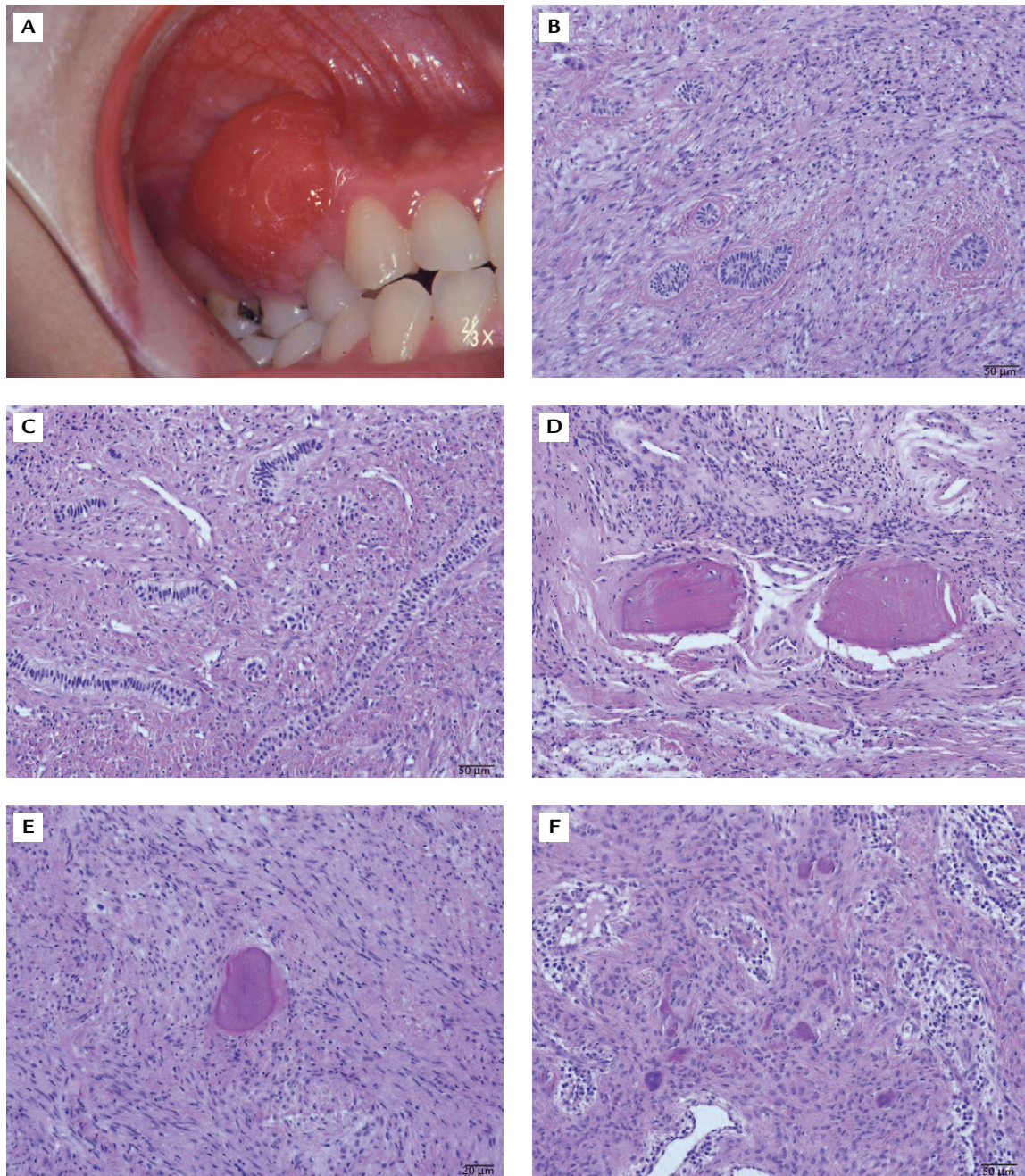


Figure 1. Clinical and histological photographs of peripheral odontogenic fibroma (PODF). (A) PODF (case 1) presenting as a red mass on the buccal gingiva of tooth #13 to tooth #15. (B) PODF (case 11) showing nests of odontogenic epithelium with juxta-epithelial hyalinization in a cellular, fibro-collagenous stroma. (C) PODF (case 11) exhibiting strands of odontogenic epithelium in a fibro-collagenous stroma. (D) PODF (case 12) demonstrating two calcified foci of osteoid in a cellular, fibro-collagenous stroma. (E) PODF (case 11) showing one calcified focus of cementoid in a cellular, fibro-collagenous stroma. (F) PODF (case 6) demonstrating several calcified foci of cementicle-like materials in a cellular, fibro-collagenous stroma.

Figure 2D). Calcifications were noted in all three cases. The mineralized components were identified as osteoid (2 cases, Figure 2E) or cementoid (1 case) material. No multinucleated giant cells or granular cells were found in any of the three CODFs.

Discussion

There have been a few retrospective studies on PODF.⁹⁻¹⁶ In general, our results were similar to those reported in other studies with regard to

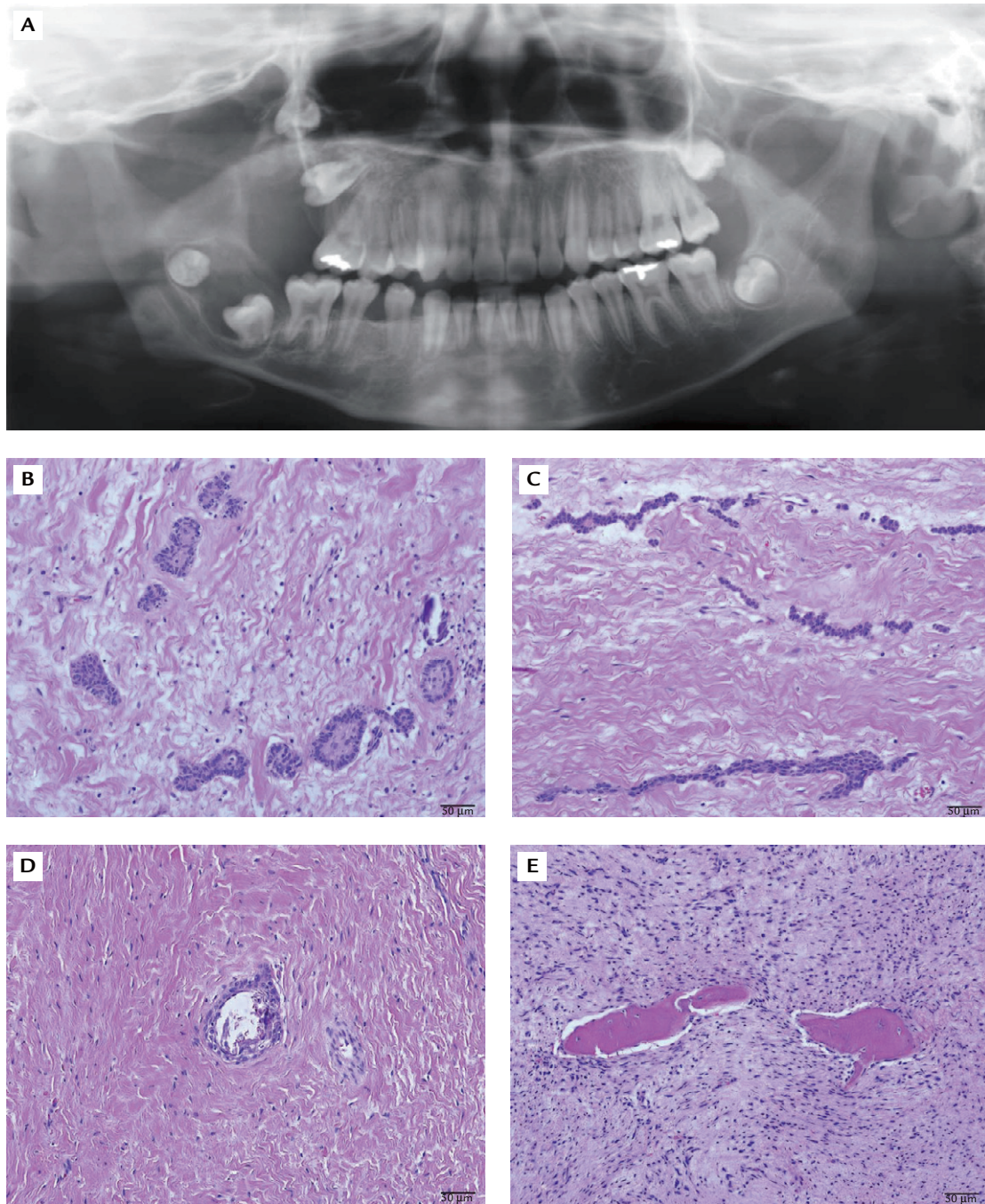


Figure 2. Radiographic and histological photographs of central odontogenic fibroma (CODF). (A) CODF (case 15) presenting as dentigerous cyst-like radiolucency, with a little radiopacity at the peripheral area, in the right posterior mandible. The right lower second and third molars were included in the lesion. (B) CODF (case 15) showing nests of odontogenic epithelium in a predominantly myxomatous stroma. (C) CODF (case 15) exhibiting strands of odontogenic epithelium in a fibro-collagenous stroma at the peripheral area of the lesion. (D) CODF (case 15) showing a focus of dystrophic calcification in a nest of odontogenic epithelium. (E) CODF (case 14) demonstrating two calcified foci of osteoid in a cellular, fibro-collagenous stroma.

patient sex^{10,11} and age,^{9,14,15} tumor size¹⁶ and location,¹⁵ signs and symptoms,^{12,15} initial diagnosis,^{9,14} and recurrence rate.^{9,11} Lin et al have performed a retrospective analysis of 25 PODFs in Taiwanese patients,⁹ and have shown a mean age of

37 years, with the peak incidence in the second to third decades of life. There was a predilection for female patients (female:male=1.8:1) and a site preponderance for the maxilla. Although the patients in the present study belonged to the same

racial group (Taiwanese), evident discrepancies in the sex or site of predilection were noted. We suggest that the discrepancies might be attributed to the differences in the sample size and the scarcity of the lesions.

The duration of PODF varies greatly. Buchner et al have found a duration of 3 months to 2 years.¹¹ Mulcahy and Dahl have shown a mean duration 45 months (range: 10 days to 10 years).¹² The present study demonstrated a mean duration of 18 months (range: 5–48 months). PODF is considered as a slow-growing benign tumor. Therefore, it is reasonable to have a lengthy duration of the lesions.

PODFs with diffuse manifestations, which mainly affect the maxillary and mandibular gingiva, have been reported by several authors.^{17,18} One of our patients (case 8) presented with gingival fibromatosis over the mandibular anterior teeth. Although the lesion was limited to the mandible, this lesion might represent a minor form of the diffuse type of PODE.

PODF is frequently misdiagnosed as pyogenic granuloma.^{9,14,19} Clinically, pyogenic granuloma is a smooth or lobulated mass. The surface of the lesion is usually ulcerated and the color can range from pink to purple.²⁰ These clinical features of pyogenic granuloma are very similar to those of PODF and make it difficult to differentiate it from PODE. In fact, PODF is also not easily distinguished from other common fibrous gingival lesions.¹ Manor et al have suggested that PODE, the most common peripheral odontogenic tumor, should be considered for the differential diagnosis of gingival lesions.¹⁹

Although PODFs are believed to have a low recurrence rate,¹ Daley and Wysocki¹⁵ have shown a significantly high recurrence rate of 38.9%. This discrepancy might have been due to differences in the racial group, sample or lesion size, and initial surgery used to remove the tumor.

The histopathological characteristics of our PODFs were similar to those reported by others with regard to the surface epithelium,^{10,12} presence of epithelial down-growth,^{10,14} stromal composition,¹⁰ inflammatory condition of the stroma,¹⁰ morphology of odontogenic epithelium,^{11,14,15}

presence of juxta-epithelial hyalinization,^{11,15} and type¹² and frequency^{9,10} of calcification. Under electron microscopy, the hyaline cuffing around epithelial islands (or juxta-epithelial hyalinization) represents a condensed layer of fibers that are arranged more or less parallel to the cell membrane.¹⁵ The significance of this phenomenon is unclear. The frequency of calcification in PODF has varied greatly from 38.9%¹⁵ to 100%.⁹ Only a few studies have demonstrated the presence of giant cells¹² or granular cells^{7,14,15} in the stroma.

Siar and Ng have reported the histopathological features of 46 PODFs in Malaysians.¹⁴ Of the 46 PODFs, 28.2% demonstrated surface ulceration, 80.4% basal cell budding, 86.9% a fibrous stroma, 10.9% a myxoid stroma, 2.2% granular differentiation of stromal cells, 63% a sparse amount of odontogenic epithelium, and 50% the presence of calcification. In contrast, our series of PODFs showed a higher frequency of surface ulceration (58.3%), epithelial down-growth (91.7%), myxoid stroma (25%), a sparse amount of odontogenic epithelium (100%), and the presence of calcification (100%), as well as a lower frequency of fibrous stroma (75%) and granular differentiation of stromal cells (0%).

With regard to CODF, the clinicopathological data have changed as more cases have been reported.²¹ CODF affects patients aged 4–80 years (mean: 40 years). A predilection for female patients and an equal distribution in the maxilla and mandible are frequently found.¹ However, a site preference for the anterior maxilla or for the posterior mandible has also been observed.¹

Kaffe and Buchner have reported that the majority of CODFs present as a unilocular (55%), radiolucent (88.2%) lesion with a well-defined border (73.3%).²² A mixed radiolucent and radiopaque lesion was found in only 10.7% of the cases in the mandible.²² We showed a mixed radiolucent and radiopaque lesion in two of our three CODFs. The discrepancy was probably due to the small sample size of CODFs in this series.

One of our three CODFs (case 15) presented, by panoramic radiography, as a dentigerous cyst-like radiolucent lesion with a little radiopacity. Daniels

also has found two CODFs,²¹ including one from his case report with a radiographic presentation of a dentigerous cyst-like lesion. Although our case number was limited, we suggest that CODF should be included in the differential diagnosis of pericoronal lesions in the posterior mandible.

There have been a limited number of studies that have focused on the histopathological features of CODF. Handlers et al have described the clinicopathological features of 19 CODF cases.²³ The tumors consisted mainly of collagenous stroma with or without focal myxoid areas (16/19, 84%). Only three cases contained predominantly myxomatous stroma. Odontogenic epithelium of varying amounts could be noted throughout the lesions. Calcifications were noted in only two of the 19 cases, and mild to moderate inflammation was seen in seven.

In conclusion, PODF occurred more commonly than CODE. Our PODF cases demonstrated an equal sex distribution, and they were found more frequently in patients in the third to fourth decade of life. The most commonly affected site was the mandibular gingiva, especially the anterior and premolar gingiva. A swelling or a mass was the most common initial clinical presentation. Only three CODF cases were found in this study; therefore, we could not draw any conclusion about CODF in Taiwanese patients.

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