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EMANUEL MENDES SOUSA

FIBROMA ODONTOGÊNICO CENTRAL:
ESTUDO CLÍNICO-PATOLÓGICO E IMUNO-HISTOQUÍMICO
DE 5 NOVOS CASOS

RIO DE JANEIRO
Março, 2018

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Dissertação de Mestrado apresentada ao Programa de Pós-Graduação em Clínica Odontológica, da Faculdade de Odontologia, da Universidade Federal do Rio de Janeiro, como requisito parcial à obtenção do título de Mestre.

Orientador: Prof. Mário José Romañach Gonzalez Sobrinho

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DEDICATÓRIA

Dedico esse trabalho a minha esposa Mariana Thiel. Por todo amor, incentivo, dedicação e esforço para que me tornasse um profissional cada vez mais qualificado.

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EPÍGRAFE

“Feliz aquele que transfere o que sabe e aprende o que ensina”.

Cora Coralina

RESUMO

O objetivo deste estudo é descrever as características clinicopatológicas e imuno-histoquímicas de 5 novos casos de Fibroma Odontogênico Central (FOC). Cinco casos diagnosticados como FOC foram obtidos ao longo de um período de 20 anos (1997 a 2017) a partir dos arquivos do Laboratório de Patologia Oral do Departamento de Patologia e Diagnóstico Oral da Faculdade de Odontologia da Universidade Federal do Rio de Janeiro (FO-UFRJ), Brasil. Os achados clínicos e radiográficos dos pacientes foram coletados nos prontuários dos pacientes. Todos os pacientes eram mulheres com média de idade de 42,2 anos (variando de 19 a 63 anos). Quatro casos (80%) afetaram a porção posterior da mandíbula e um caso (20%) ocorreu na região posterior da maxila. Dois casos foram classificados como FOC convencional rico em epitélio; os outros três casos foram diagnosticados como FOC associado ao GCCG, variante de células granulares do FOC e variante ossificante do FOC. Radiograficamente, os tumores apareceram como lesões radiolúcidas multiloculares (60%), biloculares (20%) e uniloculares (20%) com expansão e ruptura das corticais ósseas (80%) e deslocamento dentário (40%). Todos os casos foram tratados por excisão cirúrgica conservadora, sem evidência de recidiva após acompanhamento de 7 meses a 15 anos. As ilhas epiteliais de todos os casos foram positivas para citoqueratina AE1/AE3 em padrão citoplasmático e CD138 em padrão de membrana. As células estromais estreladas e fusiformes foram negativas para α-actina de músculo liso e positivas para citoqueratina AE1/AE3 em um caso. Células dendríticas de Langerhans entrelaçadas ao redor de ilhas epiteliais foram evidenciadas por CD1a em um caso, o qual mostrou células granulares estromais positivas para CD138 e CD163. O índice de Ki-67 foi baixo (<1%) nos componentes epiteliais e estromais de todos os casos. Os FOCs são tumores odontogênicos incomuns de morfologia típica e comportamento clínico não agressivo. Na presente série de casos, FOCs afetaram as regiões posteriores da mandíbula (quatro casos) e maxila (um caso) de cinco mulheres de meia-idade do Brasil.

Palavras-chave: Fibroma odontogênico central, histopatologia, imuno-histoquímica

ABSTRACT

The aim of this study is to describe the clinicopathological features of 5 new cases of central odontogenic fibroma (COF) and the immunohistochemical findings of 4 of them. Five cases diagnosed as COF were retrieved over a 20-year period (1997 to 2017) from the files of the Oral Pathology Laboratory of the Department of Oral Diagnosis and Pathology, School of Dentistry of the Federal University of Rio de Janeiro – Brazil. Clinical and radiographic findings of the patients were collected from the patients' charts. All patients were women with mean age of 42.2 years (ranging from 19 to 63 years). Four cases (80%) affected the posterior mandible and one case (20%) occurred in the posterior maxilla. Two cases were classified as epithelial-rich conventional COF; the other three cases were diagnosed as COF associated to CGCG, granular cell variant of COF, and ossifying variant of COF. Tumors appeared as multilocular (60%), bilocular (20%) and unilocular (20%) radiolucencies with expansion and rupture of bone cortices (80%) and tooth displacement (40%). All cases were treated by conservative surgical excision, with no evidence of recurrence after follow-up ranging from 7 months to 15 years. The epithelial islands of all cases were positive for cytokeratin AE1/AE3 in cytoplasmic pattern and CD138 in membrane pattern. The stellate and spindle-shaped stromal cells were negative for α-smooth muscle actin (SMA), and positive for cytokeratin AE1/AE3 in one case. Langerhans dendritic cells entwined around epithelial islands were highlighted by CD1a in one case, which showed stromal granular cells positive for CD138 and CD163. Ki-67 index was low (<1%) in both epithelial and stromal components of all cases. COFs are uncommon odontogenic tumors of typical bland morphology and non-aggressive clinical behavior. In the present series, COFs affected the posterior regions of mandible (four cases) and maxilla (one case) of five middle-aged women from Brazil.

Key words: Central odontogenic fibroma, histopathology, immunohistochemistry

SUMÁRIO

1. INTRODUÇÃO

Segundo a classificação da Organização Mundial de Saúde, o fibroma odontogênico central é definido como um tumor odontogênico benigno originado do ectomesênquima e caracterizado por apresentar quantidade variável de epitélio odontogênico inativo em meio a um estroma de tecido conjuntivo fibroso. É considerado uma neoplasia rara que representa de 0.1% a 5,5% de todos os tumores odontogênicos na maioria dos estudos retrospectivos encontrados na literatura.[1-2]

Acomete pacientes em uma ampla faixa etária, sendo mais frequente entre a 2ª e 4ª década de vida, com maior prevalência em indivíduos do gênero feminino. Apresenta-se, na maioria dos casos, como uma lesão de crescimento lento e assintomático que pode promover abaulamento das corticais ósseas adjacentes. A frequência deste tumor é semelhante na maxila e na mandíbula, sendo que na maxila localiza-se predominantemente na região anterior, enquanto na mandíbula, o local de maior ocorrência é a região posterior.[1-2]

Radiograficamente, caracteriza-se como uma imagem radiolúcida uni ou multilocular com margens bem definidas, podendo apresentar focos de calcificação em seu interior. O fibroma odontogênico central é subdividido histologicamente em tipo simples (pobre em epitélio) e tipo OMS (rico em epitélio), além de apresentar variantes como ossificante ou células granulares.[1-2] Histopatologicamente, a característica mais consistente é um tumor predominantemente composto por colágeno maduro com numerosos fibroblastos intercalados e presença de pequenos ninhos e/ou cordões inativos de epitélio odontogênico. A lesão responde bem ao tratamento cirúrgico conservador por enucleação associado à curetagem, sendo as recidivas muito incomuns.[1-4]

A maioria dos casos de fibroma odontogênico central têm sido reportados na literatura em relatos simples de casos clínicos ou pequenas séries de casos.[5-14] Embora existam estudos de séries de casos sobre fibroma odontogênico central, nenhum foi realizado até o presente momento na cidade do Rio de Janeiro. Além da coleta de dados no laboratório de Patologia Oral da FO-UFRJ, uma revisão da literatura de todas as séries com mais de 5 casos de fibroma odontogênico central foi realizada, incluindo dados como gênero, idade, localização da lesão, diagnóstico definitivo, aspectos clínicos, aspectos radiográficos, histopatológicos, imuno-histoquímicos e tratamento.

2. PROPOSIÇÃO

O presente estudo tem como objetivo realizar um estudo clínicopatológico e imuno-histoquímico de 5 casos de fibromas odontogênicos centrais diagnosticados no Departamento de Patologia e Diagnóstico Oral da Faculdade de Odontologia da Universidade do Rio de Janeiro (FO-UFRJ) no período compreendido entre 1997 e 2017 além de uma revisão da literatura das principais séries de casos publicados.

3. ARTIGO

CENTRAL ODONTOGENIC FIBROMA: A CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY OF 5 NEW CASES

Running title: Central odontogenic fibroma

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ABSTRACT

The aim of this study is to describe the clinicopathological features of 5 new cases of COF and the immunohistochemical findings of 4 of them. Five cases diagnosed as central odontogenic fibroma (COF) were retrieved over a 20-year period (1997 to 2017) from the files of the Oral Pathology Laboratory of the Department of Oral Diagnosis and Pathology, School of Dentistry of the Federal University of Rio de Janeiro – Brazil. Clinical and radiographic findings of the patients were collected from the patients' charts. All patients were women with mean age of 42.2 years (ranging from 19 to 63 years). Four cases (80%) affected the posterior mandible and one case (20%) occurred in the posterior maxilla. Two cases were classified as epithelial-rich conventional COF; the other three cases were diagnosed as COF associated to CGCG, granular cell variant of COF, and ossifying variant of COF. Tumors appeared as multilocular (60%), bilocular (20%) and unilocular (20%) radiolucencies with expansion and rupture of bone cortices (80%) and tooth displacement (40%). All cases were treated by conservative surgical excision, with no evidence of recurrence after follow-up ranging from 7 months to 15 years. The epithelial islands of all cases were positive for cytokeratin AE1/AE3 in cytoplasmic pattern and CD138 in membrane pattern. The stellate and spindle-shaped stromal cells were negative for α-smooth muscle actin (SMA), and positive for cytokeratin AE1/AE3 in one case. Langerhans dendritic cells entwined around epithelial islands were highlighted by CD1a in one case, which showed stromal granular cells positive for CD138 and CD163. Ki-67 index was low (<1%) in both epithelial and stromal components of all cases. COFs are uncommon odontogenic tumors of typical bland morphology and non-aggressive clinical behavior. The present series of COFs affected the posterior regions of mandible (four cases) and maxilla (one case) of five middle-aged women from Brazil.

Key words: Central odontogenic fibroma, histopathology, immunohistochemistry.

INTRODUCTION

Central odontogenic fibroma (COF) is an uncommon and poorly understood benign mesenchymal odontogenic tumor. COF usually appears as an asymptomatic swelling in the tooth-bearing areas of the anterior maxilla and the posterior mandible of women in second to third decades of life.[1] The radiographic appearance consists of a well-defined and corticated unilocular or multilocular radiolucency, occasionally containing radiopaque foci, showing divergence or resorption of adjacent teeth.[1-2] Most patients with COF are treated by conservative surgical excision with the attempt of maintenance of associated teeth, recurrence being rarely reported.[1-4]

Microscopically, COF exhibits non-encapsulated proliferation of a cellular fibromyxoid tissue with presence of many (epithelium-rich type) to scattered (epithelium-poor type) inactive-looking odontogenic epithelial islands and cords, which may be even absent in the latter.[1-5] In addition, different microscopical findings have been reported within the spectrum of COF, such as variable amounts of stromal granular cells intermingled with epithelial islands, deposition of cementoid calcifications and/or amyloid-like material closely related to langerhans dendritic cells entwined around epithelial islands, and COF associated with central giant cell granuloma.[1,5-14]

To the best of our knowledge, approximately 180 cases of COF have been reported in the English-language literature to date, with only few series of cases[5-13] (**Table 1**). The aim of this study is to describe the clinicopathological features of 5 new cases of COF and the immunohistochemical findings of 4 of them.

MATERIAL AND METHODS

Five cases diagnosed as central odontogenic fibroma (COF) were retrieved over a 20-year period (1997 to 2017) from the files of the Oral Pathology Laboratory of the Department of Oral Diagnosis and Pathology, School of Dentistry of the Federal University of Rio de Janeiro – Brazil. Clinical and radiographic findings of the patients were collected from the patients' charts and tabulated in Microsoft Excel® for data analysis. The diagnosis of COF of each case was confirmed after reviewing of hematoxylin and eosin-stained sections according to the current WHO criteria.[1] Immunohistochemical analysis was performed in formalin-fixed paraffin-embedded tissues (FFPET) from diagnostic biopsies of four cases, with antibodies directed to cytokeratin AE1/AE3 (dilution 1:400, clone AE1/AE3, Dako, Carpinteria), CD1a (dilution 1:500, clone 010, Dako, Carpinteria, CA, USA), CD138 (dilution 1:200, clone MI15, Dako, Carpinteria, CA, USA), smooth muscle actin (dilution 1:200, clone 1A4, Dako, Carpinteria, CA, USA), and Ki-67 (dilution 1:200, clone MIB-1, Dako, Carpinteria, CA, USA). The antibodies CD68 (dilution 1:300, clone KP-1, Dako, Carpinteria, CA, USA) and CD163 (dilution 1:300, clone 10D6, Leica Biosystems, USA) were performed only in the granular cell-predominant COF case. Paraffin sections (3 μm thick, on silane-coated histologic slides) from FFPET were dehydrated and deparaffinized according to standard procedures. Heat-induced antigen retrieval was then performed. The slides were incubated overnight with primary antibodies and the secondary antibody used was EnVision®+Dual Link/Peroxidase (Dakocytomation®). Positive and negative controls were included in all reactions. Expressions of the immunomarkers were recorded as negative or positive, and the expression of Ki-67 (nuclear positivity) was evaluated in 2 selected areas representative of the tumor using a 40X objective. The labeling index for each case was expressed as a percentage, expressing the number of positive tumor cells

per total number of tumor cells. A descriptive analysis of the clinical, radiographic, morphologic and immunohistochemical features are described and discussed in the present study.

RESULTS

The clinical findings of five COF cases are presented in **Table 2**. All patients were women whose ages ranged from 19 to 63 years (mean age of 42.2 years). Four cases (80%) affected the posterior mandible and one case (20%) occurred in the posterior maxilla. Asymptomatic swelling was observed in all cases, expansion and rupture of cortical bone were found in four cases (80%), and tooth displacement in two cases (40%). Radiographically, three cases were multilocular (60%), one bilocular (20%) and one unilocular (20%). Three tumors (60%) were located between the roots of adjacent teeth, one in a pericoronary position (20%) and one in an edentulous body of the mandible (20%). Size ranged from 4.5 to 2 cm, with a mean of 3.4 cm in largest dimension. All cases were treated by conservative surgical excision, with no evidence of recurrence after follow-up ranging from 7 months to 15 years. Two cases were classified as epithelial-rich COF showing cellular fibroblastic connective tissue with abundant islands and strands of odontogenic epithelium, which sometimes showed vacuolated clear cells (**Figures 1 and 2**). The other three cases were diagnosed as COF associated to CGCG (**Figure 3**), granular cell variant of COF (**Figures 4 and 5**), and ossifying variant of COF (**Figures 6 and 7**), the latter showing many foci of dentinoid/cementoid calcification. The epithelial islands of all cases were positive for cytokeratin AE1/AE3 in cytoplasmic pattern and CD138 in membrane pattern. The stellate and spindle-shaped stromal cells were negative for α-smooth muscle actin (SMA) in all cases, and positive for cytokeratin AE1/AE3 in one case of epithelial-rich COF (**Figure 2**). Langerhans dendritic cells entwined around

epithelial islands were highlighted by CD1a in one case of granular cell variant of COF, which showed stromal granular cells positive for CD138 and CD163 (**Figure 5**). Ki-67 index was low (<1%) in both epithelial and stromal components of all cases.

DISCUSSION

COF accounts for less than 5% of all odontogenic tumors but its real incidence may be lower because COF have previously been confused with hyperplastic dental follicles. Although it is difficult to determine whether a case is COF or hyperplastic dental follicle only by interpreting an article, and assuming that some occasional old cases may not be truly COFs, we have found nine studies with more than five cases of COF in the English-language literature.[5-13] Tumors affected predominantly women (43 cases, 55.8%) in comparison to men (34 cases, 44.2%) with average age of 30.5, varying from five to 80 years. The main radiographic appearance of COF is of a well-defined multilocular radiolucency measuring from 1 to 4 cm, with slight predilection for the mandible (50 cases, 51.5%) when compared with the maxilla (47 cases, 48.5%).[7] The posterior region of the mandible (33 cases, 34%) was predominantly affected, followed by posterior maxilla (22 cases, 22.6%), anterior maxilla (12 cases, 12.3%), and anterior mandible (4 cases, 4.1%). Additionally, twenty-six cases were equally located in unspecified sites of the mandible (13 cases, 13.5%) and maxilla (13 cases, 13.5%). We herein present five illustrative COF cases from Brazil, as asymptomatic swellings with radiographic appearance of multilocular or bilocular radiolucencies affecting mainly the posterior mandible of women with median age of 42.2 years.

Microscopically, COF is characterized by variable amounts of inactive-looking odontogenic epithelium and calcifications in a mature fibrous connective tissue.[1] From the present five cases, cases 1 and 2 were conventional epithelium-rich COFs intimately

related with the roots of posterior lower teeth, without resorption. Case 3 showed association with multinucleate giant cells in a hemorrhagic stroma in an edentulous posterior lower alveolar ridge, similarly to that described by Odell *et al.*[8] and Tosios *et al.*[9] Case 4 was predominantly composed by granular cells, with occasional calcifications, located between the roots of maxillary molars. Case 5 was associated with the crown of an unerupted third molar with size large enough to differentiate from a hyperplastic dental follicle, showing limited amount of odontogenic epithelial islands and striking formation of dentinoid or cementoid calcifications, which led us to consider it an example of ossifying variant of central odontogenic fibroma, as described by Eversole.[10]

Immunohistochemistry findings of COF may be useful in order to highlight the epithelial component of epithelium-poor lesions or to contribute on the understanding of its pathogenesis. Cytokeratin AE1/AE3 was strongly positive in odontogenic epithelium of all present cases, and interestingly also in stellate and spindle-shaped connective tissue cells of case 1, a finding not described before that may indicate an origin from primitive odontogenic ectomesenchyme. CD138 (syndecan-1) is a cell surface proteoglycan that modulates epithelial-stromal interactions, cell-cell adhesion, and cell proliferation. In the present study, odontogenic epithelium showed membrane positivity for CD138 in all cases; and interestingly, the stromal granular cells of case 4 were also positive in a cytoplasmic pattern, as also observed by Mesquita *et al.*,[14] indicating reciprocal interactions between odontogenic epithelium and granular cells. CD1a-positive Langerhans cells within the odontogenic epithelial islands were found in one case of granular cell variant of COF, as also previously described by Mosqueda-Taylor *et al.*,[11] Mesquita *et al.*,[14] and Eversole.[10] Indeed, the granular cells were also positive in membrane pattern for CD163, a monocyte/macrophage-derived differentiation antigen limited to neoplasms of monocyte/histiocyte derivation, and negative for CD68,

indicating a histiocytic differentiation of stromal granular cells of COF for the first time. Ki-67 index was less than 1% confirming the non-aggressive behavior of the lesion.

All of present cases were treated conservatively, with no recurrence being observed after an average of 51.6 months of follow-up, but associated teeth were removed in continuity with tumors of cases 2 and 5. Similarly, only three[8,13] from 98 cases of COF reviewed from nine series of the literature showed recurrences, indicating a non-aggressive behavior of COFs, despite the possibility of loss of associated tooth due commitment of periodontal ligament by the tumor.

In summary, COFs are uncommon odontogenic tumors of typical bland morphology and non-aggressive clinical behavior. In the present series, COFs affected the posterior regions of mandible (four cases) and maxilla (one case) of five middle-aged women from Brazil. Clinical and radiographical correlation are recommended to avoid microscopical misinterpretation of this intriguing entity, particularly in those COFs with predominance of granular cells, multinucleate giant cells, and calcifications.

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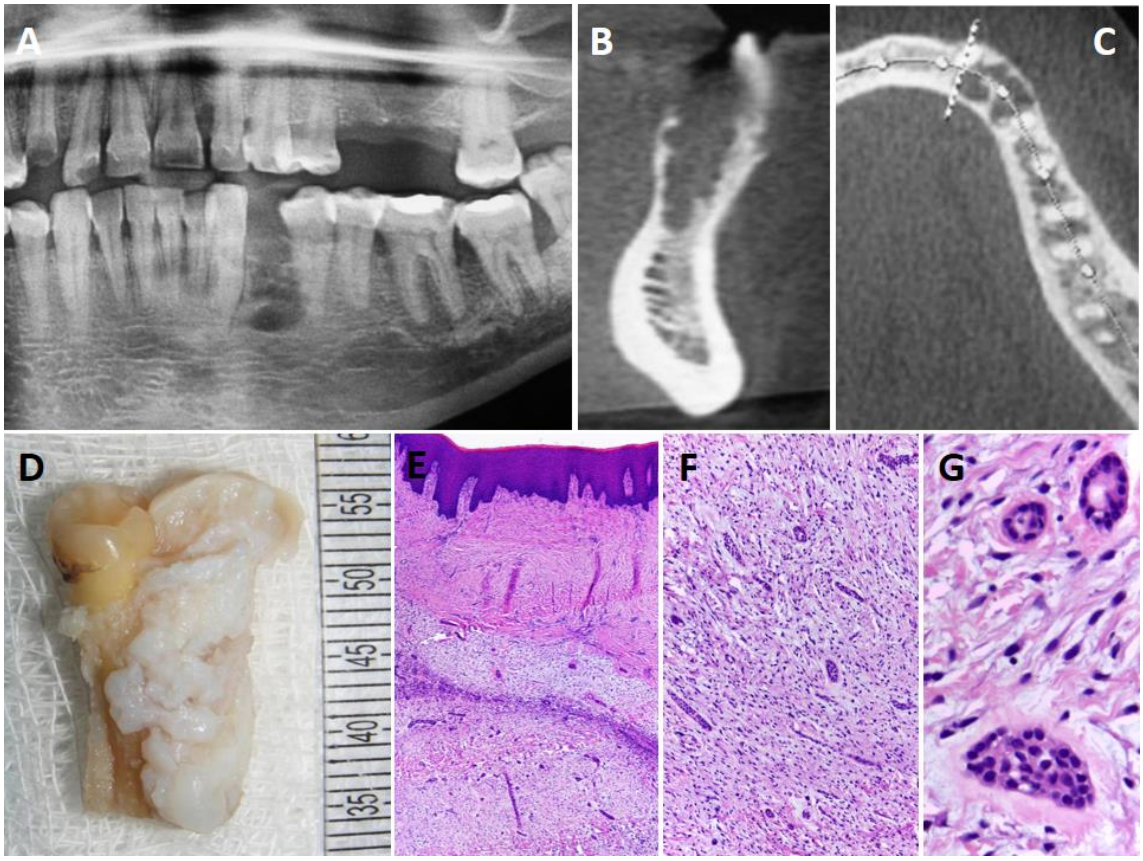

Figure 1: Radiographic and morphologic features of epithelial-rich central odontogenic fibroma (case 2): (A) Panoramic radiograph showing a multilocular radiolucency in the left posterior mandible between the roots of canine and first premolar. **(B-C)** CT images showing expansion and disruption of bone cortices. **(D)** Gross appearance showing an irregular whitish myxoid mass measuring 2 cm. Note the close relation between the lesion and the first premolar root. **(E)** Cellular fibroblastic connective tissue with abundant islands of odontogenic epithelium is observed in the deep areas of connective tissue (HE, 40X). **(F-G)** Nests of odontogenic epithelium with juxta-epithelial hyalinization in a cellular, fibrocollagenous stroma is also observed (H&E, F – 100X, G – 400X).

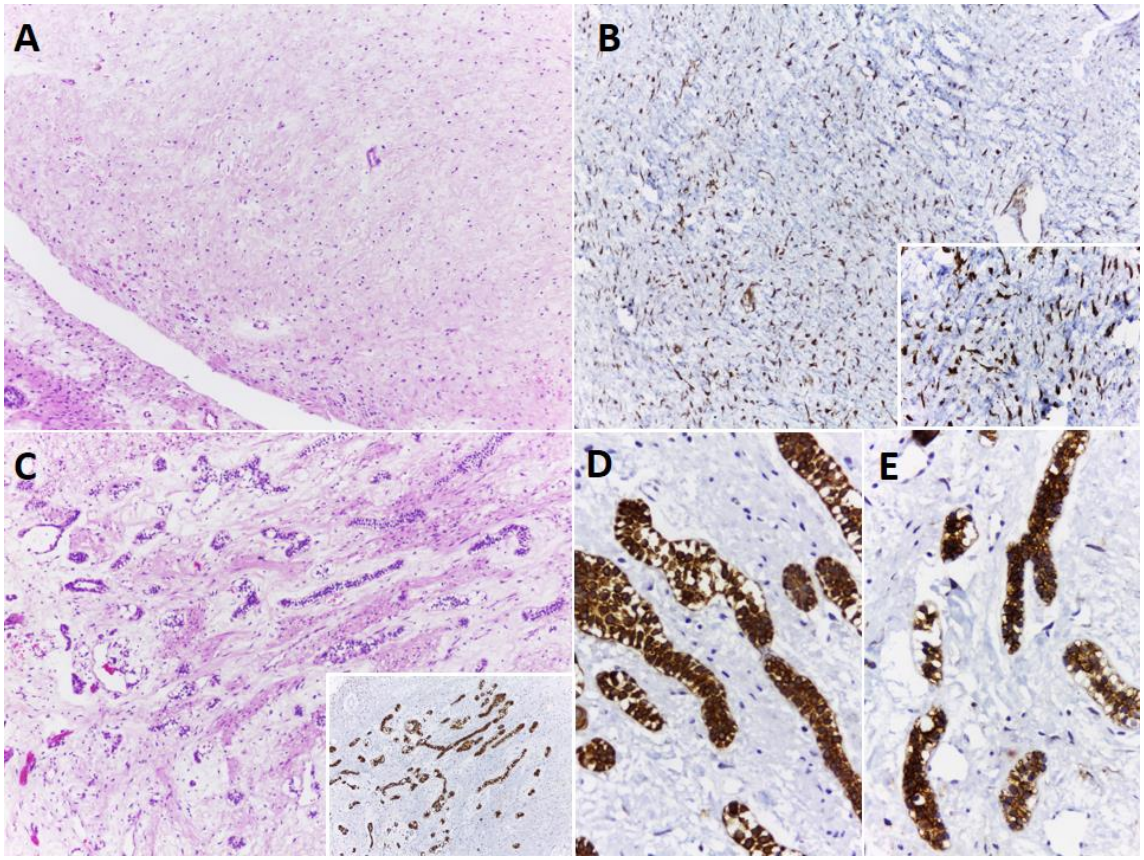

Figure 2: Histopathological and immunohistochemical features of epithelial-rich central odontogenic fibroma (case 1): (A) Myxoid area containing many spindle-shaped, stellate, and rounded cells with scant epithelial islands (H&E, 100X). **(B)** The stellate and spindle-shaped connective tissue cells were positive for cytokeratin AE1/AE3 (immunoperoxidase, 100X). **(C)** Cellular fibroblastic connective tissue area with abundant islands and strands of odontogenic epithelium, some of them displaying vacuolated cells (H&E, 100X). The epithelial islands were positive for **(D)** AE1/AE3 and **(E)** CD138 (Immunoperoxidase, 400X).

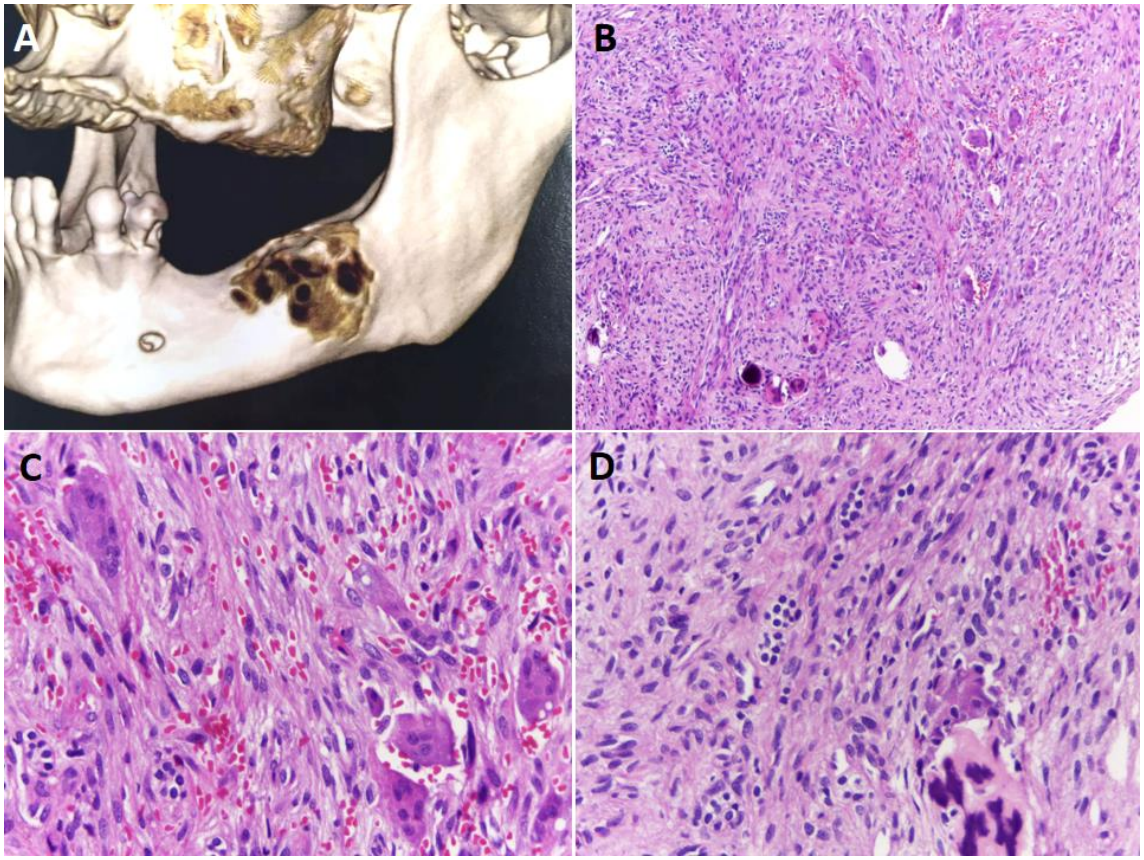

Figure 3: Radiographic and histopathological features of hybrid central odontogenic fibroma with central giant cell lesion (case 3): (A) CT scan showing a multilocular radiolucency in the left edentulous alveolar ridge. **(B)** Fibroblastic connective tissue showing multinucleated giant cells and epithelial islands of odontogenic cells with small and round foci of calcification. **(C-D)** Multinucleated giant cells clearly intermingled with epithelial islands of odontogenic cells in a cellular fibrous stroma is observed. Hemosiderin and foci of calcification are also noted (H&E, B – 100X, C-D – 400X).

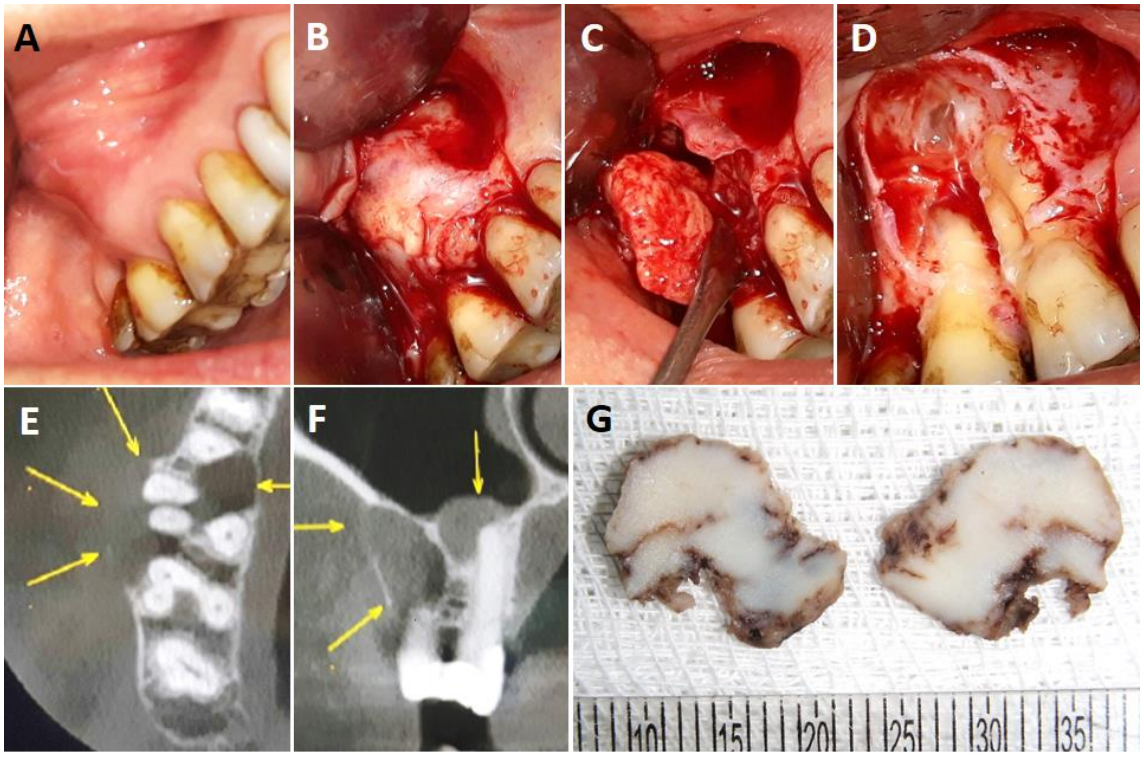

Figure 4: Clinical and radiographic features of central odontogenic fibroma, granular cell variant (case 4): (A) Intraoral examination revealed expansion of vestibular bone cortice of posterior maxilla without tooth displacement. **(B-D)** Intraoperative images showing the close relation between the lesion and roots of involved teeth. **(E-F)** CT images showing a perirradicular bilocular radiolucency in the posterior maxilla with expansion and disruption of bone cortices. **(G)** Gross appearance showing a smooth-surfaced nodular mass measuring 1 cm, with whitish cut surface and fibroelastic consistency.

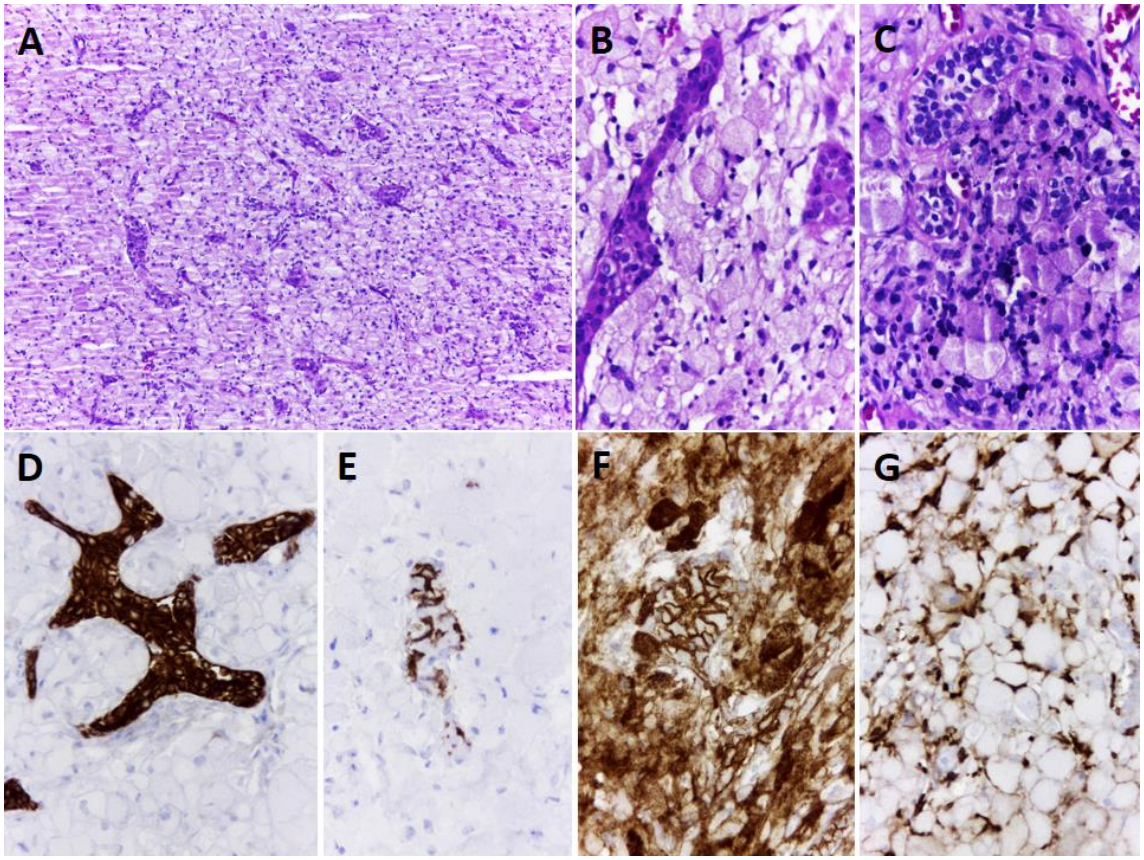

Figure 5: Histopathological and immunohistochemical features of central odontogenic fibroma, granular cell variant (case 4): (A-C) Microscopic findings characterized by fibrous connective tissue showing large round cells with abundant cytoplasm containing eosinophilic granules associated with islands and cords of odontogenic epithelium. **(C)** Small round foci of calcified material were also observed (H&E, A – 40X, B-C – 400X). The epithelial islands were positive for **(D)** AE1/AE3 and **(E)** CD1a. **(F)** Positive expression of CD138 in both granular cells and odontogenic epithelium. **(G)** The granular cells were also positive for CD163 (Immunoperoxidase, D-E – 400X).

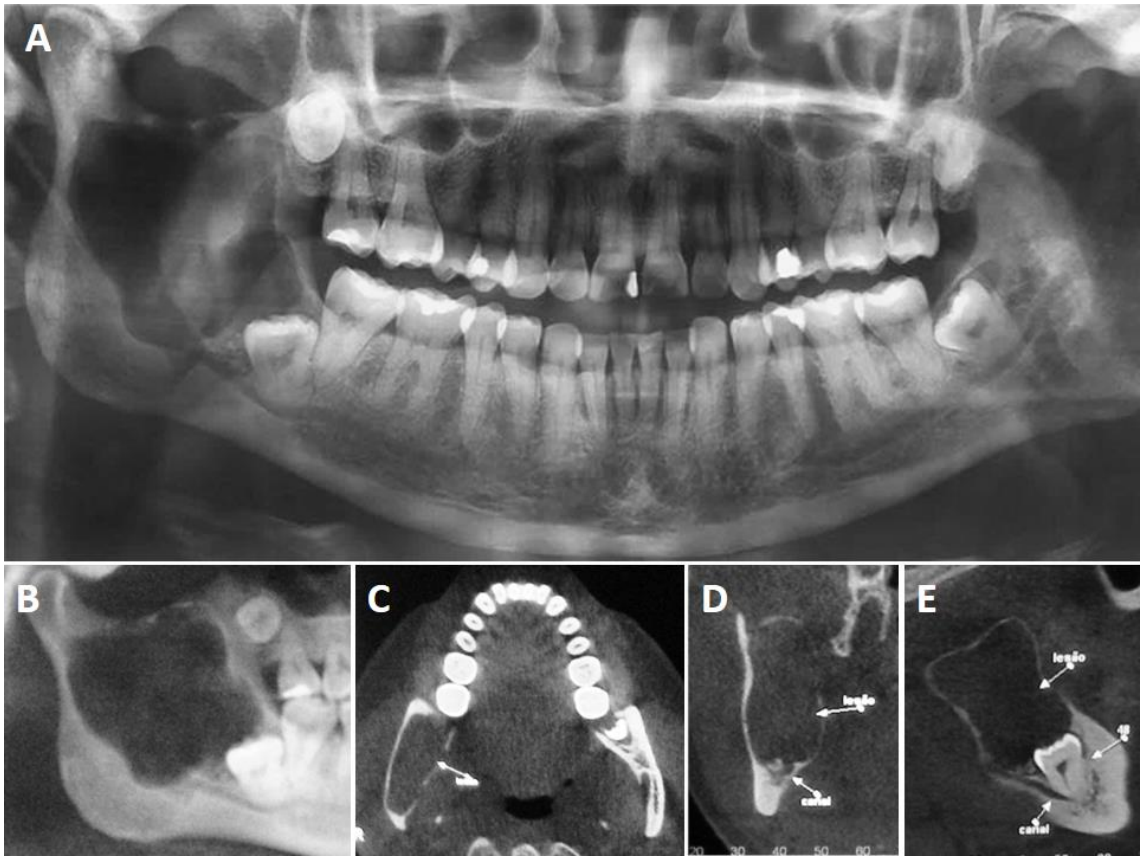

Figure 6: Radiographic features of central odontogenic fibroma, ossifying variant (case 5): (A) Panoramic radiograph showing a unilocular radiolucency in the right posterior mandible, angle and ascending ramus associated with crown of #36. **(B-E)** CT images showing a pericoronal unilocular radiolucency with expansion and disruption of bone cortices.

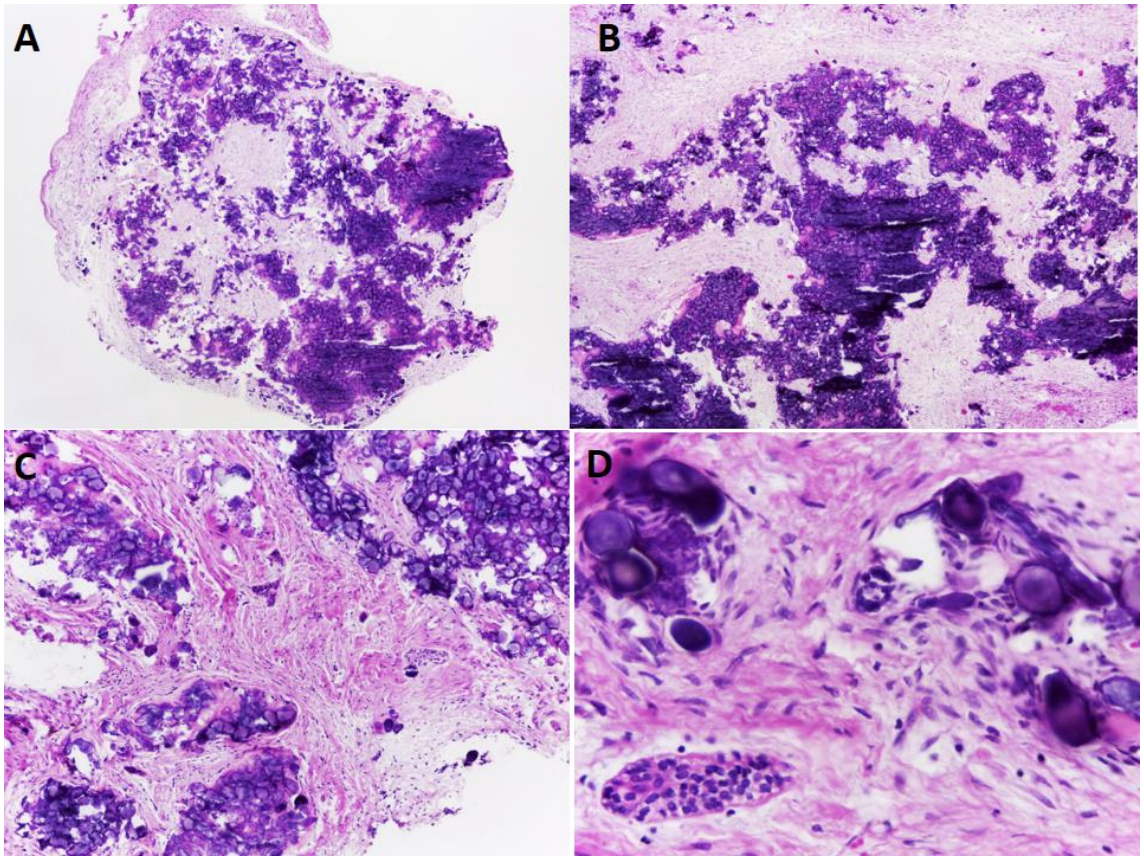

Figure 7: Histopathological features of central odontogenic fibroma, ossifying variant (case 5): (A-C) Large calcified foci of mineralized materials in a cellular, fibrocollagenous stroma were observed. **(D)** Large foci of calcifications associated with odontogenic epithelium (HE, A – 40X, B-C – 100X, D – 400X).

Table 1. Summarized clinicopathologic data from series of central odontogenic fibroma cases published in the English-language literature.

	Authors (year), country/region	N	Gnd (F:M)	Age (avg)	Site (n)		Subtype	Radiographic features	Recurrence, Follow-up (months)
					Mandible	Maxilla			
1	Doyle (1985)[5], USA	6	4F:2M (2:1)	16-59 (40.5)	Mand, post (5)	Max, ant (1)	Conventional COF	RL (4) Mixed RL-RO (2)	No, 12-36 (26.4)
2	Handlers (1991)[6], USA	19	14F:5M (2.8:1)	14-72 (37.2)	Mand, post (2) Mand, ant (1)	Max, post (8) Max, ant (8)	Conventional COF	Multilocular RL (6) Unilocular RL(2)	No, 3-36 (19)
3	Kaffe and Buchner (1994)[7], Israel	5	3F:2M (1.5:1)	9-18 (14.6)	Mand, post (3)	Max, post (2)	Conventional COF	Well defined unilocular RL (2) Well defined multilocular RL (2) Poorly defined not loculated RL (2)	Not available
4	Odell (1997)[8], UK	8	7F:1M (7:1)	5-50 (26.3)	Mand, post (5) Mand, unsp (1)	Max, post (2)	COF-CGCG	Unilocular RL (3) Multilocular RL (1)	Yes, after 3y (2 cases) 36
5	Tosios (2008)[9], USA	7	1F:6M (1:6)	15-59 (37.1)	Mand, post (7)	-	COF-CGCG	Well defined RL (7)	No, 28-117 (60.6)
6	Mosqueda-Taylor (2011)[11], Latin America	14	8F:6M (1.3:1)	14-51 (31.8)	Mand, post (4) Mand, ant (2)	Max, post (6) Max, ant (2)	ConventionalCOF	Well defined unilocular RL (10) Well defined multilocular RL (2) Partially defined multilocular RL (2)	No, 3-356 (52.5)
7	Eversole (2011)[10], USA	25	(1.5:1)	10-80 (40.1)	Mand, unsp (12)	Max, unsp (13)	Conventional COF (17) Amyloid/dendritic cell associated COF (4) COF-CGCG (2) COF, ossifying variant (2)	Well defined RL (25)	Not available, (40.8)
8	Hrichi (2012)[12], Spain	8	3F:5M (1:1.6)	11-38 (19.8)	Mand, post (5) Mand, ant (1)	Max, post (2)	Conventional COF	Unilocular RL (7) Multilocular Mixed RL-RO (1)	No, 60
9	Wu (2013)[13], Taiwan	6	5M	10-51 (27.8)	Mand, post (2)	Max, post (2) Max, ant (1)	Conventional COF	Not available	Yes, after 8 months (1case), 10-79
10	Present study, Brazil	5	5F	19-63 (42.2)	Mand, post (4)	Max, post (1)	Conventional COF (2) COF-CGCG (1) COF, granular cell variant (1) COF, ossifying variant (1)	Multilocular RL (3) Bilocular RL (1) Unilocular RL (1)	No, 7-180 (51.6)

Table 2. Clinical features of 5 new cases of central odontogenic fibroma from Rio de Janeiro-Brazil.

N	Age, Gnd	Location	Subtype	Radiographic features, Size	Tooth displacement	Treatment	Recurrence, Follow-up
1	19, F	Posterior mandible, body and ramus region	Epithelial-rich COF	Perirradicular multilocular radiolucency, 3.5 X 2 cm	No	Conservative excision	No,15 years
2	40, F	Posterior mandible, premolar region	Epithelial-rich COF	Perirradicular multilocular radiolucency; expansion and disruption of bone cortices, 2 X 1.5 cm	Yes	Conservative excision with tooth extraction	No,4 years
3	42, F	Posterior mandible, molar region	COF-CGCG	Multilocular radiolucency in edentulous alveolar ridge with expansion and disruption of bone cortices, 3 X 2 cm	No	Conservative excision	No, 1 year
4	63, F	Posterior maxilla, molar region	COF, granular cell variant	Perirradicular bilocular radiolucency with expansion and disruption of bone cortices, 4 X 3 cm	No	Conservative excision	No, 11 months
5	47, F	Posterior mandible, angle and ascending ramus	COF, ossifying variant	Pericoronal unilocular radiolucency with expansion and disruption of bone cortices, 4.5 X 3.5 cm	Yes	Conservative excision with tooth extraction	No, 7 months

4. CONCLUSÕES

Os COFs são tumores odontogênicos incomuns com morfologia típica e comportamento clínico não agressivo. Na presente série, os COFs afetaram as regiões posteriores da mandíbula (quatro casos) e da maxila (um caso) de cinco mulheres de meia-idade do Brasil. A correlação clínica e radiográfica é recomendada durante a interpretação microscópica dessa entidade intrigante, particularmente naqueles FOCs com predomínio de células granulares, células gigantes multinucleadas e calcificações.

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6. ANEXOS

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1. Oral Medicine and Pathology
Clinicopathological as well as medical or surgical management aspects of diseases affecting oral mucosa, salivary glands, maxillary bones, and temporomandibular joints, as well as orofacial neurological disorders, Craneomandibular disorders and Orofacial pain neck and facial pathology, and systemic conditions with an impact on the oral cavity. Gerodontology.

2. Oral Surgery
Surgical management aspects of diseases affecting oral mucosa, salivary glands, maxillary bones, teeth, temporomandibular joints, oral surgical procedures. Surgical management of diseases affecting head and neck areas.
Laser in Dentistry. IMPLANTOLOGY.

3. Medically compromised patients in Dentistry
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