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CASE REPORT

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Cemento-ossifying fibroma with aneurysmal bone cyst-like cystic hemorrhagic degeneration in the mandible: a case report and literature review

Fibroma cemento-ossificante com degeneração hemorrágica cística semelhante a um cisto ósseo aneurismático na mandíbula: relato de caso e revisão da literatura

Dhara Schrok Monteiro de ATAIDE[1], Kaique Alberto PRETO[1], Gabriela Lopes dos SANTOS[1], Marcelo Júnior ZANDA[2], Denise Tostes OLIVEIRA[1]

1 - Universidade de São Paulo, Faculdade de Odontologia de Bauru, Departamento de Cirurgia, Estomatologia, Patologia e Radiologia, Área de Patologia, Bauru, SP, Brazil.
2 - Universidade de São Paulo, Centro de Pesquisa Clínica, Faculdade de Odontologia de Bauru, Bauru, SP, Brazil.

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ABSTRACT

Although rare, the aneurysmal bone cyst remains the most frequently associated lesion with cemento-ossifying fibroma in jawbones, with a higher prevalence in young people in their second decade of life. Nowadays, the concept of a secondary aneurysmal bone cyst has been replaced by that of cystic hemorrhagic degeneration, producing an aneurysmal bone cyst-like appearance in the fibro-osseous lesion. Objective: This study aims to report an uncommon case of cemento-ossifying fibroma associated with aneurysmal bone cyst-like cystic hemorrhagic degeneration in the mandible of a middle-aged woman and to review its clinical, imaging and histopathological features. Case report: A 44-year-old Caucasian woman was referred for evaluation of a painless, slow-growing swelling in the region of teeth 33, 34, and 35, which presented normal pulpal vitality. Cone-beam computed tomography revealed a periapical hypodense area with hyperdense foci involving the roots of the affected teeth, associated with the expansion and rupture of the buccal cortical bone. The diagnosis established was cemento-ossifying fibroma with aneurysmal bone cyst-like cystic hemorrhagic degeneration. Conclusion: The cemento-ossifying fibroma associated with aneurysmal bone cyst-like cystic hemorrhagic degeneration, as described in this case, is uncommon in the jawbones. The correlation of clinical, imaging, and microscopic features is crucial for an accurate diagnosis.

KEYWORDS

Aneurysmal bone cyst; Cemento-ossifying fibroma; Fibro-osseous lesion; Odontogenic tumor; Ossifying fibroma.

RESUMO

Embora raro, o cisto ósseo aneurismático continua sendo a lesão mais frequente associada ao fibroma cemento-ossificante nos ossos maxilares, com maior prevalência em jovens na segunda década de vida. Atualmente, o conceito de cisto ósseo aneurismático secundário foi substituído por um de degeneração hemorrágica cística, produzindo uma aparência semelhante a um cisto ósseo aneurismático na lesão fibro-óssea. Objetivo: O objetivo deste estudo foi relatar um caso incomum de fibroma cemento-ossificante associado à degeneração hemorrágica cística semelhante a um cisto ósseo aneurismático na mandíbula de uma mulher de meia-idade e revisar suas características clínicas, imaginológicas e histopatológicas. Relato de caso: Uma mulher caucasiana de 44 anos foi encaminhada para avaliação de um aumento indolor e de crescimento lento na região dos dentes 33, 34 e 35, que apresentavam vitalidade pulpar preservada. O exame de tomografia computadorizada de feixe cônico revelou

uma área hipodensa periapical com focos hiperdensos envolvendo as raízes dos dentes afetados, acompanhada de expansão e ruptura da cortical óssea vestibular. O diagnóstico estabelecido foi de fibroma cemento-ossificante com degeneração hemorrágica cística semelhante a um cisto ósseo aneurismático. Conclusão: O fibroma ossificante central associado a uma degeneração cística hemorrágica semelhante a um cisto ósseo aneurismático, conforme descrito em nosso caso, é incomum nos ossos maxilares e a correlação das características clínicas, imaginológicas e microscópicas é crucial para seu diagnóstico preciso.

PALAVRAS-CHAVE

Cisto ósseo aneurismático; Fibroma cemento-ossificante; Lesão fibro-óssea; Tumor odontogênico; Fibroma ossificante.

INTRODUCTION

Recently, the 5th edition of the World Health Organization Classification of Head and Neck Tumours defined the cemento-ossifying fibroma (COF), also called central ossifying fibroma, as a rare, bening, and locally aggressive mesenchymal odontogenic tumor [1,2]. It is thought to arise from the multipotent cells of the periodontal ligament, which can form cementum, lamellar bone, and fibrous connective tissue, resulting in a benign odontogenic tumor composed of fibrous connective tissue associated with varying amounts of mineralized tissue [1-3]. COF shows a female predominance and typically manifests in the third and fourth decades of life [1,2,4,5].

More often than not, this odontogenic tumor is asymptomatic, but it can present with pain and swelling, leading to moderate deformity in the posterior mandible. Although uncommon, the coexistence of secondary lesions such as aneurysmal bone cyst (ABC) in COF has been widely documented [6-19], complicating both diagnosis and management. However, according to the recent World Health Organization classification, the concept of a secondary aneurysmal bone cyst has been replaced by of the term cystic hemorrhagic degeneration [1]. This aneurysmal bone cyst-like cystic hemorrhagic degeneration can occur in a range of other neoplasms and fibro-osseous lesions, including COF and fibrous dysplasia [1]. It is important to emphasize that ABCs rarely occur in the jawbones, where they present as expansive and destructive osteolytic lesion containing blood-filled cavities [3].

In this paper an uncommon case of cemento-ossifying fibroma associated with aneurysmal bone cyst-like cystic hemorrhagic degeneration in the mandible of a middle-aged woman was reported and review the clinical, imaging, and histopathological features of this hybrid tumor.

CASE REPORT

Appropriate consent was obtained from the present patient for the use of the information and the pictures.

A 44-year-old Caucasian woman was referred to the dentist for evaluation of a painless, slow-growing lesion in the mandible with an unknown duration of evolution. Intraoral examination revealed a normochromic, sessile, firm-to-palpation enlargement in the region of teeth 33, 34 and 35, which presented normal pulpal vitality (Figure 1A-B). Her medical history was unremarkable, and there was no history of trauma associated with the lesion. Cone-beam computed tomography revealed a periapical hypodense area with hyperdense foci involving the roots of the affected teeth, accompanied by expansion and rupture of the buccal cortical bone (Figure 1C-D).

The presumptive diagnosis was an odontogenic tumor or a fibro-osseous lesion. After obtaining written informed consent, an excisional biopsy was performed, and a friable, bloody area was extruded from the center of the surgical specimen (Figure 1A-B). During the surgical procedure, the lesion was easily detached from the neighboring mandibular bone. The material was submitted for histopathological analysis. Microscopic examination of the lesion revealed highly cellular connective tissue containing mineralized tissue with a pattern resembling bone and dental cementum (Figure 2A-B), as well as extensive cystic hemorrhagic degeneration with blood-filled spaces lacking endothelial lining in the central region of the lesion (Figure 2C-D). The final diagnosis was cemento-ossifying fibroma with aneurysmal bone cyst-like cystic hemorrhagic degeneration. After one year of follow-up, the patient exhibited normal healing without clinical and radiographic signs of recurrence.

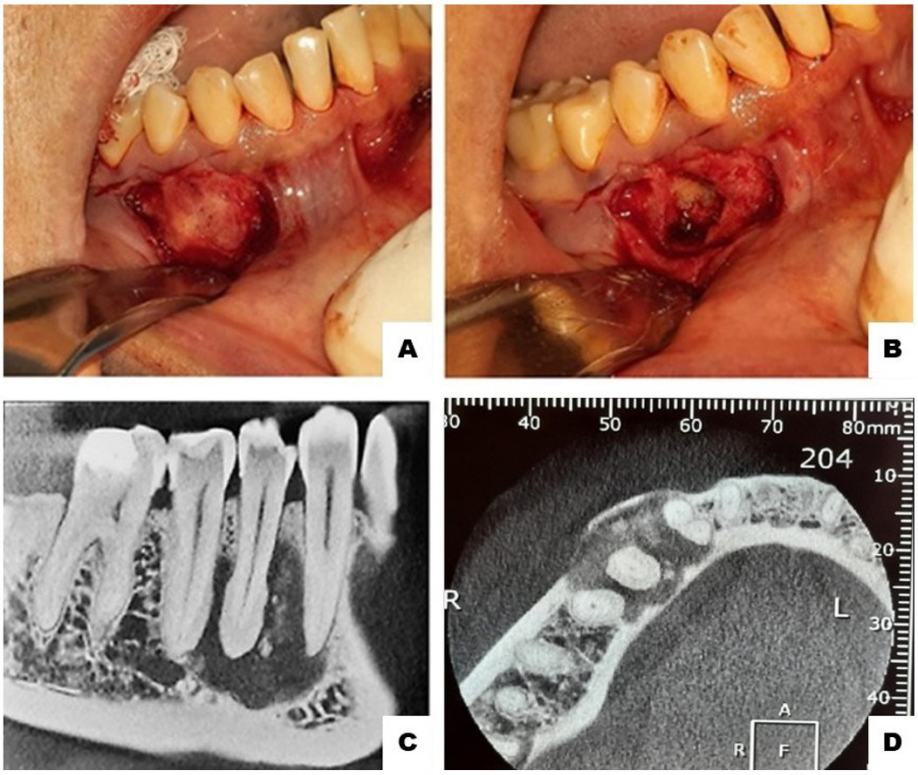

Figure 1 - (A) Clinical and imaging features of the central cemento-ossifying fibroma with aneurysmal bone cyst-like cystic hemorrhagic degeneration. (B) Intraoperative clinical view of the lesion showing a friable, bloody area extruding from the center of the surgical specimen. (C) Cone-beam computed tomography in coronal reconstruction demonstrates a multilocular hypodense area with hyperdense foci and well-defined borders, located between teeth 43 and 45, without causing displacement or resorption of the involved teeth. (D) Axial reconstruction reveals vestibulolingual cortical expansion and thinning of the mandibular lingual and buccal cortical bones at the lesion site, with areas of rupture.

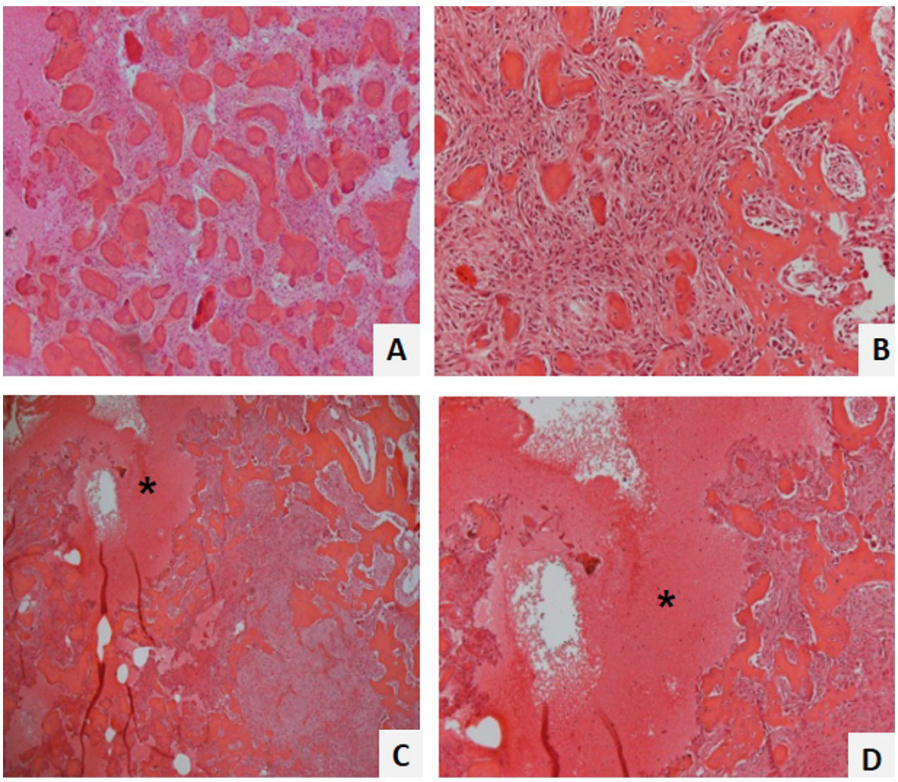

Figure 2 - Microscopic features of central cemento-ossifying fibroma with aneurysmal bone cyst-like cyst hemorrhagic degeneration. The lesion shows variable production of fibrous and mineralized tissue with a pattern resembling bone and dental cementum (A and B), as well as extensive cystic hemorrhagic degeneration with blood-filled spaces lacking endothelial lining, similar to an aneurysmal bone cyst in the central region of the lesion (black asterisk) (C and D). (Hematoxylin and Eosin, Original magnification: A = 100×, B = 40×, and C = 100×).

Literature review

A literature review was conducted to investigate the occurrence of cemento-ossifying fibroma with aneurysmal bone cyst in the jawbones using search terms : ("Cemento-Ossifying Fibroma" OR "Ossifying Fibroma" OR "Cemento-Ossifying Lesion" OR "Cemento-Ossifying Tumor") AND ("Aneurysmal Bone Cyst" OR "ABC" OR "Aneurysmatic Bone Cyst") AND ("Jaw" OR "Jaws" OR "Mandible" OR "Maxilla" OR "Mandibular" OR "Maxillary" OR "Jawbone") across major databases (PubMed, Scopus, Cochrane Library, EMBASE, BIREME, SCIELO, and Web of Science) and grey literature (Google Scholar), without any time filter. In the first step, a primary selection was performed based on the following criteria: (1) manuscripts in English, Portuguese, and Spanish; (2) exclusion of duplicate articles; (3) inclusion of complete published articles, such as original research, retrospective studies, and case reports. Subsequently, the following eligibility criteria were applied: (1) diagnosis of COF with ABC in the maxilla or mandible, confirmed by histopathological analysis; (2) complete clinical information of the patients (sex, age, and lesion location); and (3) photomicrographs of the lesion. Twenty-five cases of COF with ABC from 13 published manuscripts were selected based on the eligibility criteria, as shown in Table I.

DISCUSSION

Based on the literature review, aneurysmal bone cyst was previously considered the most frequent lesion associated with cemento-ossifying fibromas, however, the coexistence of these lesions is uncommon [3,5]. In the latest edition of the World Health Organization Classification of Head and Neck Tumors, the concept of a secondary aneurysmal bone cysts has been replaced by that of aneurysmal bone cyst-like cystic hemorrhagic degeneration [1-4].

Table I illustrates the published cases of COF associated with aneurysmal bone cyst in the jawbones. Most cases occurred in male patients (52%) with a male-to-female ratio of 1.08:1. The age of patients ranged from 3 to 47 years, with a higher prevalence in young people in their second decade of life (Table I). Contrasting with the literature review findings, this reported case of COF associated with ABC-like cystic hemorrhagic degeneration occurred in a female patient over 40 years old.

The mandible remains the most common site of COF associated with ABC, accounting for 64% of reported cases, while the maxilla is affected in only 36% (Table I). According to the literature review, the imaging findings vary widely, with a tendency toward a multilocular appearance (66.7%) (Table I). Typically, the lesion shows a radiolucent/hypodense density (52% of cases), but it can also be mixed (36%) or radiopaque/hyperdense (12%), often with well-delimited margins involving vital teeth, as described in Table I. This hybrid lesion can be confused with other osteolytic cysts and tumors due to its variable imaging characteristics. Cortical bone expansion and rupture, as observed in the present case, are more frequently observed in larger lesions [17] and maxillary sinus involvement is reported when the lesion occurs in the maxilla [5,10-12,16].

Due to its highly variable clinical and radiographic presentation, this lesion can mimic several osteolytic conditions and is often presumptively diagnosed as odontogenic cysts and tumors (26.31% of cases), COF (21.05%), other fibro-osseous lesions of the jaws (23.68), ABC (7.9%), central giant cell granuloma (7.9%), vascular lesions (5.26%), osseous neoplasms (5.26%), or bone fracture (2.63%) [6-18]. As seen in the literature, the clinical diagnostic hypothesis of the reported case was an odontogenic tumor or fibro-osseous lesion, with the simultaneous occurrence of COF associated with aneurysmal bone cyst-like cystic hemorrhagic degeneration being detected only through histopathological examination.

Microscopically, COF presents typical characteristics of cellularized connective tissue interspersed with mineralized resembling trabecular bone and cementum. However, the association of these findings with cystic hemorrhagic degeneration containing blood-filled spaces lacking endothelial lining, as described in this paper, is rare [1]. In the last decades, the coexistence of these lesions was named secondary ABC associated with COF [1,6-18]. The concept of a secondary aneurysmal bone cyst has now been replaced by that of cystic hemorrhagic degeneration producing an aneurysmal bone cyst-like appearance in the fibro-osseous lesion. This change is based on the observation that cystic alterations commonly found in fibro-osseous lesions of the jawbones lack the *USP6* rearrangement, which is present in 70% of true

Table I - Clinical and radiographic features, differential diagnosis and evolution of 25 cemento-ossifying fibromas with aneurysmal bone cyst reported in the literature

Authors, year	Sex	Age (years)	Location	Radiographic Locules	Radiographic Density	Size (cm)	Differential diagnosis	Treatment	Recurrence (after six months)
Robinson et al. [6], 1985	M	13	Maxilla	Multilocular	Mixed	NI	FD	Enucleation	Yes
Padwa et al. [7], 1997	F	3	Mandible	Unilocular	Mixed	4 x 6	NI	Enucleation	No
Noffke et al. [8], 1998	M	4	Mandible	Multilocular	Mixed	7 x 6	FD and JOF	Mandibulectomy (partial)	No
Saheeb et al. [9], 2007	M	5	Maxilla	NI	Radiolucent	3 x 5	Odontogenic cyst, Periapical cemental dysplasia and FD	Enucleation	No
Sun et al. [10], 2010	M (6) F (5)	0-10 (1), 11-20 (6), 21 - 40 (2), +40 (2)	Mandible (9) Maxilla (2)	Multilocular (8), Unilocular (3)	Radiolucent (9), Mixed (2)	1.5 - 8.5	Cyst (5), OF (2), bone fracture (1), OKC (2) Ameloblastoma (1)	Mandibulectomy partial + BG (6), Curettage (4), Mandibulectomy (total) (1)	No (8), Yes (1) NI (2)
Silva et al. [11], 2011	F	9	Maxilla	Unilocular	Radiopaque	NI	FD and osteosarcoma	Enucleation	Yes
Sankaranarayanan et al. [12], 2011	F	6	Maxilla	Unilocular	Radiopaque	3 x 3	ABC	Maxillectomy (partial)	No
Triantafillidou et al. [13], 2012	F	7	Maxilla	Unilocular	Radiolucent	NI	CGCG, ABC and vascular malformation	Curettage	Yes
Urs et al. [14], 2013	F (2), M (1)	10, 14, 11	Mandible (2), Maxilla (1)	Multilocular (2), Unilocular (1)	Mixed (2), Radiolucent (1)	0,3 - 6	FD (2), OF (2), CGCG (2), ABC (2), ameloblastoma, osseous neoplasm, and central hemangioma	Mandibulectomy partial (1), and Enucleation + Curettage (1)	No (3)
Reddy et al. [15], 2014	F	16	Mandible	Multilocular	Radiolucent	3 x 5	Ameloblastoma, COF and FD	Mandibulectomy partial	No
Gotmare et al. [16], 2017	M	8	Mandible	Multilocular	Radiolucent	NI	NI	Mandibulectomy partial	No
Sarode et al. [17], 2018	M	10	Maxilla	Multilocular	Mixed	6 x 8	NI	Maxilectomy partial	No
Toferer et al. [18], 2021	M	21	Mandible	Multilocular	Radiopaque	8.5	POF with ABC	Mandibulectomy partial	No

M: Male; F: Female; NI: Not Informed; ABC: Aneurysmal Bone Cyst; FD: Fibrous Dysplasia; COF: Cemento-Ossifying Fibroma; POF: Psammomatoid Ossifying Fibroma; JOF: Juvenile Ossifying Fibroma; OF: Ossifying Fibroma; OKC: Odontogenic Keratocyst; CGCG: Central Giant Cell Granuloma; BF: Bone Graft.

aneurysmal bone cyst cases [1]. Additionally, immunohistochemical stains are not essential for the diagnosis of COF with aneurysmal bone cyst-like cystic hemorrhagic degeneration [1-4].

Furthermore, unlike our clinical case, regarding treatment, in the cases described in the literature, only 20.83% of patients presenting COF associated with ABC were treated with curettage, while the majority (58.33% of cases) underwent more aggressive approach, such as resections, mandibulectomies or maxillectomies [6-18]. In contrast, our case had a favorable prognosis with a less invasive approach, involving enucleating of the lesion without bone resection, and showed no signs of recurrence after a 3-year follow-up. However, although rare, the recurrence of COF with ABC was described in four clinical cases reported in the literature (17.4%) [5,9,10,12].

The etiology of COF remains unknown, and its association with aneurysmal bone cyst-like cystic hemorrhagic degeneration is also unclear. Genetic studies have implicated mutations in the *CDC73* and *GDD1* genes in the development of COF in conditions such as hyperparathyroidism-jaw tumor syndrome and gnathodiaphyseal dysplasia syndrome [1,20,21]. Additionally, disruptions in the Wnt/β-catenin signaling pathway and copy number variations on chromosomes 7 and 12 have been suggested in the pathogenesis of COF [1,22]. However, the genetic characteristics of non-syndromic, sporadic COF remain unidentified [1].

While theories regarding the pathogenesis of ABC include circulatory disturbances, vascular malformations, and post-traumatic changes [23], the recent rejection of the term secondary ABC in the latest WHO classification further deepens the uncertainty surrounding the etiology of this hemorrhagic cystic degeneration resembling an aneurysmal bone cyst. This reclassification is primarily based on differences in *USP6* gene translocations observed between true aneurysmal bone cysts and those previously referred to as secondary aneurysmal bone cysts in fibro-osseous lesions [1]. Consequently, further research is needed to investigate and clarify the etiopathogenesis of hemorrhagic cystic degeneration in fibrous osseous lesions such as COF.

CONCLUSION

Cemento-ossifying fibroma is a rare odontogenic tumor, and its occurrence in association with aneurysmal bone cyst-like cystic hemorrhagic degeneration, as described in this reported case, is uncommon in the jawbones. The correlation of clinical, imaging, and microscopic features is crucial for accurate diagnosis of cemento-ossifying fibroma associated with aneurysmal bone cyst-like cystic hemorrhagic degeneration.

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Author's Contributions

DSMA – Conceptualization, Data Curation, Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing. KAP - Data Curation, Funding Acquisition Investigation Methodology, Validation, Writing – Original Draft Preparation, Writing – Review & Editing. GLS - Data Curation, Validation, Writing – Original Draft Preparation, Writing – Review & Editing. MJZ - Data Curation, Validation, Writing – Review & Editing. DTO – Conceptualization, Formal Analysis, Supervision, Validation, Writing – Original Draft Preparation, Writing – Review & Editing.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Regulatory Statement

This study is in accordance with the ethical principles of the Declaration of Helsinki for Medical Research. Appropriate consent was obtained for the presented patient for the use of the information and the pictures.

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Denise Tostes Oliveira
(Corresponding address)
Universidade de São Paulo, Faculdade de Odontologia de Bauru, Departamento de Cirurgia, Estomatologia, Patologia e Radiologia, Área de Patologia, Bauru, SP, Brazi
Email: denisetostes@usp.br

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