Case Report

Hybrid Central Odontogenic Fibroma with Central Giant Cell Granuloma: A Systematic Review and a Report of a Challenging Case

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ABSTRACT

Central odontogenic fibroma (COdF) is a rare benign tumor originating from odontogenic mesenchyme; a subset of cases exhibits hybrid features, particularly with central giant cell granuloma (CGCG). This study presents a rare case of epithelium-rich COdF associated with CGCG and a systematic review of this type of hybrid lesion. We report a 10-year-old male with a unilateral mandibular swelling and a progressively enlarging radiolucent lesion. Imaging and histopathological evaluation identified a benign mixed odontogenic tumor with epithelial-rich COdF features and multinucleated giant cells. Genetic testing for the SH3BP2 gene mutation, commonly associated with cherubism, was negative. Surgical resection and reconstruction were performed, with no recurrence observed at a 1-year follow-up. A review was conducted on hybrid COdF/CGCG lesions in PubMed, Embase, Scopus, Web of Science, and Wiley Online. Analyzing clinical, radiographic, and histopathological patterns, our findings highlight the necessity of molecular and histopathological differentiation for accurate diagnosis and treatment planning.

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Introduction

Central odontogenic fibroma (COdF) is an uncommon tumor that may develop from stem-like mesenchymal cells associated with tooth-supporting and developmental structures [1]. This lesion presents diagnostic challenges due to its overlap with other lesions [2].

COdF shows various histopathological characteristics. Two subtypes have been historically described including the rare simple type (epithelium-poor), featuring fibroblasts and occasional epithelial rests, and the more common epithelium-rich type, with dense fibrous tissue and epithelial strands. Lesions without epithelium may also be classified as COdF [3-4]. The 2022 WHO classification of odontogenic lesions broadened COdF's spectrum to include ossifying, amyloid (associated with amyloid deposits), granular cell, and hybrid odontogenic fibroma associated with central giant cell granuloma (CGCG) [1].

CGCG is a nonmalignant intraosseous lesion with a controversial etiology [5]. It is mainly made up of stromal cells with a spindle-like shape, such as fibroblasts, which promote the proliferation by attracting monocytes that turn into multinucleated giant cells [6-7]. CGCG predominantly affects the anterior region of the jaws, with a female predilection and a higher incidence of unilocular lesions. Multilocular lesions, while less common, are often larger [6, 8].

Cherubism and CGCG share similar histopathologi-

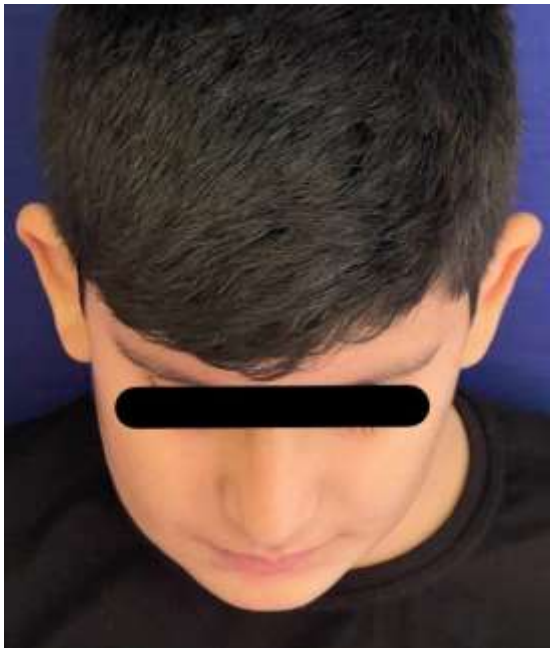

Figure 1: Extraoral view, unilateral facial swelling involving the right mandibular region

cal features. The gene responsible for cherubism was SH3BP2, but no SH3BP2 mutations were found in CGCG [9].

Interestingly, CGCG can occur alongside another benign jaw lesion, like ossifying fibroma and COdF as hybrid lesion but this condition is extremely rare [10]. In 1985 in Germany, for the first time, a case was reported involving bilateral CGCG; the CGCG on the left side displayed histological features of a COdF [11-12]. In 1992, histopathology analysis of the lesion revealed regions of cellular fibroblastic tissue containing strands of odontogenic epithelium associated with areas exhibiting features resembling CGCG [13].

This paper aims to report a challenging case with DNA examination of SH3BP2 and to provide a systematic review and analysis of previously reported hybrid COdF/CGCG cases.

Case Presentation

A 10-year-old male, suffering from unilateral swelling of the right mandible, was referred to an oral and maxillofacial surgeon. Clinical data revealed an extensive and destructive lesion of the mandible and facial asymmetry. Extraoral photographs showed swelling in the distal of the right mandibular molar (Figure 1). Differential diagnoses included rhabdomyosarcoma, chondrosarcoma, odontogenic myxoma, and conventional ameloblastoma.

Blood analysis revealed normal levels for all parameters, including alkaline phosphatase, calcium, and phosphate. However, the patient's fasting blood sugar was in the impaired range at 104 mg/dL and a borderline sodium level of 145 mmol/L.

Radiology images demonstrated erupting permanent teeth, and the right mandibular ramus exhibited radiopacity (Figure 2a). A comparison of cone-beam computed tomography (CBCT) examinations of both jaws revealed an increase in the size of the pathological lesion, suspected to be a CGCG (Figure 2b). The lesion's dimensions increased in the anterior-posterior and vertical planes, with rougher septa inside the lesion. Parathyroid scintigraphy was performed and revealed no abnormal retention of Technetium 99m sestamibi (TC-MIBI) from the mandible to the base of the heart, effectively ruling out parathyroid adenoma from the differential diagnosis.

An incisional biopsy was performed, and the obtained specimen was evaluated independently by two different pathologists. In the first report, microscopic findings revealed the presence of giant cells without evidence of malignancy. It was suggested that, since unilateral cherubism is extremely rare, and CGCG was

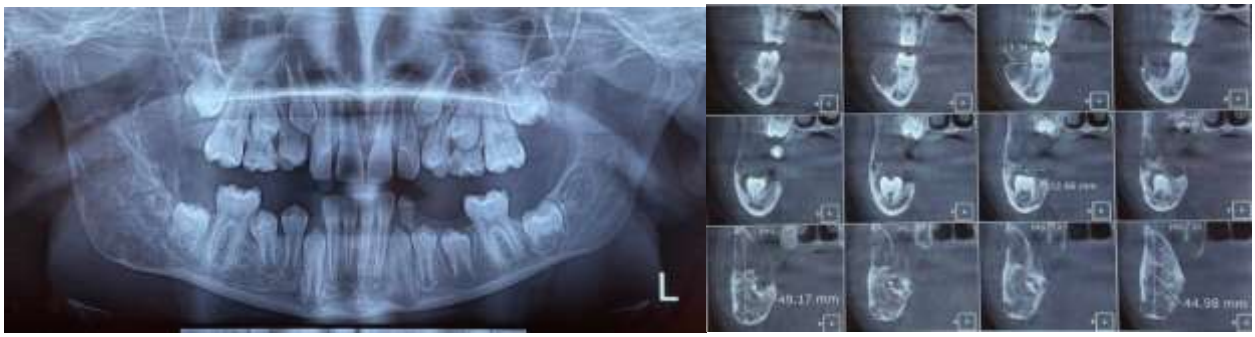

Figure 2: a: Pre-surgical panoramic view. The patient was in the mixed dentition stage demonstrating a radiopaque lesion in the right mandibular ramus, **b:** Pretreatment cone-beam computed tomography (CBCT) images demonstrating an extensive intraosseous lesion involving the right mandibular ramus

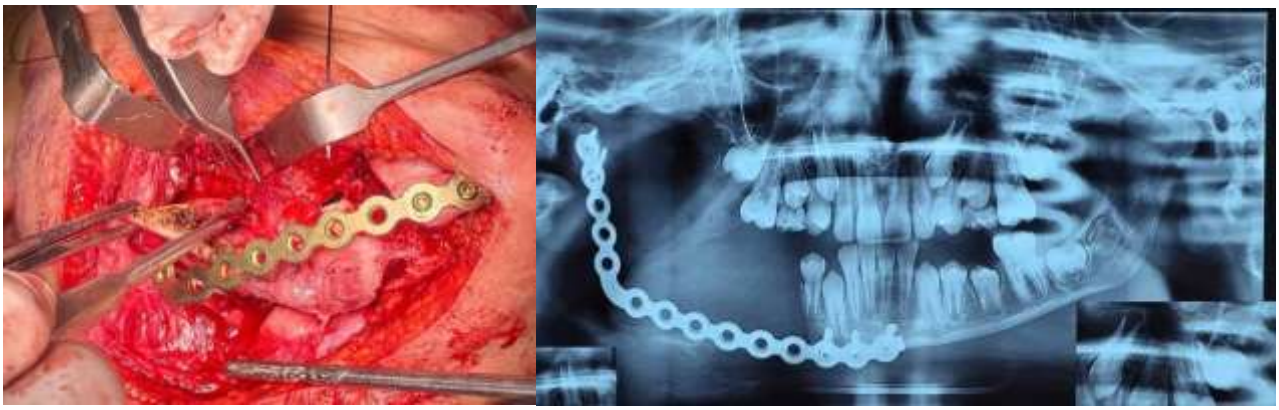

Figure 3: a: Patient treated by mandible segmental resection and reconstruction by plate, **b:** post-surgical panoramic view

among the differential diagnoses, testing for the SH3-B-P2 gene mutation would be helpful to rule out cherubism, genetic test performed and results were negative.

The second report, described a neoformed structure with features consistent with CGCG. The stroma appeared cellular and fibrotic with variations in size of giant cells and diffused distribution. This report also confirmed no malignancy and diagnosed the lesion as an aggressive type of CGCG.

Based on the incisional biopsy, surgical resection and reconstruction using plates (Figure 3a-b) were performed as a therapeutic measure due to the aggressive behavior and extent of the lesion. Following complete surgical excision of the lesion, the final pathology report described a submandibular lymph node dissection, which revealed one reactive lymph node free of tumor. The mandibular mass, measuring 8.5cm, was identified as a benign mixed odontogenic tumor (epithelium-rich odontogenic fibroma) associated with a giant cell granuloma (Figures 4a-b). This was established as the final diagnosis.

The postoperative course was uneventful, and the p-

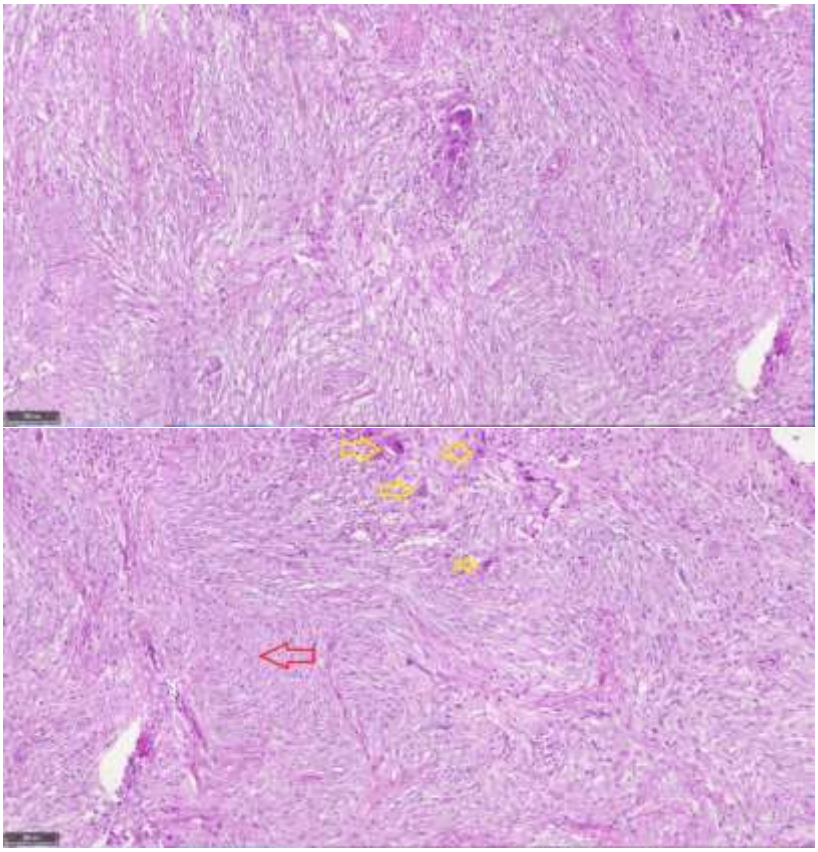

Figure 4: a, b: Microscopic view, foreign body reaction pattern into an odontogenic fibroma lesion, multinucleated giant cells (yellow arrow) and fibrotic tissue (red arrow) in figure b (magnification 200×)

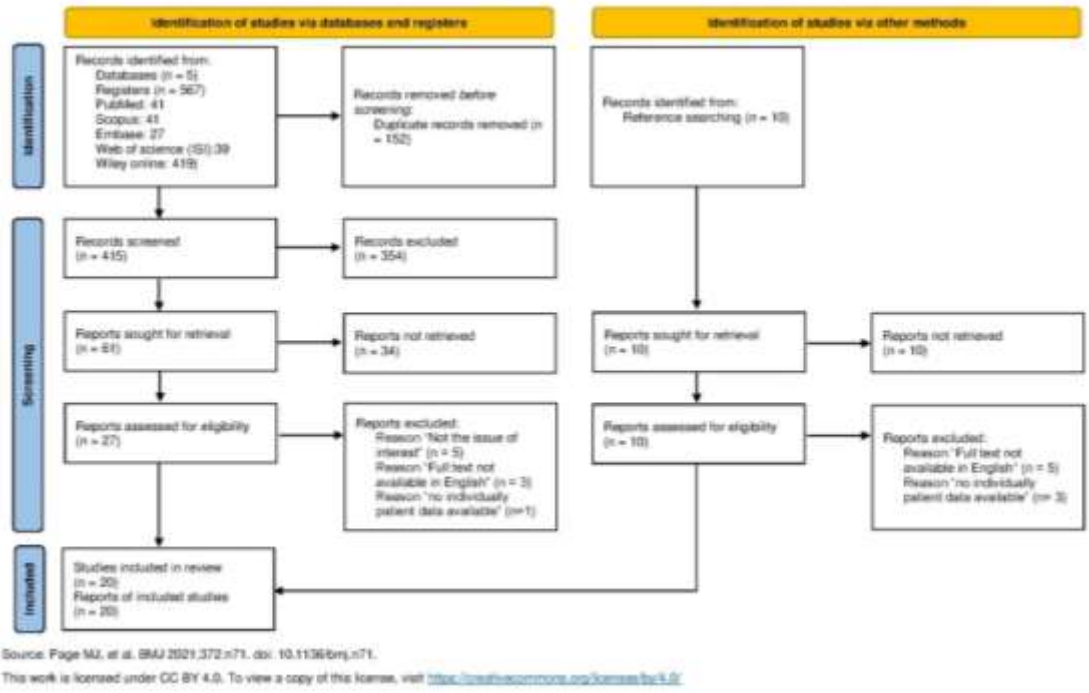

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Figure 5: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of the study selection process

atient was discharged in good condition. At a 1-year follow-up, there was no evidence of recurrence.

Method

Eligibility Criteria

Studies were considered eligible if they met the following criteria: (i) study type: case reports or case series providing individual patient data; (ii) population: patients diagnosed with COdF, in a hybrid lesions; (iii) language: English; (iv) publication date: no restrictions; (v) data availability: individual patient data.

Information Sources

A search was conducted in PubMed, Embase, Scopus, Web of Science, and Wiley Online from inception to [July, 2025]. Screening reference lists of included articles (via manual search) was also conducted.

Search Strategy

The search strategy combined controlled vocabulary and free-text terms related to COdF and CGCG. The following keywords were used: "central odontogenic fibroma", "hybrid central odontogenic fibroma", "odontogenic tumor", "central giant cell granuloma", "giant cell granuloma", and "central giant cell granuloma lesions". Boolean operators (AND/OR) were applied as appropriate. Medical Subject Headings (MeSH) terms were used when applicable in PubMed ("Granuloma, Giant Cell") and searches were limited to articles published in English.

Study Selection

Two reviewers independently screened titles and abstracts of retrieved articles. Full-text articles were assessed for eligibility, and disagreements were resolved by discussion or consultation with a third reviewer. The study selection process is presented in a PRISMA flow diagram (Figure 5).

Data Extraction

Data were extracted independently by two reviewers using a standardized form that included patient demographics, clinical, radiographic, and pathologic characteristics, treatment modalities, and outcomes. Discrepancies were resolved by consensus. Extracted patient-level data were entered into IBM SPSS Statistics 26 for descriptive statistical analysis.

Risk of Bias / Quality Assessment

The quality of included articles was independently assessed by two reviewers using the Joanna Briggs Institute (JBI) critical appraisal tools; the results of the mean rates of reviewers are in Table 1. All the articles' quality met the needs of inclusion criteria and was included based on the reviewers' decision.

Data Synthesis

Descriptive statistics, including frequencies and percentages, were calculated using IBM SPSS Statistics 26. Due to the nature of the included studies, no inferential statistical analysis was performed.

Table 1: Number of articles based on quality assessment score percentage. ("The percentage scores for each study were calculated using the formula: (number of 'Yes' responses ÷ total number of questions) × 100.")

Quality assessment rate percentage	Number of articles
100%	13
More than 80%	6
More than 60%	1

This case report was approved by the Tehran University of Medical Sciences institutional review board with ethic approval of (IR.TUMS.AMIRALAM.REC. 1403.010).

Results

From 20 eligible studies, a total of 40 patients met the inclusion criteria and were included in the analysis. The descriptive characteristics of these cases are summarized in Table 2.

Discussion

In this study, we report a rare and challenging case of hybrid COdF associated with CGCG and, additionally, present a systematic review of previously published cases. Due to the extreme rarity of this hybrid lesion (less than 50), and variable behavior, this condition presents a challenging diagnosis and consequently complicates treatment planning [14]; hence, this combined approach allows for a more informed perspective on di-agnosis, treatment plan, and prognosis of such unusual cases.

Each of the two parts of this condition has its different differential diagnoses, such as cherubism [15], aneurysmal bone cyst [16-17], and brown tumor [18] for CGCG and ameloblastoma, odontogenic myxoma [19], and cemento-ossifying fibroma [20] for COdF. Due to this, clinicians should maintain a broad differential diagnosis and also utilize the capacity of the genetic tests. The mean age for hybrid COdF and CGCG is 30.52± 9.12 (min: 5, max: 73), which demonstrates a wide age range. Moreover, there were no statistically significant differences in gender distribution, which further complicates the diagnostic process. Based on the analysis of 40 reported cases, the majority of lesions could be differentiated with features like location, pain, swelling,

Table 2: Descriptive analysis of cases with hybrid central odontogenic fibroma (COdF) + central giant cell granuloma (CGCG) (percentages for each variable were calculated only among patients with available data for that exact variable) COdF: central odontogenic fibroma; CGCG: central giant cell granuloma; Man: mandible; Max: maxilla; cm: centimeter

Variable Category		Variable	Results
•	Demographics	Sex	Female: 25/40 (62.5%) Male: 15/40 (37.5%)
		Age	Mean age: 30.52
		Location	Posterior Man: 34/39 (87.2%) Posterior Max: 3/39 (7.7%) Anterior Man: 2/39 (5.1%)
•	Clinical	Pain	No pain: 11/12 (91.7%) Paresthesia: 1/12 (8.3%)
		Swelling	With swelling: 9/11 (81.8%)
		Number of Lesion(S)	All patients (40) had one lesion (100%)
•	Radiographic	Cortical Expansion	21/24 (87.5%)
		Size (Biggest Dimension, CM)	2.42 ±1.06
		Pattern	Unilocular: 14/24 (58.3%) Multilocular: 10/24 (41.7%)
		Radiodensity	Radiolucent: 33/34 (97.1%) Mixlucency: 1/34 (2.9%)
		Root Resorption	4/15 (26.7%)
		Tooth Displacement	12/16 (75%)
•	Pathologic	Pattern Of Odontogenic Epithelium	Only Islands: 2/17 (11.8%) Only Strands: 3/17 (17.6%) Strands + Islands: 4/17 (23.5%) Strands + Nests: 2/17 (11.8%) Strands + Cords: 1/17 (5.9%) Strands + Islands + Cords: 5/17 (29.4%)
		Stroma (predominance)	Fibrous: 1/16 (6.3%) Cellular: 6/16 (37.5%) Mixed: 9/16 (56.3%)
•	Treatment	Treatment Plan	Curettage: 20/22 (90.9%) Resection: 2/22 (9.1%)
•	Outcome	Recurrence	4/36 (11.1%)

expansion, radiodensity, and also microscopic coexistence of both CGCG and COdF features; other variables showed no predilection. However, given that the data were derived from case reports and series, this finding should be interpreted with caution and cannot be considered definitive evidence of the mentioned variables. Based on this case report, genetic analyzing can be employed to rule out other lesions.

The main treatment plans for this lesion are curettage and resection. All reported recurrences occurred after treatment with curettage (4 out of 20 patients, 20%), which may indicate a relatively high recurrence rate for this treatment modality, but repeating it can prevent later recurrence just the same as CGCG [21]. Therefore, the surgeon should select the treatment plan considering the patient's condition, like the size of the lesion and the age, whilst curettage is still the main therapeutic preference for this lesion. Apparently, persistent following ups are positively recommended.

Conclusion

This case, with negative SH3BP2 mutation, highlights that accurate diagnosis of COdF/CGCG hybrid lesion requires integration of clinical, radiographic, histopathological, and genetic findings to differentiate it from similar entities. Our findings indicate that this tumor commonly affects the mandible, with no specific age or gender predilection, and shows a higher recurrence rate following conservative curettage compared with resection. Further case reports and studies are needed to better understand the behavior and pathogenesis of this hybrid lesion.

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Ethical Approval

This case report was approved by the Tehran University of Medical Sciences institutional review board with ethic approval number of (IR.TUMS.AMIRALAM.REC.1403.010).

Consent

Written informed consent was obtained from patient (or their legal guardians in the case of minors) for participation in this study and for the publication of clinical data and images.

Guarantor

Dr. Pouyan Aminishakib and Mr. Seyed Mohammad-Moein Hosseini accept full responsibility for the integrity of the work as a whole, from inception to published article.

Conflict of Interest

Authors declare no Conflict of interest statement.

References

[1] Bilodeau EA, Collins BM. Odontogenic Cysts and Neoplasms. Surg Pathol Clin. 2017; 10: 177-222.

[2] Roza ALOC, Sousa EM, Leite AA, Amaral-Silva GK, Morais TML, Wagner VP, et al. Central odontogenic fibroma: an international multicentric study of 62 cases. Oral Surg Oral Med Oral Pathol Oral Radiol. 2021; 131: 549-557.

[3] Poomsawat S, Choakdeewanitthumrong S, Kitisubkanchana J, Kosanwat T. Central odontogenic fibroma: retrospective study of six cases with variable histopathologic features using 2022 WHO classification. BMC Oral Health. 2024; 24: 1297.

[4] Neville BW, Damm DD, Allen CM, Chi AC. Oral and maxillofacial pathology. 5th ed. Philadelphia: Elsevier; 2023. p. 732-733.

[5] Jadu FM, Pharoah MJ, Lee L, Baker GI, Allidina A. Central giant cell granuloma of the mandibular condyle: a case report and review of the literature. Dentomaxillofac Radiol. 2011; 40: 60-64.

[6] Ramesh V. Central giant cell granuloma: An update. J Oral Maxillofac Pathol. 2020; 24: 413-415.

[7] Vered M, Buchner A, Dayan D. Central giant cell granuloma of the jawbones-new insights into molecular biology with clinical implications on treatment approaches. Histol Histopathol. 2008; 23: 1151-1160.

[8] Tahmasbi-Arashlow M, Patel PB, Nair MK, Liang H, Cheng YL. Cone-beam computed tomographic imaging of central giant cell granuloma: A comprehensive review. Imaging Sci Dent. 2022; 52: 123-131.

[9] de Lange J, van Maarle MC, van den Akker HP, Redeker EJ. DNA analysis of the SH3BP2 gene in patients with aggressive central giant cell granuloma. Br J Oral Maxillofac Surg. 2007; 45: 499-500.

[10] Alsufyani NA, Aldosary RM, Alrasheed RS, Alsaif RF.

A systematic review of the clinical and radiographic features of hybrid central giant cell granuloma lesions of the jaws. Acta Odontol Scand. 2021; 79: 124-131.

[11] Wangerin K, Harms D. Seltene Variationen des ameloblastischen Fibroms [Rare variations of ameloblastic fibroma]. Dtsch Z Mund Kiefer Gesichtschir. 1985; 9: 227-231.

[12] Ide F, Matsumoto N, Kikuchi K, Kusama K. Hybrid Central Odontogenic Fibroma/Central Giant Cell Lesion: A Missing Report. Head Neck Pathol. 2018; 12: 298-299.

[13] Allen CM, Hammond HL. Central odontogenic fibroma, WHO type: A report of three cases with an unusual associated giant cell reaction. Oral Surg Oral Med Oral Pathol. 1992; 73: 62-67.

[14] de Carvalho Kimura T, Sari Precetti R, Kaline Farias Bezerra H, Roger Santos Silva A, Carolina Prado Ribeiro A, Agustin Vargas P. Central odontogenic fibroma with giant cell granuloma-like features: a case report and comprehensive literature review. J Oral Diagn [Internet]. 2024 Dec 10 [cited 2025 Aug. 16];10. Available at: https://joraldiagnosis.com/revista/article/view/277

[15] Cariati P, Monsalve Iglesias F, Fernández Solís J, Valencia Laseca A, Martinez Lara I. Cherubism. A case report. Reumatol Clin. 2017; 13: 352–353.

[16] Roychoudhury A, Rustagi A, Bhatt K, Bhutia O, Seith A. Aneurysmal bone cyst of the mandible: report of 3 cases. J Oral Maxillofac Surg. 2009; 67: 1996-2004.

[17] Chandolia B, Bajpai M, Arora M. Central giant cell granuloma with aneurysmal bone cyst in a 28-year male patient: a rare concurrence. J Coll Physicians Surg Pak. 2018; 28: S128-S129.

[18] Arunkumar KV, Kumar S, Deepa D. Brown tumor in mandible as a first sign of vitamin D deficiency: a rare case report and review. Indian J Endocrinol Metab. 2012; 16: 310-315.

[19] Daniels JS. Central odontogenic fibroma of mandible: a case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004; 98: 295-300.

[20] Woo SB. Central cemento-ossifying fibroma: primary odontogenic or osseous neoplasm? J Oral Maxillofac Surg. 2015; 73: S87-S93.

[21] Greenberg MS, Glick M. Hematologic diseases. In: Greenberg MS, Glick M, editors. Burket's oral medicine: diagnosis and treatment. 10th ed. Hamilton: BC Decker; 2003. p. 429-453.