Research Article

Benign Hybrid Lesions of the Jaws: A Systematic Review of the Literature

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ABSTRACT

Background: Hybrid lesions of the jaws are rare pathological entities defined by the coexistence of two or more histopathologically distinct cystic and/or tumoral components within a single anatomical site. The World Health Organization (WHO) classification of odontogenic tumors and cysts does not currently recognize them, and their epidemiological, clinical, radiological, and therapeutic profiles remain poorly characterized. This systematic review aimed to synthesize the available literature on the epidemiology, clinical and radiological presentation, histopathology, management, and outcome of benign hybrid lesions of the jaws.

Methods: A systematic review was conducted according to PRISMA guidelines, searching PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar (search finalized February 28, 2025), using a PICOS-structured question and Boolean combinations of MeSH and free-text terms ("hybrid lesion," "odontogenic tumor," "non-odontogenic tumor," "jaw," "maxilla," "mandible," "alveolar bone"). Case reports, case series, cohort, case-control, cross-sectional, and interventional studies in humans, in English or French, reporting hybrid lesions confined to the jaws, were eligible. Methodological quality was appraised using the Joanna Briggs Institute (JBI) critical appraisal checklists appropriate to each study design.

Results: Of 379 records identified (364 from database searching plus 15 from manual search), 56 studies were included (47 case reports, 6 case series, 3 retrospective studies), reporting 129 patients (age range 2–81 years, most frequently 15–29 years; 70 males (54.3%), 59 females (45.7%)). The mandible was affected in 96 cases (74.4%) and the maxilla in 31 (24.0%). Most lesions comprised two histopathological components (120/129, 93.0%); the most frequent combinations were Central Giant Cell Granuloma (CGCG) with central odontogenic fibroma (17 cases) and with cemento-ossifying fibroma (15 cases). Painless swelling was the most common clinical finding (67/88 evaluable cases, 76.1%). Panoramic radiography was the most frequently used imaging modality (52/70, 74.3%), most often showing well-defined (44/92, 47.8%) radiolucent (45/92, 48.9%) or mixed (43/92, 46.7%) images. Surgical treatment (enucleation, 37.9%; excision, 24.1%; resection, 9.2%, among others) was used in all definitively treated cases; intralesional corticosteroids failed in three CGCG-suspected cases. Among 53 patients with adequate follow-up (3 months–10 years), only one recurrence (1.8%) was recorded, involving a CGCG-cemento-ossifying fibroma hybrid lesion.

Conclusions: Hybrid lesions of the jaws predominantly affect the mandible of young adults, most commonly combine two components (frequently CGCG-based), and follow a generally favorable course after surgical treatment, with a low recurrence rate. Their absence from current WHO classification schemes hinders standardized diagnosis and management; formal recognition and prospective, multicenter studies are warranted.

Key Words: Hybrid lesion; Odontogenic tumor; Central giant cell granuloma; Jaw; Maxillofacial pathology; Systematic review

Abbreviations: AM: Ameloblastoma; AOT: Adenomatoid Odontogenic Tumor; CEOT: Calcifying Epithelial Odontogenic Tumor; CGCG: Central Giant Cell Granuloma; COF: Central Odontogenic Fibroma; FA: Ameloblastic Fibroma; FCO: Cemento-Ossifying Fibroma; IARC: International Agency for Research on Cancer; JBI: Joanna Briggs Institute; JOF: Juvenile Ossifying Fibroma; KD: Dentigerous cyst; KOC: Calcifying Odontogenic Cyst; OKC: Odontogenic Keratocyst; PICOS: Population, Intervention, Comparator, Outcome, Study design; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; WHO: World Health Organization.

Introduction

The jaws are a privileged site for the development of cystic and tumoral lesions, owing to the persistence of residual odontogenic tissue capable of transforming into benign or malignant proliferative lesions [1]. Odontogenic tumors are approximately five times less frequent than odontogenic cysts, and non-odontogenic lesions of the jaws, while rarer still, are also predominantly benign [2]. The growing diversity of maxillofacial lesions, combined with improved understanding of their clinical behavior, the identification of new tumor entities, increasingly specific

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immunohistochemical markers, and advances in molecular biology, has progressively refined the accuracy of lesion classification; as a result, the WHO/International Agency for Research on Cancer (IARC) classification undergoes periodic revision. The fifth edition of the WHO classification of head and neck tumors introduced several updates to the chapter on tumors of the oral cavity and mobile tongue relative to the 2017 (4th) edition, incorporating new clinical, histopathological, and molecular data [3].

Hybrid lesions of the jaws are characterized by combined microscopic associations resulting from the coexistence of two or more types of cysts and/or tumors [4]. They constitute a single lesional entity that displays, on histopathological examination, distinct features belonging to two or more well-individualized lesions [5]. These rare lesions are notable for their considerable histopathological diversity [4], a rarity reflected in the small number of cases reported in the literature [6]. Although the WHO classification of jaw cysts and tumors has been periodically updated, hybrid lesions have not been addressed in the most recent revision [7]. Given their rarity and lack of recognition in current classification systems, their clinical course, appropriate therapeutic approach, and prognosis remain largely unknown [8]; these lesions represent a major diagnostic challenge and require rigorous, well-structured therapeutic strategies to minimize the risk of recurrence [7].

We therefore conducted a systematic review of the literature to characterize the epidemiological profile, etiopathogenesis, clinical and radiological features, and management modalities of benign hybrid lesions of the jaws. This review was conducted in strict accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement, ensuring methodological rigor, transparency, and reproducibility of the study selection, data extraction, and analysis process [9].

Materials and Methods

• Protocol and research question

The working group comprised a dental medicine doctoral candidate and a university hospital assistant, who jointly conducted the search, critical appraisal, and data extraction, with regular group meetings. The research question was structured using the PICOS framework: Population patients with hybrid lesions of the jaws; Intervention diagnosis and management of these patients; Comparator comparison between different hybrid lesion associations; Outcome epidemiological, clinical, radiological, and therapeutic profile; Study design all study types except those specifically excluded. This yielded the research question: "What are the epidemiological, clinical, and radiological features, and the management modalities, of hybrid lesions of the jaws?"

• Search strategy

Four electronic databases MEDLINE *via* PubMed, Scopus, Web of Science, and Google Scholar — were searched using Boolean combinations (AND/OR) of MeSH terms and free-text keywords: "odontogenic tumor*," "non-odontogenic tumor*," "hybrid lesion*," "jaw*," "maxilla*," "mandible*," "maxillary*," "mandibular*," and "alveolar bone*." The exhaustive electronic search was finalized on February 28, 2025. Manual searching was also performed to identify additional eligible records.

• Eligibility criteria

Inclusion criteria: hybrid lesions confined to the jaws; articles addressing the primary research objectives; human studies; interventional analytic studies, cohort, case-control, and cross-sectional studies, case series, and case reports; publications in French or English, with no restriction on publication date.

Exclusion criteria: articles not addressing the research objectives; purely extra-osseous lesions without clinical, radiographic, or histological bone involvement; non-human studies; narrative reviews, systematic reviews, commentaries, or letters to the editor; publications in languages other than French or English.

Article selection proceeded in three phases: (1) Title screening, with removal of duplicates; (2) Abstract screening against inclusion criteria; and (3) Full-text review against the predefined eligibility criteria.

• Data extraction and risk-of-bias assessment

Data were extracted using a predefined grid developed by the working group, capturing bibliographic identification, study objectives and design, description of the study population, variables analyzed, and critical appraisal of methodological limitations. Methodological quality of all included studies was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklists appropriate to each study design (case report, case series, or retrospective study), with

each item scored "yes" or "no" and an overall percentage score calculated to estimate risk of bias.

Results

• Study selection

The search strategy identified 379 records: 364 from the four databases (PubMed/MEDLINE, 44; Scopus, 31; Web of Science, 31; Google Scholar, 258) and 15 from manual searching. Following title, abstract, and full-text screening, 56 studies met the eligibility criteria and were included in the final analysis: 47 case reports, 6 case series, and 3 retrospective studies. Eleven articles excluded at the full-text stage were disqualified for the following reasons: narrative review design (n=1), content not matching a true hybrid lesion (n=6), language other than French or English (n=1), systematic review design (n=1), and description of a lesion without hybrid characteristics (n=2).

• Characteristics of included studies and population

The 56 included studies collectively reported 129 patients with hybrid lesions of the jaws (Table 1). Patient age ranged from 2 to 81 years, most frequently occurring in the 15–29-year age group (45% of cases). Of 129 patients, 70 were male (54.3%) and 59 female (45.7%). General health status was reported for only 22 patients: 17 were otherwise healthy, while 5 had documented comorbidities — hypertension (n=3), diabetes mellitus (n=2), type 1 myotonic dystrophy (n=1), and Gorlin-Goltz syndrome (n=1); all five received ongoing medication for these conditions.

Table 1: Number of cases by study design among the 56 included studies.

Study design	Number of patients
Case reports (n=47 studies)	47
Case series (n=6 studies)	22
Retrospective studies (n=3 studies)	60
Total	129

Note: Case-series totals (8, 2, 2, 3, 5, and 2 patients) sum to 22; retrospective-study totals (19, 34, and 7 patients) sum to 60.

• Anatomical location and lesion composition

The mandible was affected in 96 cases (74.4%), the maxilla in 31 (24.0%), both jaws simultaneously in 1 case (0.8%, a patient with Gorlin-Goltz syndrome), and the affected bone was unspecified in 1 case (0.8%, from an excisional biopsy specimen). Most hybrid lesions comprised two histopathologically distinct components (120/129 cases, 93.0%); nine cases (7.0%) showed three concomitant components, and no case combined more than three lesion types.

The morphological classification of these associations is summarized in Table 2. A tumor-tumor combination was most frequent (84 cases, 65.1%), followed by a cyst-tumor combination (34 cases, 26.4%); a cyst-cyst combination was the rarest (1 case, 0.8%).

Table 2: Morphological classification of hybrid lesion associations (n=129).

Association	n	%
Tumor + Tumor	84	65.12
Cyst + Tumor	34	26.35
Tumor + Tumor + Tumor	3	2.32
Tumor + Tumor + Cyst	6	4.65
Cyst + Cyst	1	0.78
Tumor + non-neoplastic sclerosing bone dysplasia	1	0.78

A wide diversity of specific lesion combinations was identified; the most frequent are shown in Table 3. Central Giant Cell Granuloma (CGCG) combined with Central Odontogenic Fibroma (COF) or with Cemento-Ossifying Fibroma (COF-osseous) were the two leading combinations. CGCG combined with benign fibro-osseous lesions overall (fibrous dysplasia, juvenile ossifying fibroma, or cemento-osseous dysplasia) accounted for 7.75% of all cases (10 patients: fibrous dysplasia, 6; juvenile ossifying fibroma, 3; cemento-osseous dysplasia, 1).

Table 3: Most frequent specific hybrid lesion combinations identified.

Combination	n cases
GCCG + FOC	17
GCCG + FCO	15
KOC + AM	12
KOC + FA	10
KD + Odontoma	10
AOT + CEOT	9
GCCG + fibrous dysplasia	6
AOT + Ameloblastoma	4
KOC + Odontoma	4
GCCG + JOF	3
GCCG + Ameloblastoma	3
GCCG + OKC	3

- **Clinical features**

Detailed clinical data were available for 88 of the 129 cases. The most frequent extraoral sign was swelling (67/88, 76.1%), painless in 43 cases (48.9%) and painful in 18 (20.5%); lymphadenopathy (2 cases, 2.3%), trismus (3 cases, 3.4%), and functional impairment (4 cases, 4.5%) were less common, and no case of paresthesia or purulent discharge was reported. No extraoral sign was present in 17 cases (19.3%). Intraorally, swelling was again the leading finding (32/88, 36.4%), followed by tooth mobility (10 cases, 11.4%), abnormal mucosa (8 cases, 9.1%, including 4 ulcerations), and bleeding (5 cases, 5.7%); 19 cases (21.6%) showed no intraoral sign.

- **Radiological features**

The imaging modality was specified in 70 cases: Panoramic radiography was the first-line examination (52 cases, 74.3%), followed by computed tomography (CT, 17 cases, 24.3%) and cone-beam CT (11 cases, 15.7%), generally obtained as second-line studies. Radiological signs were reported in 92 cases: Lesions were radiolucent in 45 (48.9%) and showed a mixed radiographic pattern in 43 (46.7%); most were well-defined (44 cases, 47.8%). Unilocular lesions (27 cases, 29.3%) were more common than multilocular lesions (19 cases, 20.7%). Additional findings included cortical expansion (13 cases, 14.1%), cortical thinning (5 cases, 5.4%), cortical perforation (9 cases, 9.8%), tooth displacement (13 cases, 14.1%), and root resorption (16 cases, 17.4%); extension into adjacent structures was uncommon, most often involving the mandibular canal (5 cases, 5.4%).

- **Histopathological features and diagnostic concordance**

Histopathological examination is the diagnostic gold standard for hybrid lesions, since clinical and radiological data, while useful for orientation, were insufficient alone to establish certainty. A marked discordance was observed between the initial clinical/radiological impression and the final histopathological diagnosis: Only a single case (a dentigerous cyst associated with an odontoma) showed full concordance between the provisional and final diagnosis, while preliminary incisional biopsy findings matched the final diagnosis in only 12 cases, generally because the biopsy sampled only one of the two or more coexisting components.

- **Treatment and outcome**

Treatment modality was reported for 87 of the 129 cases (Table 4). Surgical management was used in all definitively treated cases; enucleation was the most frequent approach (33 cases, 37.93%), followed by excision (21 cases, 24.13%) and resection (8 cases, 9.19%). Combined procedures (enucleation with curettage, excision with curettage, marsupialization with secondary

enucleation, or resection with reconstruction) were less common. Initial medical management with intralesional corticosteroid injections was attempted in three cases with a provisional diagnosis of CGCG; in all three, clinical worsening (increased swelling with pain) necessitated conversion to surgery, which proved effective for lesion control.

Table 4: Surgical management modalities reported (n=87).

Surgical treatment	n	%
Enucleation	33	37.93
Excision	21	24.13
Resection	8	9.19
Enucleation + curettage	6	6.89
Curettage alone	5	5.74
Excision + curettage	5	5.74
Resection + reconstruction	5	5.74
Marsupialization	2	2.29
Marsupialization + enucleation	2	2.29

Follow-up data adequate to assess recurrence were available for 53 of 129 cases, with follow-up duration ranging from 3 months to 10 years. Only one recurrence (1.8%) was recorded, in a 47-year-old patient treated by complete surgical excision of a CGCG-cemento-ossifying fibroma hybrid lesion, occurring 2 years after treatment (Table 5).

Table 5: Recurrence among 53 cases with adequate follow-up (3 months–10 years).

	n	%
No recurrence	52	98.1
Recurrence (CGCG + cemento-ossifying fibroma, at 2 years)	1	1.8
Marsupialization + enucleation	2	2.29

• Methodological quality

Applying the JBI critical appraisal checklists, the 47 case reports predominantly scored in the 75–100% range (low risk of bias per JBI criteria), with most achieving a full 8/8 score; the 6 case series scored more variably (40–80%); and the 3 retrospective studies scored 58.3–66.7% (moderate risk of bias), most often owing to unreported confounding factors and incomplete discussion of study limitations.

Discussion

• Definition and current classification status

Hybrid lesions are pathological entities showing the coexistence of two or more histopathologically distinct components at a single anatomical site, each retaining its own morphological features without mutual structural alteration; they may be benign, malignant, or combine both behaviors [10-13]. Although hybrid lesions can arise in diverse anatomical regions including the cervicofacial area, trunk, and limbs, with a reported topographic predominance in the trunk (48.1% of cases in one retrospective series) [13] those confined to the jaws are characterized by the coexistence of two or more cystic and/or tumoral entities at the same osseous site [14]. Their low incidence poses a major diagnostic and therapeutic challenge: A retrospective study of 1,767 patients with odontogenic lesions identified only 19 cases of hybrid lesions, a prevalence of 1.07%, underscoring the rarity of this entity.

The fifth edition of the WHO classification of head and neck tumours introduced limited but notable changes to the odontogenic tumor chapter relative to the 2017 edition, most significantly the addition of adenoid ameloblastoma as a newly recognized subtype of benign epithelial odontogenic tumor, alongside refined definitions of several existing entities; the classification of odontogenic cysts remained unchanged [15-20]. Hybrid lesions of the jaws, however, are still not formally addressed in this classification. Given their rarity and lack of recognition, we suggest that future revisions of the WHO classification consider incorporating hybrid lesions as a distinct category, to better reflect their specificity and improve diagnostic and therapeutic standardization.

- **Epidemiological profile**

Hybrid lesions of the jaws can occur at any age, as reflected in the wide age range observed in this review (2–81 years); pediatric cases from age 2 and a case in an 81-year-old patient were both documented among the included studies. This range is consistent with a systematic review of 39 hybrid CGCG lesions reporting an age range of 2–68 years. The 15–29-year age group was most frequently affected (45% of cases), broadly consistent with Pontes et al., who reported a mean age of 24.5 years across 203 cases [21]. The near-equal sex distribution observed here (54.3% male, 45.7% female) contrasted with the female predominance reported by Pontes et al. and by a series of 39 CGCG-hybrid cases (56.4% female) [22,23], as well as with Vijintanawan et al., who reported 23 female versus 16 male cases [24], suggesting that sex predilection may vary according to the specific lesion combinations studied.

General health status was undocumented in the large majority of publications (83% of cases), limiting exploration of any relationship between systemic conditions and the occurrence of hybrid lesions. Nonetheless, Jiji V et al., proposed that myotonic dystrophy could represent a susceptibility factor for hybrid odontogenic lesions, without elucidating the underlying mechanism [25-27], and Karimi et al., proposed a local paracrine mechanism involving multinucleated giant cell formation in hybrid lesions combining fibro-osseous and CGCG components, raising the possibility that systemic factors could modulate this pathway [28]. These hypotheses remain speculative given the scarcity of available data.

- **Pathogenic hypotheses**

The pathogenesis of hybrid lesions remains largely unelucidated, particularly regarding the mechanism by which two or three distinct histopathological components come to coexist at a single site. Several hypotheses have been proposed, primarily in studies of CGCG-hybrid lesions. The "collision tumor" theory, first proposed by Allen et al., for the CGCG-Central Odontogenic Fibroma (COF) combination, posits a fortuitous, simultaneous co-occurrence of two histologically distinct lesions at a shared anatomical site [29-35]; however, Vijintanawan et al., considered this explanation implausible given the intrinsic rarity of both entities, which makes synchronous coexistence highly improbable, and noted that collision tumors typically show simple juxtaposition without true tissue interaction, whereas hybrid lesions display close interconnection between components — including in recurrent cases, where both components persisted together, suggesting an underlying pathogenic link [36-40].

Two competing secondary-induction hypotheses have also been proposed that primary CGCG cells secrete growth factors, cytokines, and chemokines that stimulate proliferation of odontogenic cells, secondarily generating a COF [41]; or, conversely, that a primary COF undergoes a secondary giant-cell reaction triggered by trauma, hemorrhage, or inflammation [42-68]. Shetty et al., lent support to the latter model, proposing that osteoblast-mediated paracrine signals activate multinucleated giant cells within an altered fibro-osseous stroma [69], a hypothesis corroborated by Farzaneh et al.'s clinical observations [70]; considered both an induction model and an independent, concomitant origin of the two entities as plausible explanations [71-75]. Further catalogued five proposed mechanisms across the literature: Collision, transformation (a primary lesion internally transforms into a hybrid lesion, as illustrated by Yoon et al.'s report of ectomesenchymal induction from calcifying odontogenic cyst wall epithelium generating an ameloblastic fibroma), combination (fusion of two distinct pathologies at the cellular or tissue level), conversion (gradual transformation of an initial lesion into a hybrid lesion over its evolution, as illustrated by a case of ameloblastic transformation within an odontogenic keratocyst), and composition (association of components from distinct pathologies forming a composite lesion). In summary, while several hypotheses have been advanced, the underlying pathogenic mechanism of hybrid lesions remains largely unknown, and most included studies were limited to descriptive epidemiological, clinical, radiological, and therapeutic reporting.

- **Clinical and radiological correlation**

Painless swelling as the leading clinical finding (76.1% of evaluable cases) is consistent with Pontes et al., who reported swelling in 80.3% of 203 cases, and with Alsufyani et al., who reported extraoral swelling in 90.9–100% of specific CGCG-hybrid combinations. The predominantly painless, insidious presentation observed here likely reflects a generally low-grade biological potential at the early stage typical of several component subtypes, permitting gradual expansion before pain or other overt signs develop; nonetheless, Pontes et al.,

documented a substantially higher proportion of symptomatic (painful) cases (136/203, 67.0%), indicating meaningful variability in clinical presentation across cohorts, potentially reflecting inflammatory activity, bone expansion with compression of adjacent structures, or heightened osteolytic activity. A fully asymptomatic presentation, discovered incidentally on radiological examination performed for another reason, was also observed here (17 cases) and by Pontes et al. (40/203 cases, 19.7%), reinforcing the importance of radiological vigilance even in the absence of clinical signs.

Radiologically, the predominance of well-defined (47.8%) and unilocular (29.3% *vs.* 20.7% multilocular) images observed in this review is broadly consistent with Pontes et al.'s findings of predominantly unilocular, well-defined lesions, and suggests that most hybrid lesions of the jaws follow an expansile rather than infiltrative growth pattern, at least at the stage of clinical detection. However, cortical involvement (expansion, thinning, or perforation, together affecting under 30% of evaluable cases) was considerably less frequent than the 93.1% cortical involvement reported by Alsufyani et al., for CGCG-hybrid lesions specifically, a discrepancy that may reflect differences in the specific lesion subtypes, diagnostic methods, or evaluation criteria used across studies; standardized radiographic reporting criteria would facilitate more reliable cross-study comparison. The pronounced mandibular predominance observed here (74.4%) is corroborated by Pontes et al., (58.1% mandibular) and (34/39 CGCG-hybrid cases in the mandible), and may be attributable to the mandible's greater bone density and comparatively reduced medullary vascularity relative to the maxilla, together with the high representation of CGCG among hybrid-lesion components (42% of cases), a lesion itself preferentially located in the mandible.

- **Treatment and follow-up**

Surgical treatment predominated across all included studies, with enucleation (37.9%) and excision (24.1%) as the leading modalities figures closely comparable to Pontes et al., who reported enucleation in 44.8%, excision in 24.6%, curettage in 12.8%, and combined enucleation-curettage in 4.4% of 203 cases. As emphasized by Thapa et al., treatment selection should be individualized according to patient age and general health, the feasibility of rigorous long-term follow-up, lesion size, location and extent, and relationship with adjacent structures, together with the specific histopathological components identified: an isolated odontogenic keratocyst is generally managed conservatively by simple enucleation, whereas a concomitant more aggressive component (e.g., ameloblastoma) warrants a more extensive surgical approach.

The low overall recurrence rate observed here (1/53, 1.8%) is consistent with the 1.9% rate (4/203 cases, mean follow-up 34.4 months) reported by Pontes et al., who identified limited follow-up duration as the principal limitation across the reviewed literature, potentially underestimating true recurrence risk. Notably, both the recurrence identified in this review and the recurrences reported by Pontes et al. and by Alsufyani et al., involved a CGCG component (combined with COF, cemento-ossifying fibroma, or aneurysmal bone cyst) [65,66], suggesting that CGCG-containing hybrid lesions may carry a comparatively greater biological potential for recurrence than other combinations, warranting particularly close post-treatment surveillance when this component is present.

Limitations

This review has several limitations, most stemming from the nature of the underlying literature rather than the review methodology itself. First, the near-total absence of rigorously formulated etiopathogenic investigation across the included studies limits understanding of the morphogenetic mechanisms underlying these composite lesions. Second, clinical and radiographic documentation was frequently incomplete, hindering scientific reproducibility and inter-study comparability and impeding the development of standardized diagnostic criteria. Third, postoperative follow-up was insufficiently reported in many studies; the resulting lack of robust longitudinal data likely leads to underestimation of true recurrence risk. Finally, the evidence base was dominated by isolated case reports and short case series (53 of 56 included studies), which by nature lack a comparator group and carry a high inherent risk of bias and low statistical power, substantially limiting the generalizability of the epidemiological and therapeutic conclusions that can be drawn. These limitations highlight the need for prospective, multicenter studies employing standardized methodology to better elucidate the etiopathogenic mechanisms, clinical course, and optimal therapeutic approach for hybrid lesions of the jaws.

Conclusion

This systematic review of 129 reported cases across 56 studies indicates that hybrid lesions of the jaws can occur at any age, with a peak in young adulthood, an almost equal sex distribution, and a marked mandibular predominance. Their clinical presentation is variable, ranging from asymptomatic incidental findings to painful swelling, and their radiological features, while diverse, are most often well-defined and unilocular or mixed in density. Histopathological examination remains the diagnostic reference standard, most commonly revealing a two-component association, most frequently CGCG combined with central odontogenic fibroma or cemento-ossifying fibroma. Management is exclusively surgical and should be tailored to the specific components involved; recurrence is uncommon overall but appears more likely when a CGCG component is present, warranting rigorous long-term clinical and radiological follow-up. The absence of hybrid lesions from current WHO classification schemes, combined with substantial gaps in the published literature, underscores the need for further research to clarify their etiopathogenesis and for their formal inclusion in a recognized classification system, in order to optimize management and reduce the risk of under- or overtreatment.

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Conflict of Interest Statement

The authors declare no conflict of interest related to this work.

Ethics Statement

This systematic review analyzed previously published, de-identified case data and did not involve direct patient contact or new human-subjects research; institutional ethics committee approval and individual patient consent are therefore not applicable. No ethics approval or waiver statement was reported in the source thesis, consistent with standard practice for systematic reviews of published literature.

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