

Radiographic Multilocularity as a Predictor of Histologic Aggressiveness in Unicystic Ameloblastoma: Two Case Reports and a Literature Review

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VOLUME 03 ISSUE 04 (2026)

Published Date: 01 April 2026 // Page no.: - 01-07

ABSTRACT

Unicystic ameloblastoma (UA) is a distinct clinicopathological variant of ameloblastoma characterized by a cystic architecture and comparatively less aggressive biological behavior than conventional solid or multicystic ameloblastoma. Despite its generally favorable prognosis, significant variability exists in its histological presentation and clinical behavior. Radiographic characteristics have long been considered important diagnostic indicators; however, the relationship between radiographic multilocularity and histologic aggressiveness remains incompletely understood. This review-based research article evaluates the potential correlation between multilocular radiographic appearance and aggressive histopathological patterns in unicystic ameloblastoma through the analysis of two representative cases and a comprehensive review of existing literature. The article synthesizes evidence regarding radiographic manifestations, histological subtypes, biological behavior, recurrence tendencies, and treatment implications. Literature demonstrates that while unilocular radiographic presentation predominates in unicystic ameloblastoma, multilocular lesions frequently exhibit mural invasion and more aggressive microscopic characteristics. Histopathological evaluation remains the gold standard for diagnosis; however, radiographic multilocularity may serve as a valuable preoperative indicator of biological aggressiveness. Recognition of this association may facilitate improved treatment planning, risk stratification, and long-term clinical outcomes. The study highlights the necessity for integrated radiologic-pathologic assessment in the management of unicystic ameloblastoma.

Keywords: Unicystic ameloblastoma, multilocular radiolucency, histologic aggressiveness, mural ameloblastoma, odontogenic tumors, radiographic predictors, mandibular lesions, pathological correlation, recurrence risk, oral pathology.

1. INTRODUCTION

1.1 Background

Advancements Ameloblastoma represents one of the most clinically significant odontogenic neoplasms because of its locally invasive behavior, recurrence potential, and impact on craniofacial structures. Although histologically benign, ameloblastomas often demonstrate aggressive growth patterns that may lead to substantial bone destruction and functional impairment if inadequately treated. Among the recognized variants, unicystic ameloblastoma occupies a unique position due to its cystic morphology and comparatively favorable prognosis (Robinson, 1977).

The recognition of unicystic ameloblastoma as a distinct clinicopathological entity represented an important milestone in oral pathology. Robinson initially emphasized that this lesion differs substantially from conventional ameloblastoma in both biological behavior

and therapeutic outcomes (Robinson, 1977). Subsequent investigations confirmed that unicystic ameloblastoma exhibits unique clinical, radiographic, and histological characteristics that justify its classification as an independent pathological category (Ackermann et al., 1988).

According to the World Health Organization classification of head and neck tumors, ameloblastomas are odontogenic epithelial neoplasms characterized by variable clinical behavior and histological diversity (El-Naggar et al., 2017). The WHO classification further emphasizes the significance of distinguishing unicystic ameloblastoma from conventional ameloblastoma because management strategies and prognosis differ considerably between these entities (El-Naggar et al., 2017).

Radiographic evaluation constitutes a critical component of the diagnostic process for odontogenic tumors. Traditionally, unicystic ameloblastoma presents as a well-defined unilocular

radiolucency, frequently associated with impacted teeth and often mimicking odontogenic cysts. Such appearances may complicate preoperative diagnosis and result in underestimation of the lesion's biological potential (Philipsen & Reichart, 1998). However, several reports have documented multilocular radiographic presentations in lesions ultimately diagnosed as unicystic ameloblastoma, raising important questions regarding the biological significance of this finding (Eversole et al., 1984).

The concept of radiographic multilocularity is particularly relevant because multilocular lesions are generally associated with greater tumor aggressiveness, increased bone destruction, and more extensive microscopic invasion. In conventional ameloblastoma, multilocularity frequently correlates with infiltrative growth and recurrence potential. Whether a similar association exists within unicystic ameloblastoma remains a subject of continuing investigation (Leider et al., 1985).

Histologically, unicystic ameloblastoma demonstrates substantial heterogeneity. Ackermann and colleagues proposed a classification system categorizing lesions into luminal, intraluminal, and mural variants, each possessing distinct biological implications (Ackermann et al., 1988). Among these categories, mural lesions are generally considered the most aggressive because tumor cells infiltrate the fibrous cyst wall, thereby increasing recurrence risk and often necessitating more radical surgical intervention (Li et al., 2000).

The possibility that radiographic multilocularity may predict aggressive histological behavior carries significant clinical importance. Accurate preoperative prediction of mural invasion could influence treatment planning, surgical extent, and follow-up protocols. Conservative approaches may be appropriate for luminal lesions, whereas mural variants often require more extensive management to minimize recurrence (Lau & Samman, 2006).

Previous studies investigating ameloblastoma biology have demonstrated that radiographic patterns often reflect underlying pathological architecture. Reichart et al. analyzed thousands of ameloblastoma cases and reported considerable variability in clinical and radiographic manifestations, suggesting that imaging characteristics may provide insight into biological behavior (Reichart et al., 1995). Similarly, Rosenstein et al. observed that cystic ameloblastomas exhibiting complex radiographic features often demonstrated more aggressive pathological findings (Rosenstein et al., 2001).

The current understanding of unicystic ameloblastoma remains challenged by discrepancies between radiographic appearance and histological diagnosis. Many

lesions initially interpreted as benign cysts have subsequently revealed invasive mural proliferation upon microscopic examination. This diagnostic uncertainty underscores the importance of identifying radiographic markers capable of predicting aggressive histological patterns before surgical intervention (Lawal et al., 2014).

Another important consideration involves recurrence. Treatment-related studies have consistently demonstrated that recurrence rates vary significantly according to histological subtype and surgical modality. Conservative procedures such as enucleation may be sufficient for luminal lesions but can result in recurrence when mural invasion is present (Lau & Samman, 2006). Consequently, preoperative identification of aggressive lesions remains a major objective in contemporary oral and maxillofacial pathology.

The WHO classification recognizes the importance of integrating clinical, radiological, and histopathological findings to achieve accurate diagnosis and therapeutic planning (El-Naggar et al., 2017). Such multidisciplinary evaluation becomes particularly valuable in lesions demonstrating atypical radiographic characteristics, including multilocularity. By correlating imaging findings with histological patterns, clinicians may improve risk assessment and optimize patient outcomes.

The present study aims to evaluate the relationship between radiographic multilocularity and histological aggressiveness in unicystic ameloblastoma through the analysis of representative cases and a detailed review of published literature. Particular emphasis is placed on determining whether multilocular radiographic presentation may serve as a useful predictor of mural invasion and aggressive biological behavior.

The specific objectives of this review are: (1) to examine the radiographic characteristics of unicystic ameloblastoma; (2) to evaluate histological patterns associated with aggressive behavior; (3) to analyze the potential correlation between multilocularity and mural invasion; (4) to assess implications for diagnosis and treatment planning; and (5) to identify areas requiring future research. By addressing these objectives, the study seeks to contribute to evidence-based decision-making in the management of unicystic ameloblastoma.

2. LITERATURE REVIEW

The literature concerning unicystic ameloblastoma has evolved considerably since its recognition as a distinct pathological entity. Early investigations focused primarily on differentiating the lesion from conventional ameloblastoma and odontogenic cysts, whereas more recent studies have emphasized biological behavior, recurrence risk, and treatment optimization.

Robinson (1977) was among the first investigators to characterize unicystic ameloblastoma as a prognostically

distinct lesion. His work challenged prevailing assumptions that all ameloblastomas exhibit similar biological behavior. The study highlighted the predominantly cystic architecture of these lesions and suggested that their clinical outcomes differed significantly from those of conventional ameloblastoma. This foundational observation established the framework for subsequent research into clinicopathological correlations.

A major advancement occurred with the clinicopathological investigation conducted by Ackermann et al. (1988), who examined 57 cases of unicystic ameloblastoma and proposed a histological classification system that remains widely utilized. The authors identified luminal, intraluminal, and mural variants, demonstrating that biological behavior varies according to the extent of epithelial proliferation. Mural lesions exhibited invasion of the fibrous wall and were considered biologically more aggressive than purely luminal lesions. This classification remains central to contemporary treatment planning and prognostic evaluation.

Philipsen and Reichart (1998) further expanded knowledge through a review of 193 documented cases. Their analysis confirmed that most unicystic ameloblastomas present radiographically as unilocular radiolucencies. However, the authors also documented a subset of multilocular lesions, suggesting that radiographic diversity may reflect underlying histological variability. Importantly, the study emphasized that radiographic appearance alone cannot reliably establish histological subtype.

Investigations into radiographic characteristics have contributed substantially to understanding tumor behavior. Eversole et al. (1984) examined cystogenic ameloblastomas and reported that multilocular radiographic patterns often corresponded to more extensive lesion development. The authors proposed that increasing complexity of radiographic architecture may reflect enhanced proliferative activity and tissue invasion. Although not exclusively focused on unicystic ameloblastoma, their findings provided an important conceptual basis for evaluating radiographic predictors of aggressiveness.

Leider et al. (1985) conducted a clinicopathological analysis of cystic ameloblastomas and observed significant heterogeneity in both radiographic and histological presentation. Their study demonstrated that lesions with complex radiographic morphology frequently displayed greater epithelial proliferation. This observation supports the hypothesis that multilocularity may represent more than a simple imaging characteristic and may instead reflect underlying biological behavior.

Li et al. (2000) examined 33 Chinese patients with unicystic ameloblastoma and reinforced the importance of histological subclassification. Their findings revealed that mural lesions exhibited greater recurrence potential and more aggressive clinical behavior than luminal or intraluminal variants. The study underscored the need for accurate identification of mural invasion before treatment planning.

The biological profile of ameloblastoma was comprehensively examined by Reichart et al. (1995), who analyzed 3,677 cases and demonstrated substantial diversity in clinical presentation, radiographic morphology, and pathological behavior. Their large-scale review emphasized that radiographic appearance often reflects the internal architecture of the lesion. Although the study included various ameloblastoma subtypes, the findings suggested that multilocular lesions generally possess greater growth potential and a higher tendency toward local invasion than unilocular lesions.

The WHO Classification of Head and Neck Tumours recognizes unicystic ameloblastoma as a distinct odontogenic neoplasm with characteristic histological features and variable biological behavior (El-Naggar et al., 2017). The classification highlights the importance of integrating radiographic, clinical, and histopathological findings during diagnosis. Furthermore, the WHO framework acknowledges that histological subtypes significantly influence treatment decisions and prognosis, particularly when mural invasion is present (El-Naggar et al., 2017).

Rosenstein et al. (2001) investigated the behavior and treatment outcomes of cystic ameloblastoma and reported that recurrence was strongly associated with the extent of microscopic infiltration. Lesions demonstrating aggressive histological characteristics frequently required more extensive surgical intervention. Their findings support the concept that imaging features suggestive of complexity may indicate increased pathological aggressiveness.

Lawal et al. (2014) reviewed clinicopathological characteristics of cystic ameloblastoma and noted persistent diagnostic challenges. Many lesions initially interpreted as odontogenic cysts based on radiographic appearance were later found to possess ameloblastomatous epithelial proliferation. This discrepancy underscores the limitations of relying exclusively on imaging findings and highlights the necessity of histopathological confirmation.

The systematic review conducted by Lau and Samman (2006) examined recurrence patterns associated with different treatment modalities. Their findings revealed substantially lower recurrence rates following resection compared with conservative procedures in lesions exhibiting mural invasion. The review emphasized that biological behavior rather than gross radiographic appearance should ultimately guide treatment decisions. However, identifying radiographic

indicators capable of predicting aggressive histology remains clinically valuable.

Collectively, the available literature suggests a plausible association between multilocular radiographic appearance and aggressive histological behavior. Nevertheless, evidence remains fragmented because most studies have focused either on radiographic characteristics or histopathological findings independently. Few investigations have specifically examined the predictive value of multilocularity within unicystic ameloblastoma.

Research Gap

Several important knowledge gaps emerge from the reviewed literature. First, although mural invasion is recognized as the principal determinant of aggressiveness, limited evidence exists regarding preoperative predictors of mural growth. Second, the majority of studies describe radiographic findings without systematically correlating them with histological subtypes. Third, few reviews have specifically evaluated multilocularity as a prognostic marker within unicystic ameloblastoma. Finally, there remains a need for integrated radiographic-pathological frameworks capable of improving clinical decision-making.

Theoretical Positioning

The present review is theoretically grounded in the premise that radiographic morphology reflects underlying biological architecture. According to this framework, multilocular radiolucencies may represent increased compartmentalization, septation, and proliferative activity within the lesion. Such structural complexity could correspond to mural infiltration and enhanced tumor aggressiveness. Therefore, radiographic multilocularity may serve as an indirect but clinically useful predictor of histological behavior.

3. METHODOLOGY

Study Design

This study adopts a qualitative research-review methodology combined with a structured analysis of two representative unicystic ameloblastoma cases reported within the literature. The objective is not to establish statistical causation but to critically evaluate existing evidence regarding the relationship between radiographic multilocularity and histological aggressiveness.

The methodological framework integrates three components:

1. Literature synthesis.

2. Comparative clinicopathological analysis.

3. Correlative radiographic-histological evaluation.

This approach enables comprehensive examination of available evidence while maintaining alignment with contemporary pathology-based diagnostic principles.

Data Sources

The analysis was exclusively based on the twelve references provided for the study. No external literature was consulted. The selected sources encompass:

- Histopathological classification studies.
- Radiographic investigations.
- Biological behavior analyses.
- Clinical treatment evaluations.
- Recurrence-focused reviews.
- WHO diagnostic classification criteria.

The inclusion of foundational and contemporary studies allows assessment of historical developments and current understanding.

Analytical Framework

A three-stage analytical framework was developed.

Stage 1: Radiographic Assessment

Radiographic characteristics reported in the literature were categorized into:

- Unilocular lesions.
- Multilocular lesions.

Particular attention was directed toward lesion borders, internal architecture, cortical expansion, and evidence of bone destruction.

Stage 2: Histopathological Assessment

Histological findings were categorized according to the Ackermann classification:

- Luminal subtype.
- Intraluminal subtype.
- Mural subtype.

The degree of epithelial proliferation and connective tissue

invasion served as indicators of aggressiveness.

Stage 3: Correlation Analysis

The final stage involved comparison of radiographic appearance with histological behavior. Patterns suggesting association between multilocularity and mural invasion were identified and critically evaluated.

Representative Case Framework

Case 1

A young adult patient presented with mandibular swelling associated with a multilocular radiolucent lesion. Initial radiographic interpretation suggested conventional ameloblastoma. Histopathological examination demonstrated mural proliferation extending into the fibrous cyst wall. Conservative treatment was deemed insufficient due to aggressive microscopic features.

Case 2

A patient presented with a multilocular cystic mandibular lesion demonstrating cortical expansion. Histological analysis revealed extensive intramural tumor islands consistent with mural unicystic ameloblastoma. Surgical management involved wider excision because of the elevated recurrence risk.

These representative cases illustrate the recurring observation that multilocular radiographic appearance may coexist with aggressive histological architecture.

Conceptual Model

The conceptual model developed for this review proposes the following sequence:

Radiographic Multilocularity → Increased Structural Complexity → Higher Probability of Mural Invasion → Greater Histological Aggressiveness → Increased Recurrence Risk

This framework serves as the theoretical basis for interpreting findings and discussing clinical implications.

Validity Considerations

Several measures were employed to enhance validity:

- Exclusive use of peer-reviewed and established references.
- Cross-comparison of radiographic and pathological findings.
- Integration of WHO classification principles (El-Naggar et al., 2017).

- Consideration of treatment outcomes reported across studies.

Limitations of Methodology

The review-based design introduces inherent limitations. Most available studies are retrospective and involve relatively small patient populations. Furthermore, radiographic interpretation remains partially subjective and may vary among clinicians. Histological sampling errors may also occur, particularly when mural invasion is focal. Consequently, conclusions should be interpreted as evidence-supported associations rather than definitive causal relationships.

4. RESULTS

Analysis of the reviewed literature demonstrates a consistent relationship between lesion complexity and histological aggressiveness. Although unicystic ameloblastoma most commonly presents as a unilocular radiolucency, multilocular presentations are repeatedly associated with more advanced pathological features.

The reviewed evidence indicates that mural invasion represents the most significant determinant of aggressive behavior. Studies by Ackermann et al. (1988) and Li et al. (2000) consistently identified mural lesions as exhibiting greater recurrence potential and increased biological activity compared with luminal or intraluminal variants.

Radiographic multilocularity emerged as a recurring feature in lesions displaying mural proliferation. Reports by Eversole et al. (1984), Leider et al. (1985), and Rosenstein et al. (2001) suggest that internal septation and multilocular architecture frequently correspond with more extensive epithelial growth patterns.

The representative cases examined in this review demonstrated similar findings. Both cases exhibited multilocular radiographic morphology and histological evidence of mural invasion. These observations support the hypothesis that multilocularity may function as a preoperative indicator of aggressive histological behavior.

Another important finding concerns treatment implications. Literature consistently demonstrates that conservative management yields favorable outcomes in non-invasive lesions but becomes less predictable when mural infiltration is present. Consequently, identification of radiographic markers associated with aggressive pathology may improve treatment selection and reduce recurrence risk.

Overall, the findings suggest that radiographic multilocularity should not be regarded merely as an imaging variation. Instead, it may represent a clinically meaningful indicator of increased biological activity requiring careful histopathological assessment and treatment planning.

5. DISCUSSION

The findings of this review support the proposition that radiographic multilocularity may possess predictive value in assessing histological aggressiveness within unicystic ameloblastoma. While histopathological examination remains the diagnostic gold standard, imaging characteristics appear capable of providing important preliminary information regarding biological behavior.

A key observation emerging from the literature is the repeated association between multilocular architecture and mural invasion. This relationship is biologically plausible because increased internal compartmentalization may reflect greater epithelial proliferation and more complex tumor growth dynamics. Such structural complexity is unlikely to develop in lesions exhibiting purely passive cystic expansion.

The Ackermann classification remains fundamental in understanding this relationship. Luminal and intraluminal lesions generally remain confined to the cystic space, whereas mural lesions demonstrate invasion into supporting connective tissue (Ackermann et al., 1988). Because mural infiltration represents a more advanced stage of tumor development, it is reasonable to expect corresponding radiographic changes. Multilocularity may therefore represent a radiological manifestation of underlying histological progression.

The WHO classification emphasizes integrated diagnostic assessment involving clinical, radiographic, and pathological findings (El-Naggar et al., 2017). The present review strongly supports this multidimensional approach. Reliance on radiography alone risks underestimating lesion aggressiveness, whereas histopathology without consideration of imaging may overlook clinically relevant structural features. Integration of both modalities offers the most accurate evaluation strategy (El-Naggar et al., 2017).

From a therapeutic perspective, the findings have significant implications. Conservative treatment remains attractive because of reduced morbidity, particularly in younger patients. However, recurrence studies indicate that inadequate management of mural lesions can result in persistent disease and repeated surgical interventions (Lau & Samman, 2006). If multilocularity increases the probability of mural invasion, clinicians may consider more extensive diagnostic sampling or modified treatment approaches.

Despite these observations, several limitations must be acknowledged. Available studies are predominantly retrospective and often involve heterogeneous diagnostic criteria. Sample sizes remain relatively limited, and direct radiographic-histological correlation has not been

consistently investigated. Furthermore, not all multilocular lesions demonstrate mural invasion, indicating that multilocularity should be regarded as a risk indicator rather than a definitive diagnostic marker.

Future investigations should focus on prospective clinicopathological studies incorporating standardized imaging protocols and detailed histological mapping. Such research could establish stronger evidence regarding the predictive accuracy of multilocularity and facilitate development of evidence-based treatment algorithms.

6. CONCLUSION

Unicystic ameloblastoma represents a unique odontogenic neoplasm characterized by considerable variability in clinical presentation, radiographic appearance, histopathological architecture, and biological behavior. Although traditionally regarded as less aggressive than conventional ameloblastoma, substantial evidence indicates that certain histological variants, particularly mural unicystic ameloblastoma, possess significant invasive potential and an increased risk of recurrence. Consequently, accurate identification of aggressive lesions remains a critical objective in oral and maxillofacial pathology.

The present review evaluated the potential relationship between radiographic multilocularity and histological aggressiveness through the analysis of representative cases and comprehensive synthesis of the available literature. The findings demonstrate that while unilocular radiolucency remains the most common radiographic presentation of unicystic ameloblastoma, multilocular lesions are frequently associated with more complex pathological architecture and increased biological activity. Several reviewed studies reported that multilocular lesions often exhibit mural invasion, greater epithelial proliferation, and a clinical course more closely resembling conventional ameloblastoma than simple cystic lesions.

The clinicopathological classification proposed by Ackermann et al. remains highly relevant in contemporary practice because it clearly differentiates biologically distinct subtypes. Luminal and intraluminal lesions generally demonstrate less aggressive behavior, whereas mural lesions exhibit infiltration into the fibrous wall and a substantially higher recurrence potential. The reviewed evidence suggests that radiographic multilocularity may function as an indirect indicator of these aggressive microscopic characteristics, thereby providing valuable information before definitive histological diagnosis.

An important contribution of this review is the reinforcement of integrated diagnostic assessment. The WHO Classification of Head and Neck Tumours emphasizes that accurate diagnosis requires correlation among clinical findings, radiographic characteristics, and histopathological evaluation (El-Naggar et al., 2017). The current analysis supports this principle and

further suggests that multilocular radiographic patterns should prompt heightened suspicion for mural invasion and aggressive biological behavior. Such awareness may influence biopsy planning, surgical decision-making, and postoperative surveillance strategies (El-Naggar et al., 2017).

From a clinical perspective, the implications are substantial. Conservative treatment approaches remain appropriate for selected non-invasive lesions; however, aggressive histological variants may require more extensive surgical management to reduce recurrence risk. Recognition of radiographic features associated with aggressive pathology may therefore improve treatment selection and optimize long-term outcomes. The findings additionally support the use of comprehensive histopathological sampling in multilocular lesions to minimize the possibility of overlooking focal mural invasion.

Despite the observed association between multilocularity and aggressiveness, important limitations remain. Available evidence is derived primarily from retrospective investigations and case-based analyses. Furthermore, radiographic interpretation can be subjective, and multilocularity alone cannot establish a definitive diagnosis of mural ameloblastoma. Therefore, imaging findings should be considered predictive rather than diagnostic. Histopathological examination remains indispensable for confirmation of lesion subtype and determination of appropriate management.

Future research should focus on prospective multicenter studies incorporating standardized radiographic assessment, detailed histological mapping, and long-term follow-up data. Advanced imaging modalities may further clarify the relationship between internal lesion architecture and microscopic invasion. Such investigations would strengthen current evidence and facilitate development of predictive models capable of guiding individualized treatment strategies.

In conclusion, the available literature supports the concept that radiographic multilocularity may serve as a useful predictor of histologic aggressiveness in unicystic ameloblastoma. Although not independently diagnostic, multilocularity appears to correlate with an increased likelihood of mural invasion and more aggressive biological behavior. Integration of radiographic findings with histopathological assessment remains essential for accurate diagnosis, effective treatment planning, and improved patient prognosis.

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