

Unicystic ameloblastoma: analysis of surgical management and recurrence risk factors

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Abstract

Unicystic ameloblastoma is a distinct pathological variant with varying evidence published about its behaviour and surgical management. Due to a paucity of large studies in the literature with long-term follow up, the aim of this study was to analyse its surgical management and identify clinicopathological features associated with recurrences. All histopathologically confirmed lesions diagnosed at two referral centres between 1995 and 2020 were retrospectively analysed. Demographic, clinical, radiological, and histopathological features were analysed along with surgical methods and follow-up data. Univariate regression analyses were performed to identify risk factors for recurrence. Sixty-three patients were included in the study with mean age of 26.3 years and a male to female ratio of 1:0.75. The majority of lesions occurred in the posterior mandible (57.1%) and were unilocular (88.9%). Most lesions were managed with enucleation followed by application of Carnoy's solution (ferric chloride: 1g; chloroform: 3 mL; glacial acetic acid: 1 mL; ethyl alcohol 96%: 6 mL) and burring of the peripheral bone margin which resulted in the lowest recurrences (9.1%) besides resection. Significantly associated clinicopathological features with recurrences included patients who were male, large lesions (>90 mm), presence of root resorption, cortical perforation, mural subtype, and retention of associated teeth. In conclusion, decision making in the management of unicystic ameloblastoma should be based on the clinicopathological features and not be solely based on the histopathological subtype. Enucleation followed by application of Carnoy's solution and burring of the peripheral bone margin was demonstrated to be the least invasive method with an acceptable low recurrence rate. © 2021 The British Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

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Introduction

Unicystic ameloblastoma (UAM) is a benign but locally aggressive neoplasm of epithelial origin.¹ It was first reported by Robinson and Martinez in 1977 as a distinct entity due to its marked clinical and radiological characteristics as well as histopathological features.² Clinically, it presents a decade earlier when compared to conventional ameloblastoma. Radiographically, it appears as a well-demarcated, unilocular radiolucency that generally encompasses an unerupted tooth the mimics a dentigerous cyst. Histopathologically, it consists of a cystic cavity lined by

an ameloblastomatous epithelium with three distinct growth patterns. Luminal subtype is when the tumour is confined to the epithelial lining alone, while intraluminal subtype shows extension of the tumour into the lumen of the cyst. In the mural subtype the tumour invades the wall of the cyst.³

When initially described, UAM was reported to respond favourably to conservative methods when compared with its conventional counterpart.⁴ However, recent evidence has shown that mural UAM behaves more aggressively than the other two histological variants with recurrence rates post enucleation similar to that of conventional ameloblastoma.⁵ As a result, the 2017 WHO classification recommended that mural type of UAM be acknowledged as having similar aggressive behaviour to conventional ameloblastoma, although further studies are needed prior to reclassification of this variant.^{1,6}

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The management of UAM is controversial and dependent on the histological type.⁷ Conservative treatment has poorer prognostic outcomes due to higher risk of recurrence, while radical treatment is associated with significant morbidity.⁸ Due to the paucity of large studies on the management of UAM in the literature with long-term follow up, the aim of the current study was to analyse the success of various surgical methods in the management of UAM and identify clinicopathological features associated with recurrences.

Material and methods

All histopathologically confirmed UAM diagnosed at two referral centres between January 1995 and December 2020 were retrospectively analysed. Ethics consent was obtained from the Biomedical Research Ethics Committee of the institution prior to conducting the study.

The inclusion criteria included all records of patients diagnosed with UAM with detailed clinical, radiological, and histopathological features. Surgical records were analysed including follow-up visits and presence of recurrences. Records were excluded when clinico-pathological details were missing and the histopathological diagnosis including the subtype was inconclusive. Surgical methods needed to be described in detail including the use of any adjuvant methods such as application of Carnoy's solution (ferric chloride: 1g; chloroform: 3 mL; glacial acetic acid: 1 mL; ethyl alcohol 96%: 6 mL) and/or burring of the peripheral bone margin. Furthermore, records were excluded if no postoperative follow-up data were present to detect recurrences for a minimum period of 12 months.

Details recorded for each case included demographic data such as age and gender. The clinical features of each neoplasm including the presence of swelling, pain, and paraesthesia were recorded. Radiological features including location, density, size, locularity, definition of margin, cortical perforation, expansion of cortex, and presence of root resorption/displacement were analysed. The histopathological features including the subtype were noted based on the final surgical specimen and on the diagnostic criteria as defined by the WHO. Surgical methods employed to manage the lesion were recorded as well as radiographs and notes from postoperative follow up.

The location of each lesion was categorised into different regions in the jaws. The size of each lesion was measured in millimetres on panorex radiographs along the widest diameter. Lesions were classified on radiographs as either unilocular or multilocular. Root resorption of permanent dentition was evaluated on panorex radiographs for flattening of the roots of dentition associated with the lesion.

Data were analysed using Epi Info™ V7 (Centres for Disease Control) by Fisher's exact test and Student's *t* test. Variance analysis was used to correlate demographic and radiological parameters with the various histopathological subtypes. Univariate regression analysis was used to compare outcomes of various surgical methods utilised in this

study and identify factors associated with high recurrence. Statistical significance was set at $p < 0.05$.

Results

Demographics

Seventy-nine patients were diagnosed with UAM during the 25-year period of which 63 met the inclusion criteria. A total of 268 was diagnosed with ameloblastoma in the same period with UAM comprising 29.5% of all ameloblastomas. The ages of patients ranged from 10–75 years with the majority of patients presenting in their second and third decades of life (74.6%). The mean age of patients affected by UAM (26.3 years) was younger than patients diagnosed with conventional ameloblastoma (30.4 years) in the same population; however this was not statistically significant. Males ($n = 36$; 57.1%) were more commonly affected than females ($n = 27$; 42.9%).

Clinical presentation

The majority of patients presented with swelling of the affect part of the jaw ($n = 56$; 88.9%). The mean period of time from start of symptoms to presentation was 8.6 months. The mandible ($n = 59$; 93.6%) was markedly more involved than the maxilla ($n = 4$; 6.4%). Most lesions occurred in the posterior regions of the jaws ($n = 36$; 57.1%) with the molar region of the mandible being the most affected site overall ($n = 20$; 31.7%).

Radiological features

The majority of lesions presented as a unilocular radiolucency ($n = 56$; 88.9%). Seven lesions (11.1%) appeared as multilocular while only four lesions appeared mixed in density (6.3%). All lesions were well-defined with the exception of three cases which extended into the coronoid and condyle regions of the mandible. Root resorption was a prominent feature ($n = 35/58$; 60.3%) as was tooth displacement ($n = 46/58$; 79.3%). Cortical expansion was also a common ($n = 51$; 80.9%) while cortical perforation was less frequent ($n = 13$; 20.6%).

The size of the lesions ranged from 10–132 mm (mean = 70mm). Interestingly, lesions with root resorption (mean = 77.1mm) presented with significantly ($p = 0.003$) larger size compared to lesions that didn't (mean = 55.9mm). Furthermore, patients with root resorption (mean = 28.7 years) were significantly ($p = 0.014$) older than those without (mean = 19.9 years). These findings highlight that the presence of root resorption may indicate more aggressive behaviour of the lesion.

Histopathological features

The epithelial lining of UAM was fairly thin (5–10 layers) and consistently displayed basal cell palisading. The mural

subtype was most common. Intraluminal and mural subtypes were significantly larger in size on radiographs than luminal lesions. No other significant differences were found in terms of the clinicopathological features amongst the histopathological subtypes (Table 1).

Surgical management and recurrences

Sixty-three lesions were managed with various surgical methods with seven recurrences (recurrence rate: 11.1%) over a mean follow-up period of 25.6 months (Table 2). The majority of UAM were managed with enucleation followed by application of Carnoy’s solution and burring of the peripheral bone margin (n = 44; 69.8%). The defect was then packed with bismuth iodide paraffin paste (BIPP) impregnated gauze which was removed incrementally over two to three visits one week apart. This method yielded the lowest recurrence besides resection.

Marsupialisation followed by enucleation resulted in the highest recurrence of 25% (Fig. 1). Enucleation alone was not commonly used for the management of UAM as inevitable there was always a concern that tumour cells are left behind in the bony wall and the resultant recurrence rate was significantly high when compared with other methods (p = 0.02).

No recurrences were associated with resection although it was only utilised for tumours with mural subtype (n = 6/6; 100%) that caused cortical perforation (n = 5/6; 83.3%), were extensive in size (mean = 83 mm) and occurred in the mandibular posterior regions. Significantly associated clinical

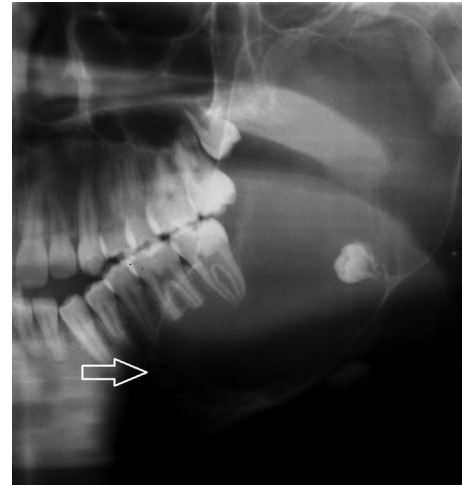


Fig. 1. Preoperative panorex radiograph showing extensive unicystic ameloblastoma into the left mandibular ramus and condyle regions that recurred post marsupialisation.

copathological features with recurrences included male gender, large lesions (>90 mm), presence of root resorption, cortical perforation, and mural subtype (Table 3).

One significant common denominator in the majority of cases that recurred was the retention of teeth associated with the lesion (Table 3). It is important to remove teeth associated with the lesion at the time of final surgical treatment as the lesion has the tendency to extend between the roots of the involved teeth. This leads to recurrences as the tumour tissue cannot be accessed in these areas.

Table 1
Demographic and radiological features of the histopathological subtypes of UAM. Data are mean (SD) or number.

Variable	Luminal (n = 16)	Intraluminal (n = 20)	Mural (n = 27)	p value
Age (years)	22.1 (4.7)	26.9 (18.3)	29.9 (16.5)	0.27
Gender (M:F)	7:9	15:5	14:13	0.49
Site:				0.42
Anterior	5	7	15	
Posterior	11	13	12	
Loculation:				0.89
Unilocular	16	19	21	
Multilocular	0	1	6	
Size (mm)	45.6 (20.9)	78.3 (26.8)	77.3 (26.3)	0.0002
Root resorption (yes:no)	05:13	14:2	16:8	0.83
Perforation of cortex (Yes:No)	1:15	2:18	10:17	0.83

Table 2
Surgical methods utilised in the management of various subtypes of unicystic ameloblastoma and number of recurrences.

	Luminal	Intraluminal	Mural	Recurrence rate (%)	95% CI	p value
Enucleation	3	1	1 (1 recurrence)	20	0.00 to 1.00	0.02
Marsupialisation followed by enucleation	2	4	2 (2 recurrence)	25	0.652 to 3.693	0.26
Enucleation, Carnoy’s, and burring of the peripheral bone margin	11	15 (1 recurrence)	18 (3 recurrence)	9.1	0.884 to 1.049	0.38
Resection	0	0	6 (no recurrence)	0	–	–

Table 3
Summary of clinicopathological features associated with recurrent unicystic ameloblastoma (UAM).

	Recurrent UAM	Non-recurrent UAM	p value
Age (years)	16.3	27.5	0.22
Gender (M:F)	7:0	29:27	0.01
Jaw (mandible:maxilla)	7:0	52:4	1.0
Size (mm)	96.3	68.2	0.09
Root resorption (yes:no)	7:0	28:23	0.03
Cortical perforation (yes:no)	4:3	9:47	0.02
Histopathological subtype (luminal and intraluminal:mural)	1:6	36:20	0.01
Extraction of involved teeth (yes:no)	3:4	40:9	0.04

Management protocol

Taking into account the clinicopathological features of UAM presented in this series as well as the treatment modalities utilised in our institution with follow-up data, a management protocol has been proposed (Table 4). The main aim of this protocol is to eliminate the tumour in the least invasive method while at the same time minimise morbidity to the patients.

Discussion

UAM remains a controversial lesion due to a lack of extensive studies focusing solely on this tumour with long-term follow-up. As the lesion mainly affects young to middle aged individuals, minimally invasive methods with low morbidity and long-term disease-free survival are important to achieve.⁷ In this study, one of the largest cohorts of UAM in the literature was showcased.

Epidemiologically, UAM comprises about 5%–22% of all variants of ameloblastoma.⁹ Siriwardena et al (2018)¹⁰ reported a higher frequency of UAM of 31.1% in their sample. Our sample showed a similar frequency of 29.5%. This highlights the fact that UAM comprises almost one-third of all ameloblastomas encountered and therefore a definitive strategy is required to manage this relatively common entity.

Demographically, males are more commonly affected than females as shown in this study while most affected patients were in the second and third decades of life.¹⁰ Our

population was slightly older than reported mainly due to delayed presentation as a large portion of our patients reside in rural areas.

The mandible was overwhelmingly involved as with conventional ameloblastoma.¹¹ Interestingly in this population, a large number of UAM occurred in the anterior region of the mandible (42.9%) which was not reported by any other study that we know of (Table 5). This may be due to genetic and environmental reasons.

The majority of UAM appeared unilocular on radiographs however a considerable number of UAM can appear multilocular especially in the posterior regions of the mandible.^{5,12} Rosenstein et al reported 29% of their lesions to be multilocular in appearance as compared to 12.7% in our sample.¹³ Multilocular features may complicate the differential diagnosis as well as the management of these lesions as smaller locules may be missed during surgical treatment.

Cortical perforation is another important radiological feature that plays a pivotal role in the management of UAM.^{7,13} Thirteen UAM (20.6%) caused cortical perforation in this sample of which ten were of the mural subtype. This finding highlights the aggressive behaviour of the mural subtype.

It has been reported that lesions associated with root resorption may indicate a potentially poor prognosis as this may indicate aggressive behaviour.⁷ Li et al reported the incidence of root resorption to be 79.3% while 60.3% of this sample showed features of root resorption.⁵ Moreover, Zheng et al reported that the presence of root resorption along with cortical perforation and mural subtype may indicate underlying aggressive biological potential which needs more invasive forms of therapy and are not appropriately suited for marsupialisation.⁷ Our findings confirm the above statement as a significant number of recurrent lesions showed signs of root resorption.

Classifying UAM based on histopathological features has been reported to be the most important diagnostic and prognostic factor of this tumour.^{1,3} The luminal and intraluminal subtypes have been described to have the same features and behaviour as odontogenic cysts.¹⁰ On the other hand, the mural subtype has the potential to invade the tumour capsule. Multiple authors have reported that the mural subtype is associated with high recurrences and we concur with these findings.^{5,7,13,14}

Table 4
Proposed surgical protocol for the management of UAM based on findings in this study.

Enucleation alone	<ul style="list-style-type: none"> • Not recommended by findings in this study • Can only be utilised in easily accessible areas with luminal and intraluminal subtypes
Marsupialisation/decompression followed by enucleation	<ul style="list-style-type: none"> • For difficult to access regions such as ascending ramus/posterior maxilla • Should be avoided in the mural subtype with cortical perforations • Post enucleation, Carnoy's solution should be applied and burring of the peripheral bone margin performed to reduce recurrences
Enucleation followed by Carnoy's solution and burring of the peripheral bone margin	<ul style="list-style-type: none"> • Most suitable method for most UAM – first line therapy • Can be utilised for cases with easily accessible cortical perforation • Less morbidity than resection with low recurrence rate
Resection with reconstruction	<ul style="list-style-type: none"> • Reserved for cases with multiple inaccessible perforations of the cortex • Extensive lesions involving condyle/coronoid process • Multilocular lesions

Table 5

Comparison of clinicopathological features and management of unicystic ameloblastoma in this study with previous reports in the last 20 years. Data are % unless otherwise stated.

	Li et al ⁵	Rosenstein et al ¹³	Lee et al ¹⁴	Meshram et al ¹⁷	Zheng et al ⁷	Nowair & Eid ¹²	This study
No. of patients	33	21	29	15	116	20	63
Mean age (No.)	25.3	35	23	13.2*	22.3	18.5	26.3
M:F ratio	1:0.57	1:1.1	1:1.4	1:0.67	1:0.87	1:0.25	1:0.75
Most common symptom	Swelling (100%)	NA	Swelling (72%)	NA	NA	Swelling (100%)	Swelling (88.9%)
Jaw:							
Mandible	91	100	86	100	100	100	93.6
Maxilla	9	0	14	0	0	0	6.4
Location:							
Anterior	6	9.5	15	6.7	12.9	0	42.9
Posterior	94	90.5	85	93.3	87.1	100	57.1
Locularity:							
Unilocular	75.8	71	90	86.7	NA	100	89.9
Multilocular	24.2	29	10	13.3	NA	0	12.7
Cortical perforation	NA	33	NA	NA	18.1	NA	20.6
Root resorption	79.3%	29	62		31.9	NA	60.3
Histopathological subtype:							
Luminal	24.2	33.3	7	40	63.8	NA	25.4
Intraluminal	30.3	19	0	53.3	22.4	NA	31.7
Mural	45.5	47.7	93	6.7	13.8	NA	42.8
Overall RR	35	43	10	0	12	0	11.1
RR: enucleation	20	64.3	50	0	NA	NA	20
RR: marsupialisation	NA	NA	NA	NA	12%	NA	25
RR: enucleation +adjuvant	16.7	NA	10	NA	NA	0	9.1
RR: resection	0	0	0	NA	NA	NA	0
Features of recurrent lesions	Posterior Maxilla; mural subtype	Mural subtype	Mural subtype; non-extraction of teeth	NA	Root resorption; cortical perforation; mural subtype	NA	Males; Root resorption; cortical perforation; mural subtype

NA: not available; RR: recurrence rate; *study only included patients under 20 years of age.

Surgical management of UAM remains controversial with some authors advocating simple enucleation owing to the cystic nature of the tumour while others promoting more radical approaches to reduce recurrences.¹² Although resection of UAM has been shown to cause the lowest recurrence rates, numerous complications can ensue even following reconstruction. These include disfigurement, dysfunction, and psychological suffering, especially amongst young patients.^{14,15} Conservative methods such as enucleation and curettage with adjuvant chemical cautery and burring of the peripheral bone margin are associated with significantly less functional and aesthetic impairment; however, they can result in a higher rate of recurrence if performed inadequately.^{12,16}

As demonstrated in this study, enucleation alone was shown to be significantly related to unacceptably high recurrence rates and supported by findings from multiple studies.^{5,13} Marsupialisation or decompression can be utilised in large lesions extending into difficult to access regions of the jaws with relatively good outcomes.⁷

It is important for the clinician to implement a treatment method that can concurrently validate the histopathological diagnosis and provide predictable outcomes. The method of enucleation of the cyst lining followed by application of Carnoy's solution and burring of the peripheral bone margin fulfils these criteria. As shown in our findings, this method provides the entire cystic lining for histopathological exam-

ination as well as achieves acceptable outcomes with low morbidity to the patient.

Owing to the retrospective design of this study, there are a few limitations that should be taken into account. Firstly, the surgical methods were not completely standardised as they were performed by different clinicians over a period of 25 years. Secondly, different radiographic devices were utilised over the study period which could affect the radiological interpretation. Lastly, numerous patients were lost to follow up as they reside in rural regions far away from our institution. This may impact the true recurrence rate of these lesions.

Conclusions

Enucleation in conjunction with Carnoy's solution and followed by burring of the peripheral bone margin was shown to be an effective method with low morbidity to the patient. Males, large lesions (>90 mm), presence of root resorption, cortical perforation, and mural subtype along with non-extraction of involved teeth were significantly associated with recurrences.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients permission

Ethics was obtained from the Biomedical Research Ethics Committee of the institution prior to conducting the study. Patients' consent was not required.

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