Conservative Treatment of Unicystic Ameloblastoma

Original Article

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ABSTRACT

Background: Treatment of unicystic ameloblastoma should be conservative as possible, to avoid serious complications resulting from radical surgery. The aim of this study was to evaluate the effect of enucleation with bone curettage followed by application of carnoy's solution in conservative treatment of unicystic ameloblastoma.

Materials and Methods: This study included 10 patients seeking treatment for unicystic ameloblastoma, which were confirmed by: preoperative CBCT that showed unilocular radiolucency, and histopathological examination of incisional biopsy specimens. Final enucleation specimens were used for additional confirmation and for unicystic ameloblastoma subtyping. Unicystic ameloblastoma was treated by enucleation with bone curettage followed by application of carnoy's solution.

Results: This study involved five males and five females, with an age ranged from 12 to 70 years, and an average age 32.8 years. All the lesions occurred in the mandible; eight lesions in posterior mandible and two lesions in anterior mandible. Four lesions were associated with impacted teeth. Root resorption occurred in six cases. Considering histopathological subtypes; three cases were luminal, one case was intraluminar, and six cases were mural. No recurrences were observed in all cases, after 30 months.

Conclusion: Unicystic ameloblastoma even mural types can be successfully treated conservatively by enucleation with bone curettage followed by application of carnoy's solution.

Key Words: Carnoy's solution, Conservative treatment, Curettage, Enucleation, Unicystic ameloblastoma.

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INTRODUCTION

Ameloblastoma is an epithelial odontogenic tumor. It is one of the most important oral tumors, with a long history of recognition and controversy. Although ameloblastoma is classified as a benign tumor, it is locally invasive with high recurrence rate. It accounts for about 1 % and 18 % of all oral and odontogenic tumors, respectively[1].

Ameloblastoma can be described as a silent lesion, as it grows slowly and usually becomes symptomatic when it reaches a large size. Most of ameloblastoma were discovered accidently during routine dental examination[2].

WHO in 2017 divided ameloblastoma into four groups; conventional (solid /multicystic), extraosseous / peripheral, unicystic, and metastasizing ameloblastoma. Conventional type is more common, more aggressive and has a higher recurrence rate after surgery. Conventional ameloblastoma has six different pathological subtypes; Follicular and plexiform types are the most common, and granular cell, desmoplastic, acanthomatous, and basal cell types. However none of them affects prognosis or biological behavior of the neoplasm[3 - 5].

Unicystic ameloblastoma (UA) accounts for about 5 % to 15 % of all ameloblastoma, with reported recurrence rates 10 % to 25. More than 90 % of unicystic ameloblastoma involve the mandible, mostly the posterior region[6]. Unicystic ameloblastoma (UA) refers to those lesions that show clinical and radiographic features of an odontogenic cyst but on histological examination show an ameloblastic proliferation into the cystic lumen, confined to the cyst lining, or invade the cystic wall, hence their name are intraluminar, luminar, or mural unicystic ameloblastoma (UA), respectively[7, 8].

Histolopathological type, size, site and clinical behavior of the lesion, as well as age and general condition of the patient should be considered in treatment planning of ameloblas¬toma. There are different modalities for treatment of ameloblastoma which can be classified generally into radical and conservative approaches[9]. Radical approach, which is the most common approach used for treatment of conventional type of ameloblastoma, included bone resection with safety margin 1 - 2 cm. Radical surgery may result in several complications such as facial disfigurement, teeth removal, masticatory malfunction, growth disturbance, even after successful reconstruction[10].

As UA less aggressive and has low recurrence rate than conventional type, conservative approaches have been

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widely used for treatment of UA such as marsupialization, marsupialization followed by enucleation, or enucleation alone or with adjunctive modalities as bone curettage, or application of liquid nitrogen or carnoy's solution[11 - 14].

Carnoy's solution is a fixative agent. It was used clinically in 1933 for the first time as a sclerosing agent for treatment of cysts and fistulae by Cutler and Zollinger[15]. As it provides mild tissue penetration, rapid local fixation of remaining cells and optimal hemostasis, it has been used as a supplementary treatment after enucleation of various cysts and tumors in oral and maxillofacial regions, particularly lesions with local invasiveness behavior such as keratocyst and ameloblastoma[13, 16].

The aim of this study was to evaluate the effect of enucleation with bone curettage followed by application of carnoy's solution in conservative treatment of UA.

PATIENTS AND METHODS

This study was approved by the ethical committee of faculty of dentistry, Mansoura University (No. A29080120). The guidelines of the Helsinki Declaration were followed. Ten patients presenting to the Outpatient Clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Mansoura University, and seeking treatment for UA, which were confirmed by: preoperative CBCT (Figure 1) that showed unilocular radiolucency, and histopathological examination of incisional biopsy specimens. Final enucleation specimens were used for additional confirmation and for UA histopathological subtyping (luminal, intraluminal or mural subtypes). An informed consent was signed from each patient.

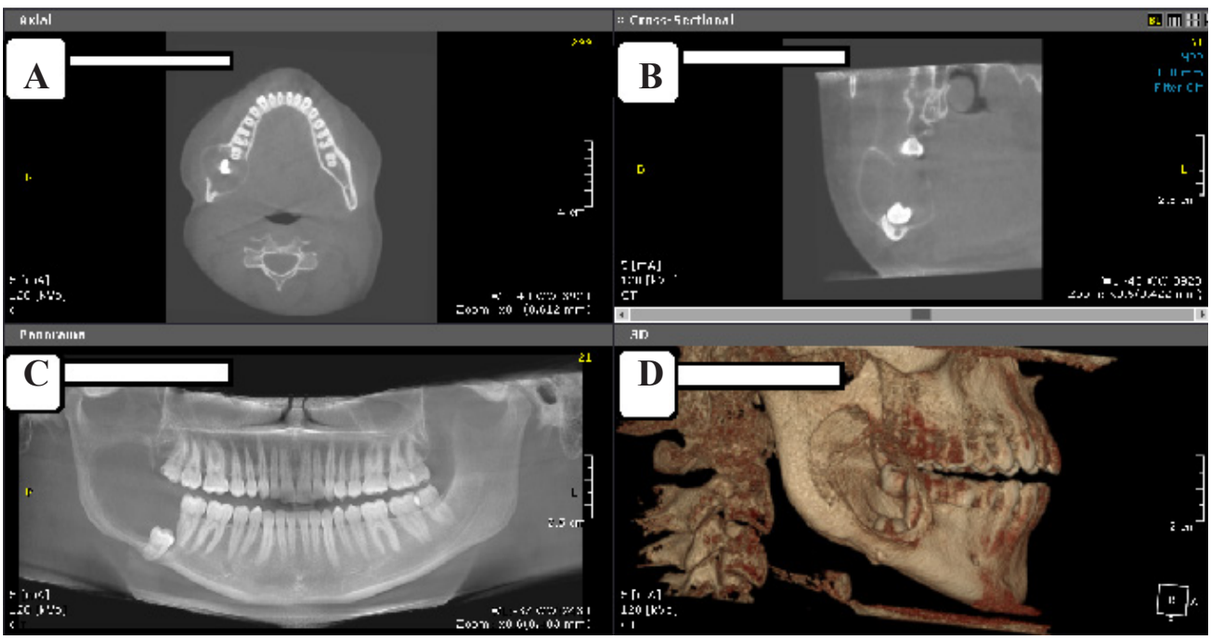

Figure 1: Preoperative CBCT showing unilocular radiolucent lesion with impacted lower eight (case 1).

All procedures were done under local anesthesia with sedation if needed. In doing enucleation of the lesion, mucoperisteal flap with sufficient size was elevated. Adequate amount of buccal bone, if needed, was removed to get enough access for tumor enucleation. (Figure 2 A) If the inferior alveolar nerve was exposed, the tumor was cautiously dissected from the nerve to avoid gross nerve trauma. The teeth related to the tumor were extracted. The surgical cavity was thoroughly inspected and any remaining tumor tissues were excised. After that, all the surfaces of the bone cavity were curetted using large round surgical bur to remove 2.5 mm of bone, according to the remaining bone thickness. During bone curettage, inferior alveolar nerve was gently retracted to avoid nerve trauma. After finishing of bone curettage, carnoy's solution was applied to the surgical cavity for three minutes using ribbon gauze saturated with carnoy's solution. (Figure 2 B) After that, the bone cavity was thoroughly irrigated with normal saline.

The mucoperisteal flap was sutured from the periphery only leaving the surgical cavity open from the crest, permitting packing of the cavity by using ribbon gauze impregnated with garamycin ointment. The pack was changed every 2 to 3 days until secondary healing was achieved.

Antibiotic (clindamycin 300 mg/ twice daily) and analgesic (ketoprufen 50 mg/ twice daily) were prescribed for each patient for seven days except in case no. 6 (age 12 y), to whom half doses were prescribed. All patients were instructed to use 2 % chlorhexidine mouth wash three times/ day for seven days to maintain good oral hygiene. All patients were evaluated clinically and radiographically at 12 and 30 months postoperatively for recurrence assessment. At 30 months a core of healed bone was incised using 2 mm trephine bur and histopathologically examined for each patient.

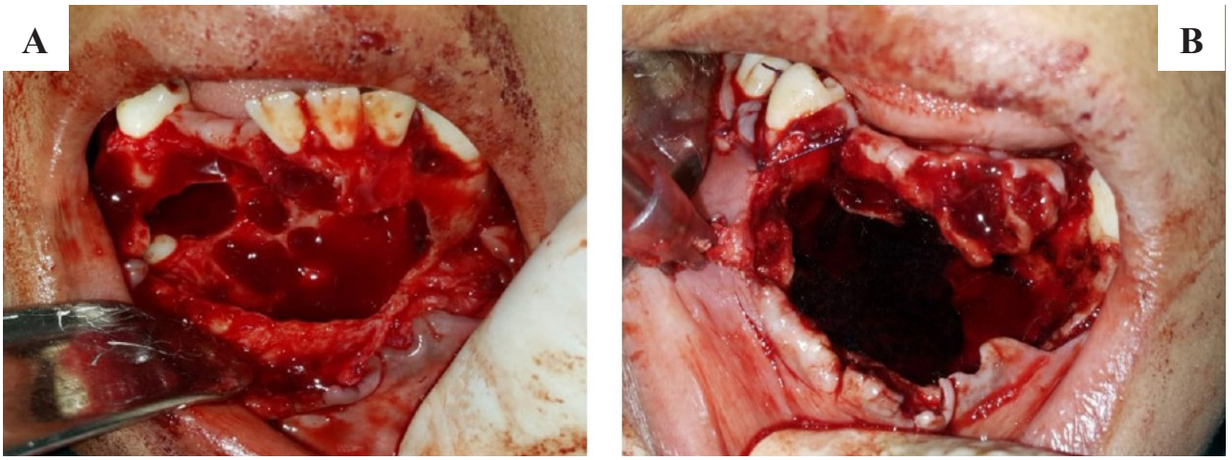

Figure 2 A: Surgical cavity after enucleation of UA. Figure **2 B:** Surgical cavity after bone curettage and application of carnoy's solution (case 6).

RESULTS

There were five males and five females (M: F ratio 1:1), with an age ranged from 12 to 70 years, and an average age 32.8 years. 70 % of lesions occurred in third and fourth decades. All the lesions occurred in the mandible, eight (80 %) lesions in posterior mandible and two (20 %) lesions in anterior mandible. Four lesions were associated with impacted teeth, with an average age 24 years, and six lesions were not associated with impacted teeth, with an average age 38.6 years. Root resorption occurred in six cases (Table 1).

Table 1: Patient age and gender, lesion site, presence or absence of impacted teeth, presence or absence of root resorption, histopathological variant, and recurrence:

Patient No.	Age (year) / Gender	Lesion site	Presence Of impacted tooth	Presence of root resorption	Histopath-ological variant	Recurrence
1	36/F	Right angle+ramus	Lower eight	-	Mural	No
2	20/M	Left/angle	-	+	Mural	No
3	25/F	Left/body+angle +ramus	Lower eight&seven	+	luminal	No
4	35/M	Anterior mandible	-	+	Intraluminal	No
5	23/F	Right/angle+body	Lower eight	+	Mural	No
6	12/M	Anterior mandible	Lower right central incisor&canine	-	Mural	No
7	29/F	Right/angle+body	-	+	Luminal	No
8	32/F	Left/ body+angle +ramus	-	+	Luminal	No
9	46/M	Right/angle+ramus	-	-	Mural	No
10	70/M	Right/angle	-	-	Mural	No

. Abbreviations: F, female; M, male; -, absence; +, presence.

Histopathological results:

All the lesions were UA, which were confirmed by histopathological examination of both incisional and final enucleation biopsies. Considering histopathological subtypes; three cases were luminal, one case was intraluminar, and six cases were mural (Figure 3 and Table 1). At 30 months the biopsied bone, showed normal bone healing without recurrence of ameloblastic cells.

Outcomes of treatment:

After 30 months no recurrences were observed in all cases. (Table 1 and Figure 4) There were no permanent nerve injuries in all cases, except in case no 2, who had preoperative inferior alveolar nerve paraesthesia, presented as lip numbness and tingling, and not resolved after surgery. In addition lingual nerve paraesthesia (numbness and tingling of tongue) occurred in the same case after surgery, and continued in the follow up intervals (Figure 5).

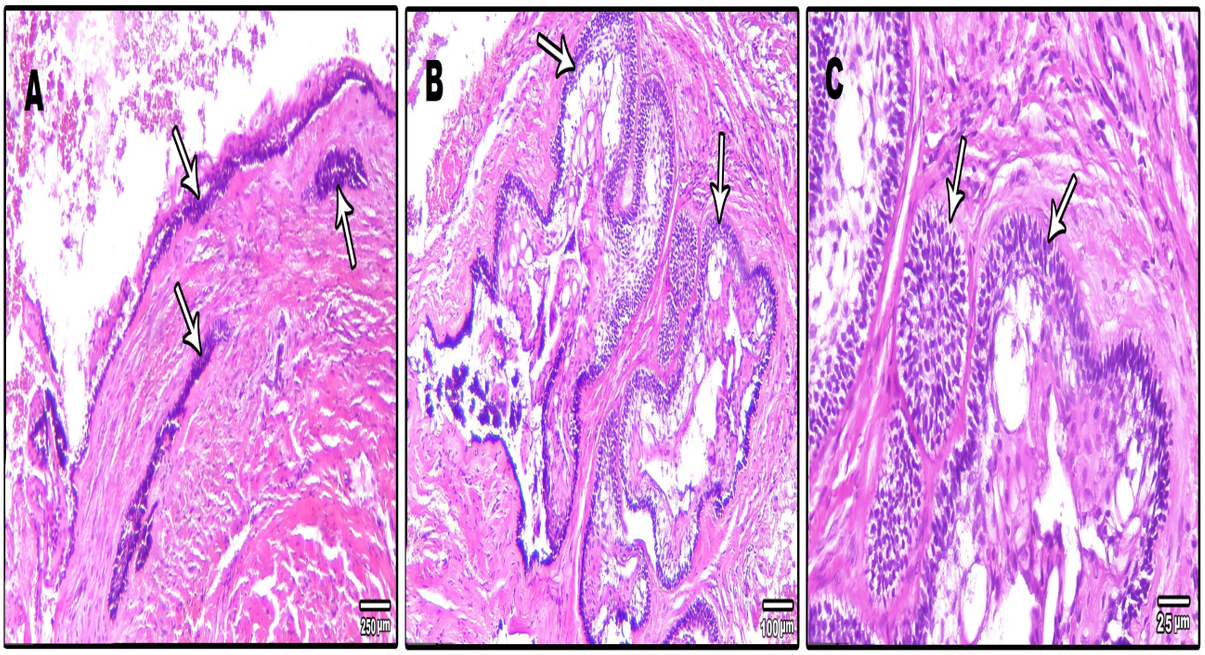

Figure 3: Histopathological analysis (H and E stain) showing: A) amelloblastic cells (arrows) invade the fibrous capsule of the cyst lining (mural UA). B and C) Follicles of cells with ameloblastic features (arrows) in fibrous connective tissue.

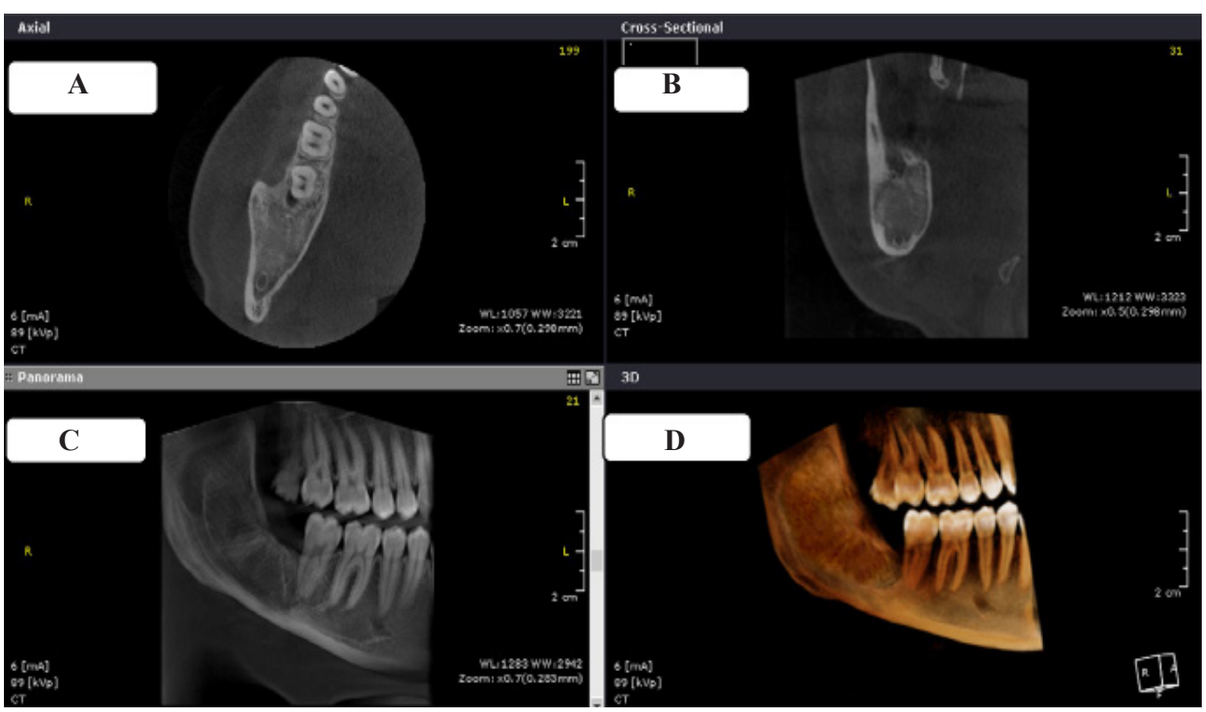

Figure 4: Postoperative CBCT showing bone healing after 30 months (case 1).

Figure 5: A- Preoperative CBCT showing unilocular radiolucent lesion with perforation of buccal and lingual cortices, B- Postoperative CBCT showing bone healing after 30 months (case 2).

DISCUSSION

Ameloblastoma is a benign, slowly growing and locally invasive epithelial odontogenic tumor. UA is the second significant clinical type of ameloblastoma. They are commonly occurred in younger patients as compared to conventional ameloblastoma[2].

In concordance with the findings of most studies, in my study there was no sex predilection and the lesions were more predominant in the mandible (100 %), mostly in posterior area (80 %) (17 - 20). In this study, 70 % of UA occurred in third and fourth decades with an average age 32.8 years. In contrary, Kessler HP *et al*[21] and Philpsen HP *et al*[22] documented that 50 % of such tumors occurred during the second decade, with an average age 22 years.

In several studies, 50 % to 80 % of UA were associated with an impacted tooth" dentigerous variant of UA" with an average age 22 years, and a few without an impacted tooth" non-dentigerous variant" with an average age 33 years[22, 23]. However in my study, only 40 % of cases were associated with impacted teeth, and 60 % of cases were not associated with impacted teeth with average ages 24 and 38.6 years, respectively.

The histopathological subtyping of UA was important, because it is generally believed that the presence of tumor cells in the fibrous capsule of UA (mural subtype), increases the incidence of recurrence after enucleation similar to conventional type. Enucleation biopsy was important for confirmation of histopathological subtyping, since it is difficult to detect mural invasions via microscopic examination of a piece from the lining of a UA (incisional biopsy). Because of that a thorough microscopic examination to the whole enucleation specimen was needed to detect mural invasions[8, 24].

There were a few researches concerning hitopathological subtyping of UA, in most of which mural subtype represented the predominant incidence; 45 %[25], 48 %[19], 49 %[8] and 93 %[13]. Similarly, in my study mural subtype of UA represented the prevalent incidence (60 %) over the luminal (30 %) and intraluminal (10 %) subtypes. In contrary, Meshram *et al*[7] reported that most of the patients[14 - 15] had luminal or intraluminal variant of UA, and one only had mural variety.

Ameloblastoma still one of the most controversial lesions in relation to the type of treatment. Treatment may be radical or conservative. Although radical approach has a documented low recurrence rates, it usually results in morbidity and serious complications, even after successful reconstruction. So, the treatment should be directed to be conservative as possible, which supported by the fact that ameloblastoma, particularly unicystic type, is a slow growing, locally invasive, and very rare metastasizing benign tumor[9, 12, 13].

The recurrence rate after conservative treatment of UA was documented from 10 to 25 %[26]. Marsupialization, marsupialization followed by enucleation, or enucleation alone or with adjunctive modalities as bone curettage, application of liquid nitrogen or carnoy's solution are the most commonly conservative approaches used for treatment of unicystic ameloblastoma[11 - 14].

According to the systematic review of Lau SL *et al*[26] about recurrence rates after different treatment modalities of UA, the recurrence rates were 3.6 % for resection,

16 % for enucleation and application of carnoy's solution, 18 % for marsupialization alone or followed by enucleation, and 30.5 % for enucleation alone. Nakamura N *et al*[12] compared long-term results of 78 ameloblastoma (27 cases were unicystic), and they documented 7.1 % and 33.3 % recurrence rates after radical and conservative treatments, respectively. Their study included 27 cases with UA, they found no recurrence after radical surgery (0 / 13) and marsupialization alone (0 / 3), and 2 cases were recurrent after marsupialization followed by enucleation + curettage (2 / 11).

Also Lee PK *et al*[13] reported 10 % recurrence rate after treatment of 29 patients with UA (93 % mural type) with enucleation followed by application of carnoy's solution. They proposed a possible benefit of carnoy's solution against recurrence. However, Sampson *et al*[14] reported 100 % recurrence rate after treatment of 26 mandibular ameloblastoma (four were unicystic) with curettage alone. From the aforementioned studies[12 - 14, 26] the recurrence rate was more in the following sequence; enucleation, followed by enucleation with curettage, followed by enucleation with application of carnoy's solution.

In my study UA was treated conservatively with enucleation and bone curettage followed by application of carnoy's solution. There was no recurrence even in mural types (6 / 10), which considered aggressive resembling conventional ameloblastoma. These results might be attributed to the use of combined three modalities of treatment; enucleation with bone curettage followed by application of carnoy's solution.

Although carnoy's solution acts as a scavenger that fixes and eliminates remnants of tumor tissues after enucleation and/or curettage, it is a mild, not deeply penetrating and cauterizing agent with an average 1.54 mm bone penetration depth[16]. So it has not the ability to remove the moderate or deep tumor tissues that may penetrate bone. Marx *et al*[27] reported that tumor cells of conventional ameloblastoma can penetrate bone from 2 to 8 mm beyond its radiographic border. That can explain the recurrence of UA in several studies[12 - 14, 26] after treatment with enucleation only or enucleation followed by application of carnoy's solution.

In this study, carnoy's solution was used after bone curettage using large round surgical bur to remove about 25-mm from the entire bone surfaces, enabling carnoy's solution to penetrate the bone more deeply and enhancing its action.

In my study there were no inferior alveolar nerve affections, which may related to proper and gentle handling of inferior alveolar nerve during enucleation and curettage. Also, carnoy's solution was not applied directly over the nerve and its application not exceed three minutes, according to the recommendation of Ferich *et al*[28] to avoid chemical inferior alveolar nerve impairment. Lingual nerve paraesthesia occurred after surgery in patient number two. This might result from the lingual tissue manipulation as the lesion produced cortical bone perforation and soft tissue involvement. Sampson *et al*[14] recommended a more aggressive treatment to excise the tumor and inhibit recurrence, if cortical bone perforation and soft tissue involvement were found.

From this study it may be concluded that UA even mural subtypes can be successfully treated conservatively by enucleation with bone curettage followed by application of carnoy's solution. However, this result needs to be confirmed by longer follow up periods and larger studies. Also additional studies may be conducted to show the effect of this conservative approach on conventional type of ameloblastoma.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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