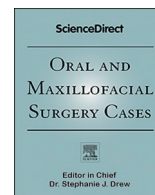




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Conservative treatment of unicystic mural ameloblastoma

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ABSTRACT

Mural ameloblastoma is a subtype of Unicystic Ameloblastoma characterised by the expansion or infiltration of tumour nodules into the fibrous wall of the cyst. The behaviour of this subtype is highly aggressive, with a risk of recurrence comparable with that of Conventional Ameloblastoma. Consequently, the preferred treatment for Unicystic mural Ameloblastoma is broad resection of the tumour. In this case report we describe the successful conservative treatment of a Unicystic mural Ameloblastoma associated with an impacted tooth. The conservative treatment consisted in a initial marsupialization followed by the enucleation of the lesion performed with a lateral corticotomy to create a “bone door” and the relocation of the “bone door” using micro-plates and titanium screws.

Our conservative approach preserved the integrity of the inferior alveolar nerve as well as mandibular functionality and resulted in a good aesthetic outcome.

Due to the behaviour of this lesion, a strict follow up is mandatory. In our experience, follow-up is conducted as long as possible regardless of the surgical treatment. This protocol includes Cone Beam CT performed 1 year after surgery and panoramic radiology (OPG) once a year until 5 years after surgery. OPG is then repeated every 3 years in patients with Unicystic Ameloblastoma and every 2 years in those with Conventional Ameloblastoma or ameloblastoma with mural invasion. Suspected recurrence should be evaluated by CBCT.

1. Introduction

Ameloblastoma is a benign tumour of epithelial origin. It is locally aggressive, increases to large volumes and has a high risk of recurrence. The most common variants are conventional ameloblastoma (CA) and unicystic ameloblastoma (UA). CA is the most aggressive form and has a tendency of recurring multiple times, whereas UA is a peculiar subtype distinguished by a more benign, less aggressive behaviour [1].

In 1988, Ackermann [2] divided UAs into three growth patterns: luminal, intraluminal and mural. In the intraluminal subtype, the

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ameloblastic node protrudes from the cystic border into the lumen. In the luminal variant, the tumour node are contained within the ameloblastic cystic surface, and mural ameloblastomas are characterised by the expansion or infiltration of tumour nodules into the fibrous wall of the cyst.

The intraluminal and luminal variants are considered to be less aggressive and to have a lower risk of recurrence, whereas the mural subtype is highly aggressive, with a risk of recurrence comparable with that of CA. The behaviour of the mural subtype is supported by the study by Li et al. [3], in which high levels of proliferating cell nuclear antigen and Ki-67 antigen were found in mural ameloblastomas. These findings are consistent with the ability of tumour islands in the fibrous wall to invade the surrounding cancellous bone. Consequently, the preferred treatment for mural UA is broad resection of the tumour [4,5].

However, in this case report we describe the successful conservative treatment of a mural UA associated with an impacted tooth. Our conservative approach preserved the integrity of the inferior alveolar nerve (IAN) as well as mandibular functionality and resulted in a good aesthetic outcome.

2. Case presentation

A 31-year-old male arrived at our clinic complaining of facial deformity, intraoral mandibular swelling and biting-related ulcers since the previous month. The patient reported neither pathologies nor allergies.

Panoramic radiography (OPG) revealed absence of the medial portion of the mandibular ramus with interruption of the mandibular canal and impaction of tooth 4.8. Cone beam CT (CBCT) showed the amplitude of the lesion and cortical bone loss on both the lingual and buccal sides, as well as thinning of the bone base. In addition, the canal of the IAN was compromised (Fig. 1A).

The preliminary diagnosis was odontogenic cyst or ameloblastoma. A small portion of the cystic wall was harvested for histological examination (sample size $0.8 \times 0.6 \times 0.5$ cm). The cystic membrane was marsupialised and a gauze was placed in the cavity to maintain patency (Fig. 2).

During the first postoperative month, the surgical site was rinsed weekly and then the patient was followed-up monthly at the clinic.

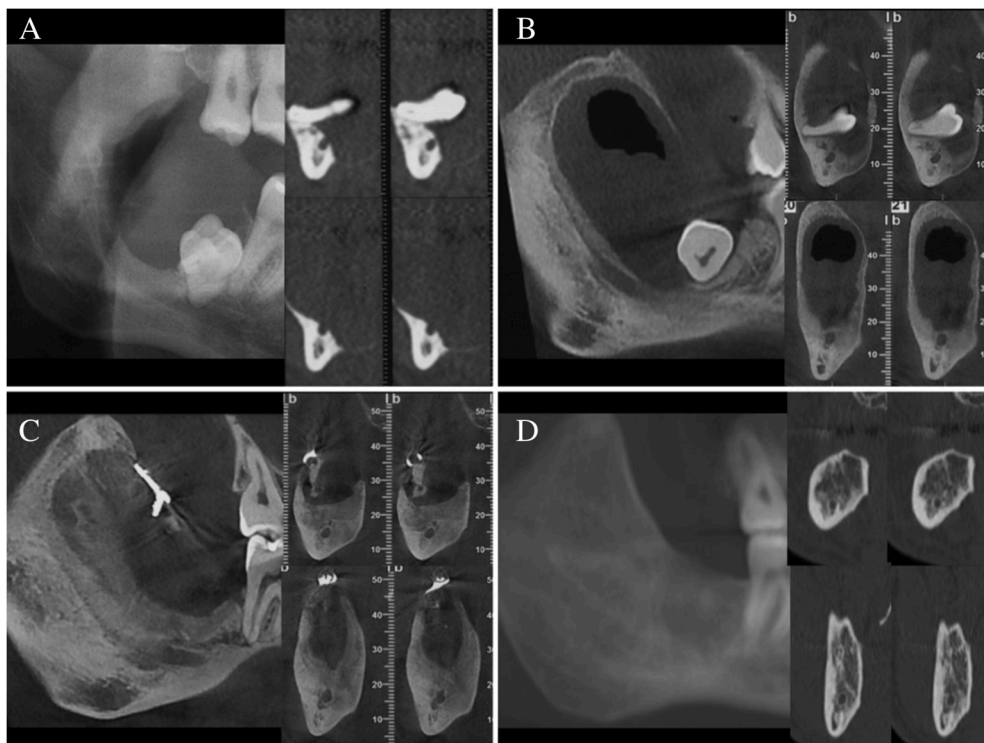


Fig. 1. Radiographic images of the Unicystic Ameloblastoma (UA): A) CBCT scans at the diagnostic phase: cortical bone loss on both the lingual and buccal side is evident, as well as thinning of the basal bone. In addition, the IAN canal was involved and compromised. B) CBCT scans 6 months after marsupialization (first surgical step): evidence of new bone formation, reappearance of cortical borders, both on the lingual and the vestibular side; volume cyst reduction and channelling of IAN canal. C) Radiographic control (CBCT) 12 months after enucleation (second surgical step) revealed almost complete remineralisation of the osteolytic area, with partial disappearance of the osseotomised and repositioned bone segment. D) CBCT scans taken 36 months from the surgical reintervention (third surgical approach): Evidence of complete repair of the bone defect, with rearrangement of the medullary bone, remineralisation of the cortical bone with complete canalisation of the mandibular canal and absence of recurrences. CBCT= Cone Beam Computed Tomography, IAN = Inferior Alveolar Nerve, UA = Unicystic Ameloblastoma.

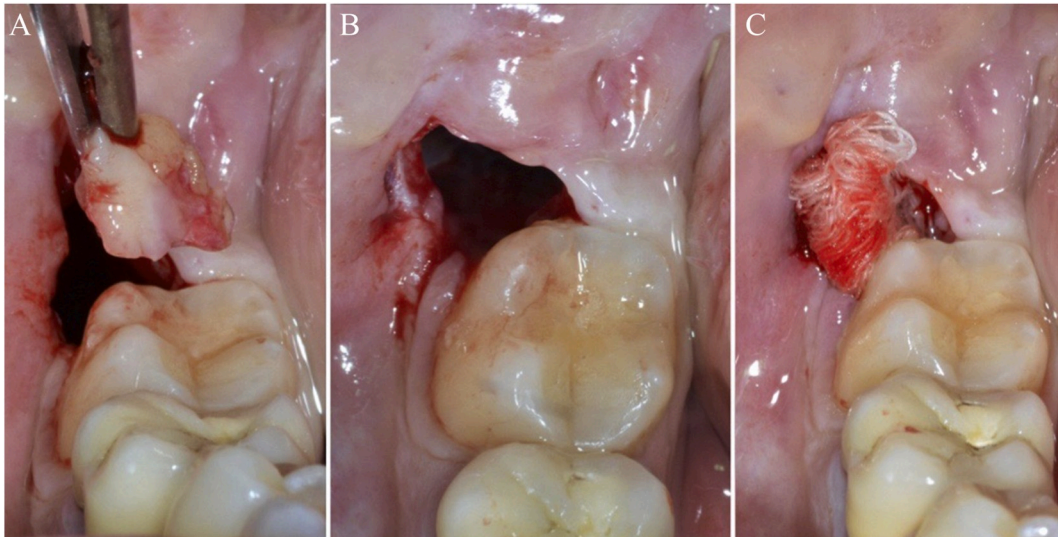


Fig. 2. Clinical images of the first surgical approach performed in order to biopsy the lesion. A) Removal of a portion of the cystic wall, harvested for histological examination. B) The cystic cavity, was periodically irrigated with hydrogen peroxide (10 vol)/chlorhexidine (0.2%). C) The cavity was filled with gentamicin-soaked gauze to maintain patency.

The histological report was compatible with a diagnosis of mural UA with a follicular pattern (Fig. 3A). Given the patient's age and functional and aesthetic considerations, the marsupialization was maintained until the cortical rim of the mandibular canal had remineralised.

At 2 months, the first post-marsupialization CBCT revealed reappearance of the cortical borders and bone neoformation. At 6 months postoperatively, a second CBCT was performed, revealing further formation of new bone, a reduction in cystic volume and channelling of the IAN canal (Fig. 1B).

A second surgery was then planned. A lateral corticotomy was performed, as described by Alling and Alling [6], to create a "bone door" to provide surgical access to the lesion, thereby allowing enucleation of the ameloblastoma, scraping off the bone walls to remove potential ameloblastic infiltrates and extraction of the impacted tooth. The "bone door" was then relocated to its original position using microplates and titanium screws (Fig. 4). The surgical specimen was sent for histological analysis.

The pathologist confirmed the diagnosis of UA with mural growth and a follicular pattern (Fig. 3B).

A CBCT, performed 6 months after the second surgery, showed progression of the osteoblastic process of bone repair. Another OPG was performed 1 year after the excision, which revealed almost complete mineralisation of the osteolytic area, with the exception of the bone surrounding the osteosynthesis plate and screws. On a third CBCT, the partial disappearance of the osteotomised and repositioned bone segment was evident and thus necessitating surgical reintervention. Additional findings included thorough ossification of the mandibular angle, both on the lingual and vestibular sides, but also a bone defect probably due to bone necrosis in the area of the plate and "bone door" (Fig. 1C). The osteosynthesis plate and screws were removed, and the inflammatory tissue was excised completely and sent for histological examination (Fig. 5).

Microscopic results revealed odontogenic epithelium arranged in a follicular pattern with isolated foci of basaloid cells with peripheral palisading in the intraosseous portion of the bone defect. (Fig. 3C).

Twelve months after the last surgery, CBCT demonstrated complete repair of the residual defect, with rearrangement of the medullary bone, remineralisation of cortical bone, complete canalisation of the mandibular canal and absence of suspicious lesions.

The patient was followed up until 24 months after the third surgery. On OPG, complete healing of the lesion, thorough ossification of the defect, no signs of recurrence and maintenance of the mandibular angle and ramus profile were observed. Clinically, the therapeutic process resulted in the absence of deformity, no alteration in the mandibular contour and no functional alterations (with respect to either laterality or protrusion). The patient remained symptom-free and had no appreciable neurological damage to the IAN. CBCT performed 36 months after the third surgery showed no evidence of recurrence and confirmed the bone healing (Fig. 1D). Nonetheless, due to the aggressive behaviour of this UA subtype and risk of recurrence, the patient will be monitored closely by long-term clinical and radiological follow-up.

3. Discussion

The differential diagnosis of large unilocular osteolytic lesions must consider UA, keratocysts and odontogenic cysts, but a final diagnosis and thus the initiation of treatment can only be made following biopsy [7]. The incisional biopsy allowed us to marsupialise the lesion while waiting for the histological result. Marsupialization is very effective in the molar area and mandibular ramus due to the bone structure and local anatomy. The healing potential of the marsupialised lesion depends on the rate of new bone regeneration,

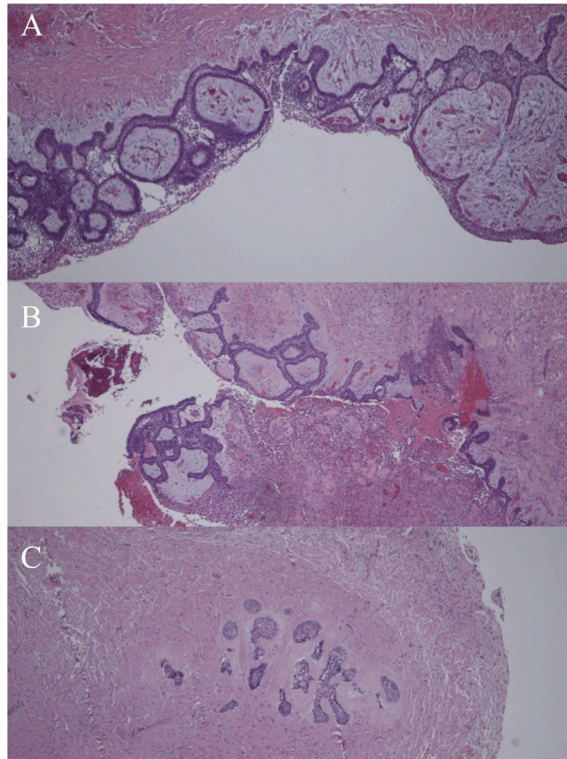


Fig. 3. Histological images of the collected samples. A) Sample at first surgical step: Hematoxylin and Eosin (H&E), 4x. Odontogenic epithelium arranged in follicular pattern. Variably sized clusters of cells composed of central loosely arranged areas with basal cell components, surrounded by columnar epithelial cells with clear and vacuolated cytoplasm and hyperchromatic nuclei. Nuclei were aligned at the periphery away from the basement membrane. Absence of significant nuclear pleomorphism and inconspicuous mitotic activity. Microcyst changes were appreciable as well as minimal stroma with moderate fibrous tissue component. B) Sample at the second surgical step. Hematoxylin and Eosin (H&E), 4x. Odontogenic epithelium arranged in follicular pattern. Sheets and nests of basoloid cells with peripheral palisading were evident. The cells showed hyperchromatic nuclei and reduced mitotic activity. The remaining mucosa presented ulcerated areas with chronic inflammation. C) Sample at the third surgical step. Hematoxylin and Eosin (H&E), 4x. Odontogenic epithelium is arranged in follicular pattern. Isolated foci of basaloid cells with peripheral palisading. Stroma presented marked reactive fibrous tissue components.

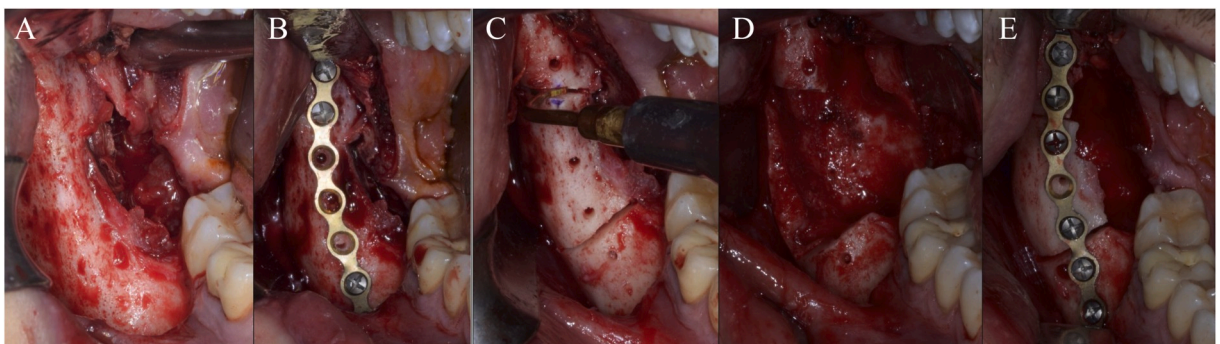


Fig. 4. Clinical images of the second surgery performed to enucleate the lesion. A) Vision of the cortical bone at the initial phase of the surgery. B) Fixing of the microplate with titanium screws in order to create a guide for relocating the osteotomized bone. C) Lateral corticotomy performed using piezoelectric instruments. D) Vision of the mandibular segment after ameloblastoma enucleation, scraping of the bone walls to remove potential ameloblastic infiltrates and extraction of the impacted tooth (4.8). E) Reposition of the removed bone portion using a microplate and titanium screws for fixation.

which is related to the patient's age and site of the pathology [8]. Among the factors that affect the marsupialization outcome are the surgical technique and tumour growth pattern [8]. Nakamura et al. [9] described two main histological patterns relevant to the pathological behaviour of the tumour: expansive lesions, which remain confined within their capsulated borders, and invasive lesions,

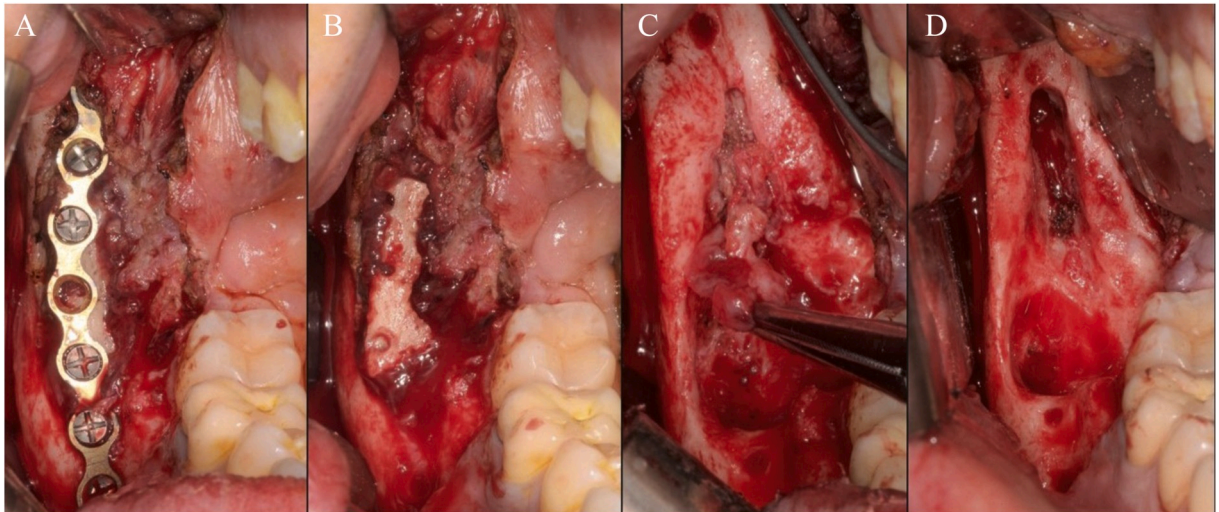


Fig. 5. Clinical images from the third surgical step: A) The previously relocated bone wall appears necrotic upon flap elevation. B) Details of the necrotic bone after fixation-plate removal. C) Excision of the inflammatory tissue encapsulating the necrotic segment. D) Vision of the mandibular ramus after necrotic bone and inflammatory tissue excision, performed along with scraping of the bone walls in the attempt of removing potential ameloblastic infiltrates.

which microscopically invade the surrounding bone outside their fibrotic capsules. The expansive subtype is usually more responsive to marsupialization, whereas the invasive subtype requires a more radical approach involving complete resection. The ameloblastic mandibular lesion in this case had a unilocular aspect with well-demarcated borders, consistent with a diagnosis of UA. However, it also included an outer layer of basaloid cells [9] and cortical bone perforation [10], both of which are associated with a worse prognosis [10]. Other negative predictive factors are the surgical approach, radiographic appearance, tumour size and histologic subtype [11,12]. Multicystic lesions, especially the follicular subtype, and unicystic mural lesions are frequently associated with recurrence [11].

The histological result in the presented case was UA with mural growth. According to the literature [1,4,5,12,13], given its risk of recurrence, UA with mural proliferation resembles CA more closely than UA. Mural ameloblastoma managed by surgical enucleation alone or in association with curettage has a recurrence rate of 35.7% [14], while the radical approach gives a very low risk of recurrence [4], and a 1-cm safety margin minimises the risk [5].

Based on the size of the lesion, the aim of surgery is to maintain the continuity of the mandible or achieve complete (partial or total) resection that can be managed by reconstruction with osteosynthesis plates alone or osteosynthesis plates plus bone grafts. In case of mandible discontinuity, treatment could result in anaesthetic deformities, facial asymmetry, dysfunctional mouth opening and chewing defects and thereby a reduced quality of life [1]. For this reason, some authors suggest a conservative approach for patients likely to comply with the demands of a long postoperative follow-up [15,16].

Our patient was initially managed conservatively to maintain the lower mandibular border as much as possible, reconstruct the vestibular and lingual cortical bone and regain the cortical rim of the mandibular canal. This approach facilitated the second surgical step while maintaining nerve integrity and function [16].

In patients treated with radical or conservative approaches, the aim of postoperative follow-up should be preventing relapse to avoid the need for radical re-intervention.

In our experience, follow-up is conducted as long as possible regardless of the surgical treatment. This protocol includes CBCT performed 1 year after surgery and OPG once a year until 5 years after surgery. OPG is then repeated every 3 years in patients with UA and every 2 years in those with CA or ameloblastoma with mural invasion. Suspected recurrence should be evaluated by CBCT.

4. Conclusions

Although mural ameloblastoma represents a variant of UA, its aggressiveness and similar recurrence rate to that of CA indicate the need for radical treatment. Nonetheless, in some patients, conservative treatment is a valid alternative and can preserve aesthetic functions and outcomes as well as quality of life. These approaches demand patient compliance and strict radiographic follow-up. In the case reported herein, good functional and aesthetic outcomes were achieved, and no relapse was observed at 3 years after surgery.

Author contribution

Prof. Consolo: Conceptualization and Supervision. Dr. Tognacci: Writing - original draft, Visualization. Dr. Bencivenni: Writing - original draft, Visualization. Prof. Felice: Writing - review & editing. Prof. Bellini: Writing - review & editing.

Consent statement

Formal consent for the publication was not elaborated and obtained because the figures used are completely anonymized and without any marks that can make the patient identifiable.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgments

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: <http://www.textcheck.com/certificate/ANe4IH>.

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