

## Peer Review File

**Article information:** <http://dx.doi.org/10.21037/fomm-21-17>

### **Reviewer A**

**Comment 1:** As an orthodontic treatment, it is a case report that has been treated very well. However, the method used for this cases with ameloblastoma-derived cysts is similar to the orthodontic treatment for cases with simple cysts, and there is no technical novelty.

### **Reply 1:**

Ameloblastoma in the children and adolescents showed wide variation in age selection. A 10-year old female with a UAM in the mandible was reported in this case report. The lower second premolar was impacted. The surgical therapy is a common treatment option of cystic lesions containing teeth. The surgical excision of the UAM with surrounding tissues and the extraction of affected teeth during the operation may result in the defects in the dentition function and aesthetics. The growth potential of adolescent patients is ignored. In the present case report, the patient received the decompression of the cystic lesions combined with orthodontic treatment. The application of decompression makes the UAM area eliminated in size. The new alveolar bone provides space for the eruption of the impacted second premolar. Appropriate timing of the orthodontic intervention made the course of treatment acceptable.

**Comment 2:** Ameloblastoma is a benign tumor with a high recurrence and surgical removal is the mainstream. Despite this background, there is a lack of scientific evidence to recommend conservative therapy.

### **Reply 2:**

Anne et al. presented a case of UA that developed prenatally and was successfully managed in the early neonatal period with marsupialization and curettage performed carefully to avoid injury to the tooth germ. After 2 years of follow-up, complete bone remodeling and normal eruption of deciduous teeth have been noted, and no residual deformity has been observed<sup>1</sup>. Saori et al. described a case of UAM of the mandible in a 7-year-old girl that mimics a dentigerous cyst given its association with an unerupted permanent mandibular first molar. Orthodontic treatment and marsupialization were useful given that it enabled the successful enucleation of the tumor without the need for tooth removal<sup>2</sup>. Several literatures about the combination of conservative surgery and orthodontic treatment indicated it an effective management options for UAM in resent years. Recognition and distinction of the different forms of ameloblastomas are fundamental, because they are intimately linked to the treatment plan and prognosis. Extensive resections have been used to treat solid ameloblastomas to prevent possible recurrences. The surgeries are invariably

associated with serious problems for the patient, such as masticatory dysfunction, mutilation, facial deformity, and abnormal mandibular movements. The rate of recurrence is a crucial factor for coherent planning, but other aspects are also important and must be considered in the therapeutic approach, including emphasizing morbidity and the patient's quality of life.

1. Morice A, et al. Conservative management is effective in unicystic ameloblastoma occurring from the neonatal period: A case report and a literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 2020;129:e234-42.

2. Saori Takahashi, et al. Unicystic Ameloblastoma in a Child Treated with a Combination of Conservative Surgery and Orthodontic Treatment: A Case Report. *J Clinical Pediatric Dentistry, J Clin Pediatr Dent* 2019;43:121-5.

**Comment 3:** Is it okay to understand that decompression alone will eliminate the ameloblastoma?

**Reply 3:**

The authors support the opinion that the combination of conservative therapy combined with orthodontic treatment is one of an effective management options for UAM. The decompression achieves the bone reconstruction effects by balancing the internal and external pressure of the tumor, eliminating or reducing the bone resorption factors of the cyst, and changing the lining epithelium of the cyst. However, the postoperative follow-up should be taken regularly to check signs of UAM recurrence.

**Comment 4:** Generally, it is necessary to remove the tumor tissue after decompression. It is said that this time it became smaller only by decompression, but what kind of judgment should be made to which such a method can be applied?

**Reply 4:**

Yes. In the present case report, after the decompression, a complete curettage was also performed to remove the tumor tissue. The indication of decompression is the unicystic type of Ameloblastoma. The dental alveolar bone in the tumor region was healed without obvious deformity.

**Comment 5:** How did you determine the type of Ameloblastoma? I think it is difficult to diagnose ameloblastoma from this tissue section alone. The palisade arrangement of the basal cell layer of the epithelium is also unclear and indistinguishable from the lining epithelium of other odontogenic cysts. In addition, it is accompanied by strong inflammation, and it is thought that the modification of inflammation is strongly applied. I think it is difficult to make a definitive diagnosis from this photo alone.

**Reply 5:**

Ameloblastomas are currently classified into three types: (1) solid or multicystic, (2) unicystic, and (3) extraosseous or peripheral type. The unicystic type is radiologically characterized by unilocular aspect. In this case the Cone-Beam computed tomography images indicated the unicystic radiolucent area. And the histological findings of the specimen obtained at the cystic wall tissue of the unerupted second premolar with Hematoxylin Eosin staining revealing an ameloblastoma.

**Comment 6:** As you know, Unicystic ameloblastoma includes Luminal unicystic ameloblastoma Mural unicystic ameloblastoma, Peripheral ameloblastoma, Desmoplastic ameloblastoma. Can you recommend this decompression therapy for which type?

**Reply 6:**

The unicystic ameloblastoma is thought to have recurrence potential, but to be less aggressive than the solid type. We prefer to recommend the decompression therapy for the Luminal unicystic ameloblastoma. In the present case report the less invasive form of therapy and follow-up were chosen.

**Comment 7:** Where did the Ameloblastoma eventually go? Did they die? Why was it able to heal without being cut off?

**Reply 7:**

We recommend conservative treatment of UAM in the adolescent cases to avoid loss or injury to the tooth, provided close follow-up is carried out all through the individual's growth for early detection of potential recurrences, growth impairments, or tooth eruption disorders. The decompression achieves the bone reconstruction effects by balancing the internal and external pressure of the tumor, eliminating or reducing the bone resorption factors of the cyst, and changing the lining epithelium of the cyst. In the present case report, after the lesion was reduced, a complete curettage was performed. The repair of bone defect may benefit from the growth potential of patient, and the physiological orthodontic tooth movement promotes bone remodeling.

**Comment 8:** The retention period is 6 months, but can we say that there will be no recurrence?

**Reply 8:**

This 'retention' means the orthodontic retention. The patient wore the Howley retainer to maintain the stability of the occlusion relationship without relapse. Postoperative follow-up of UAM is very important because more than 50% recurrences occur within 5 years. Our case report also confirmed the tendency. Radiographic and clinical follow-up is necessary for up to 10 years. The orthodontic retention and the follow-up was explained in the Discussion. The CBCT images showed stable treatment results after 34-month follow-up and no significant ameloblastoma recurrence.

**Reviewer B**

**Comment 1:** The first paragraph of the Discussion consists of a short literature review without actually discussing the case reported. Delete it or move it to the Introduction.

**Reply 1:**

The first paragraph of the Discussion was moved to the Introduction.

**Comment 2:** “The present study represents” should be “The present case report represents”

**Reply 2:**

The text description was revised.

**Comment 3:** “The present case demonstrates that the decompression technique could prevent the resection of the mandible diagnosed with a UAM.”

Wrong. It is impossible to state that with such short-term follow-up, specially taking into consideration that it was a unicystic ameloblastoma decompressed and later curetted, which brings a considerable risk of recurrence in the long term. For more information, consult reviews on the recurrence risk of unicystic ameloblastomas managed by different approaches.

**Reply 3:**

The ‘prevent’ is not correct. There were a few limitations to the current case report—The present case report was retrospective. The short-term positive effects of the patient such as: acceptable Class I canine and molar relationships were achieved, alveolar bone defects in the right mandibular second premolar and first molar was healed. However, considering the risk of recurrence of UAM, the postoperative follow-up is necessary. Radiographic and clinical follow-up should be done every 6 months for the first 2 years and then annually. These were added to the end of the Discussion.

**Comment 4:** “The decompression technique also promotes the bone formation and tooth movement in the ameloblastoma region, which enables the eruption of impacted premolar.” Tooth movement after decompression of cysts preventing its eruption is something well known. What is the novelty?

“The multidisciplinary approach including orthodontic treatment helps to reconstruct a normal and stable occlusal function.” Another well-known statement. What is the novelty?

**Reply 4:**

Treatment of an ameloblastoma often requires an occlusal reconstruction. The biologic behavior of a unicystic ameloblastoma is considered less invasive, and it responds more favorably to conservative treatment than does a multicystic ameloblastoma. Conservative therapy was performed in this patient. The eruption of the mandibular second premolar on the affected side was

disturbed by the tumor. The impacted tooth naturally erupted after the reduction of tumor volume by the decompression. The patient had an Angle Class I malocclusion with crowding. Orthodontic treatment was the only way to solve these problems completely. The reduction of the resistance of new alveolar bone formation was eliminated by decompression, the formation of new bone promoted the eruption of tooth, and the tooth movement promoted the reconstruction of bone and periodontal tissue.

This thesis has some innovation points such as: (1)Successful decompression provided conditions for new alveolar bone formation. (2)Timing of orthodontic intervention, the eruption power of crown avoided the traction of impacted premolar. (3)Physiological orthodontic force stimulates periodontal tissue healing. (4)Non-extraction design achieved the ideal molar relationship, which increase the stability of the results of orthodontic treatment. (5)Reasonable selection of indications and regular follow-up may control the risk of the recurrence of UAM.

**Comment 5:** What is the reason to include cephalometric tracings and a table with cephalometric measurements in a case report focusing on a conservative therapy for a unicystic ameloblastoma?

**Reply 5:**

Considering the integrity of the case data, the cephalometric analysis pre/post orthodontic treatment was included in the manuscript. The results indicated a slight labial proclination of both the maxillary and the mandibular incisors occurred after treatment. But the lip protrusion is acceptable after the braces debonded. The impacted lower right premolar moved into the dental arch.

**Comment 6:** All in all, the authors still have to convince me of what novelty could this case report bring to the field.

**Reply 6:**

From the perspective of orthodontists, the treatment goal of malocclusion patients is to establish an ideal and stable occlusal relationship, especially the posterior occlusal relationship. For non extraction cases, it is very important to maintain the integrity of dentition during orthodontic treatment. An adolescent patient with UAM in the mandible and the lower premolar impacted was recruited in the present case report. Usually the radical treatment could result in deformity and dysfunction of the jaw. Considering the growth potential of the mandible, we chose the conservative therapy combined with orthodontic treatment.

This thesis has some innovation points which was discussed in the ‘**Reply 4**’: (1)Successful decompression provided conditions for new alveolar bone formation. (2)Timing of orthodontic intervention, the eruption power of crown avoided the traction of impacted premolar. (3)Physiological orthodontic force stimulates periodontal tissue healing. (4)Non-extraction design achieved the ideal molar relationship, which increase the stability of the results of orthodontic

treatment. (5) Reasonable selection of indications and regular follow-up may control the risk of the recurrence of UAM.