



Original Article

Clinical and histomorphometric evaluation of decompression followed by enucleation in the treatment of odontogenic keratocyst



Ji-Su Oh, Jae-Seek You, Su-Gwan Kim*

Department of Oral and Maxillofacial Surgery, School of Dentistry, Chosun University, Gwangju, Republic of Korea

Received 8 February 2018; Final revision received 12 March 2018
Available online 18 June 2018

KEYWORDS

Epithelial thickness;
Jaw cysts;
Keratocysts;
Odontogenic tumors

Abstract *Background/purpose:* The classification and treatment of odontogenic keratocyst (OKC) are controversial. The objective of this study was to present the efficiency of decompression followed by enucleation by clinical and histomorphometric evaluation for the treatment of OKC.

Materials and methods: Thirty four OKCs of 27 patients who underwent decompression followed by enucleation were included in this study. Clinical and histomorphometric analysis were performed.

Results: The average decreasing rate was 59% in maximum diameter, 66% in the amount of the volume for the average of period of the decompression was 9.8 months. The mean of increasing rate of the thickness of the epithelial lining was 921.16%. There were no recurrences for a mean follow-up period of 5.8 years. The thin and friable cyst wall of the OKC was changed to thickened, hard type.

Conclusion: The decompression was found to be effective and reliable as a treatment of the OKC to decrease the recurrence tendency, even for Gorlin-Goltz syndrome.

© 2018 Association for Dental Sciences of the Republic of China. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The odontogenic keratocyst (OKC) was classified by The World health Organization (WHO) in 2005 as a benign tumor that has an odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme. The WHO recognized that keratocystic odontogenic tumors (KCOTs) have the potential to be aggressive and that

* Corresponding author. Department of Oral and Maxillofacial Surgery, School of Dentistry, Chosun University, 375, SeoSukDong, DongGu, GwangJu, 501-759 Republic of Korea. Fax: +82 62 228 7316.

E-mail address: sgkim@chosun.ac.kr (S.-G. Kim).

careful follow up is essential after treatment.¹ KCOT was reclassified as OKC in the classification of developmental odontogenic cysts and relocated from the neoplastic category back into the cyst category until there is more definite evidence for classifying as KCOT by WHO in 2017 with calcifying cystic odontogenic tumours.^{2,3} Because *patched homolog (PTCH)* gene mutations are only found in 30% of sporadic OKCs, such genetic alterations have been even reported among several non-neoplastic lesions, including dentigerous and orthokeratinised odontogenic cysts.^{3,4} Also, OKCs can be completely regressed following decompression and the lining of decompressed cyst changed more like oral mucosa histologically unlike neoplasms.⁵

The modality of treatment of OKC remains still controversial, even the question of nomenclature whether the OKC is a cyst or a cystic neoplasm is certainly to be answered yet.^{6,7} When surgery is selected, minimizing both the risk of recurrence and the surgical morbidity,⁶ patient assistance for periodical follow-up⁸ must be considered.⁹ Various modalities of treatment have been introduced from conservative treatment, such as simple enucleation, to aggressive and extreme treatment, such as radical resection.^{6,9} The OKC is aggressive and has a high rate of recurrence; however, with advances in the genetic and molecular research on OKC, more conservative treatment, such as marsupialization has been advocated recently.⁶

Many studies have reported the recurrence rates of OKCs treated by decompression, the changes of the volumes or diameters of OKCs after decompression, and the results of comparative analyses between decompression and other treatment methods.^{10–12} However, there are few studies that examine the changes in the histology or histomorphometry of the epithelial linings of OKCs before and after decompression.^{13,14}

The purpose of the present study was to evaluate the clinical and histomorphologic changes in OKCs before and after decompression. The nomenclature of OKC was used in the present study although all patients were diagnosed with KCOT.

Materials and methods

This study consisted of 34 specimens, histopathologically proven OKCs on the basis of the WHO classification system,¹ obtained from 27 patients. This study was approved by Institutional Review Board of Chosun University Dental Hospital (CDMDIRB-1323-128). This study also limited patients performed decompression followed by enucleation. To minimize errors that arise from differences among surgeons, all procedures were performed by the same surgeon. Clinical data and radiographs were obtained. All of the patients underwent decompression with simultaneous incisional biopsy. After making the individual obturator (Fig. 1), each patient was instructed to irrigate the cavity daily and keep the obturator in place for 24 h before enucleation to maintain its patency.

The radiographs were taken every 2 months after decompression was performed. The maximum diameter was measured using panoramic photography before decompression and immediately before enucleation. The



Fig. 1 Individual resin obturator was made for irrigation into a cystic cavity.

amount of the volume reduction was measured before decompression and just before enucleation. After calculating all of cross sectional area involved OKC in computed coronal tomography, it was added and the amount of the volume reduction was obtained. After enucleation, the average of the total thickness of the wall was measured by periodontal probe clinically. And the tissues were histologically compared with those obtained from the incisional biopsy. As described by Telles et al.,¹⁴ the thickness of the epithelial lining of each specimen was measured by same examiner. Ten points were measured in each specimen, and the mean values were calculated. The histologic images were obtained by using the ICC50 HD (Leica, Wetzlar, Germany) and the thickness was measured by using the Leica Application Suite, version 4.5 (Leica, Wetzlar, Germany).

Results

Thirty four specimens from 27 patients were included in this study. Sixteen male and eleven female patients whose ages ranged from 14 to 69 years (mean age 36.2 years) participated. Five of them were diagnosed with Gorlin-Goltz syndrome. They had 2 or 3 multiple OKCs, and lesion which was decompressed included in this study.

Twenty four OKCs were located in the mandible, and ten OKCs in the maxilla. Two patients diagnosed with Gorlin-Goltz syndrome had OKCs in both the mandible and the maxilla. Twenty six patients had unilocular OKCs, and the only patient whose OKC recurred after simple enucleation had a multilocular OKC. One patient had a secondary infection that ruptured the wall of the OKC in the mandible and induced a severe deep neck infection.

The average of maximum diameter of OKC in panoramic photography was 46.3 ± 38.8 mm before decompression. The average of maximum diameter of the OKC was 21.5 ± 38.2 mm after decompression. The average decreasing rate was $59 \pm 21\%$ and the average of period of the decompression was 9.8 months (range, 5–14 months). The average of volume of the OKC in computed tomography was 14800 ± 12100 mm³ before decompression,

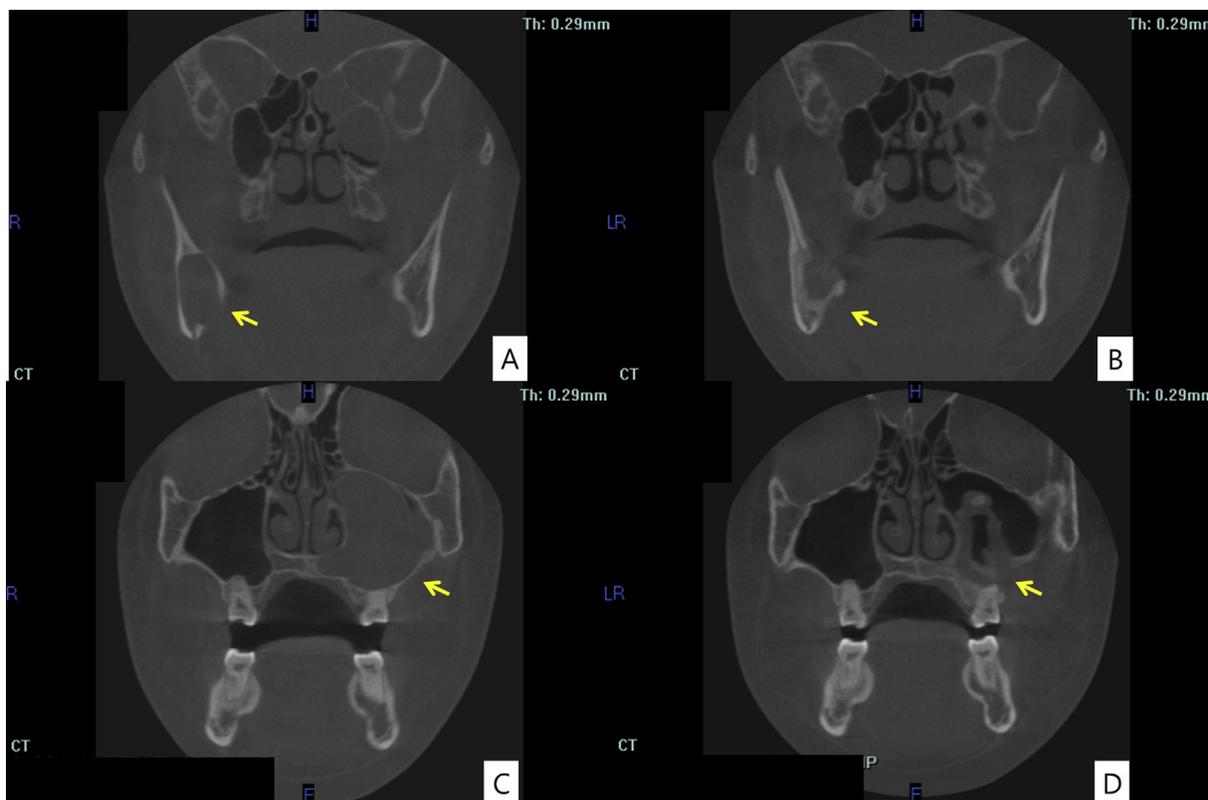


Fig. 2 Computed coronal tomography showed a multiple large OKC. (A) Large radiolucency lesion was showed on right mandibular ramus. (B) Normal bony healing was showed around OKC after 8 months of decompression. (C) OKC was observed entire left maxillary sinus including palate. (D) OKC was decreased and palate was filled with bone after 8months of decompression.

$7400 \pm 4900 \text{ mm}^3$ after decompression. The volume reduction rate was $66 \pm 28\%$ (Fig. 2).

Twenty six patients had thin and friable cyst walls that could not be caught by a pincette at the time of decompression except one patient had a secondary infection caused by rupture of the cystic wall. However, thickened, hard cyst wall could be easily removed as one mass from the surrounding bone in each patient at the time of enucleation. The average total thickness of the wall, measured by a periodontal probe, was $3.5 \pm 1.5 \text{ mm}$ (Fig. 3).

All of the patients demonstrated typical characteristics of histopathological findings except one patient who had a secondary infection before decompression. The wall of the cystic cavity was constructed of fibrous tissue covered by very thin regular parakeratinized stratified squamous epithelium that had five to eight layers. The basal cells showed columnar cells with palisading nuclei. Many epitheliums were separated from the fibrous capsule, very loose connection between epithelium and connective tissue without rete pegs even if there was not detachment. The change of the cyst wall showed that the epithelium was changed to the hyperplastic stratified squamous epithelium and dense connective tissue with infiltration of inflammation cells after decompression followed by enucleation. The thickness of the epithelial lining before decompression was $365.82 \pm 261.87 \mu\text{m}$ (Fig. 4). In contrast, the thickness of the epithelial lining after enucleation was $1849.76 \pm 1224.56 \mu\text{m}$ (Fig. 5). The mean of increasing rate of epithelial thickness was $921.16 \pm 263.17\%$.

The follow-up ranged from 4.2 years to 8.1 years with a mean follow-up of 5.8 years. A recurrence was found in a patient with Gorlin-Goltz syndrome involved lesions without decompression in the maxillary sinus. There was no recurrence in cases of decompression followed by enucleation.

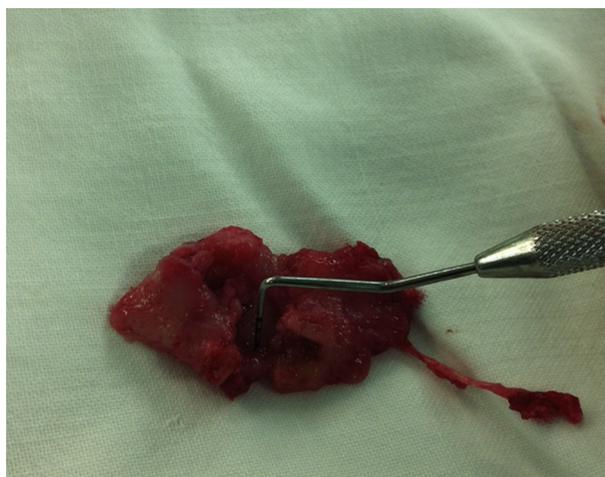


Fig. 3 An approximate the total thickness of the OKC using periodontal probe was measured after decompression followed by enucleation.

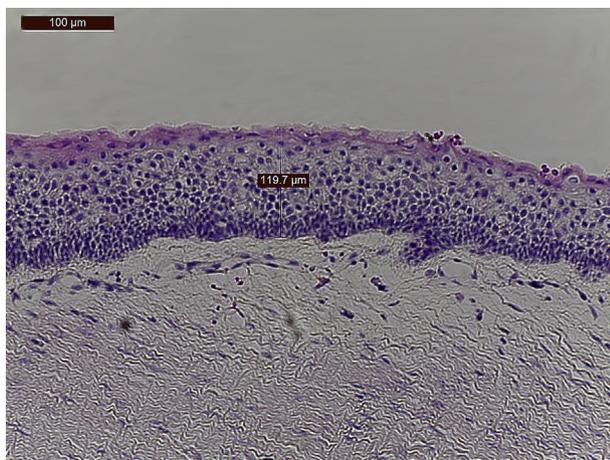


Fig. 4 The epithelial lining shows corrugated parakeratinized layer and nuclear palisaded basal layer of columnar cells before decompression.

Discussion

Brannon¹⁵ suggested that the mechanisms for recurrence of the OKC were incomplete removal, the growth of a new OKC from satellite cysts or remnant cyst after treatment, and development of a new OKC. Among them, Woolgar et al.¹⁶ reported that operative factors have a significant influence on the recurrence of the OKC through a comparative study of the clinical and histological features of recurrent and non-recurrent OKC. Besides, Forssell et al. reported that the recurrence rate of OKC enucleated in one piece was lower than recurrence rate of OKC enucleated in several pieces, it is mandatory to eradicate the whole epithelium to reduce the recurrence.¹⁷ Nevertheless, the operative problem is that OKC has a unique characteristic that the cyst wall is very thin and friable, so it is difficult to remove as a single piece because of specific features. This characteristic is associated with the high recurrence rates

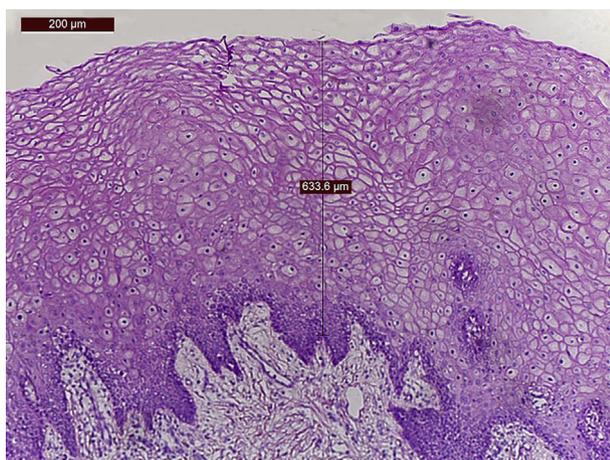


Fig. 5 The epithelial lining shows hyperplastic stratified squamous epithelium after decompression followed by enucleation.

in the jaw lesions,⁸ it explains why enucleation alone is a procedure with the highest recurrence rates.^{8,18} Decompression is one of the treatment modality to reduce recurrence by the histologic characteristic of the OKC. However, the regulatory mechanisms of how OKC is reduced and normal bone repair mechanisms are not clear.¹¹

In fact, marsupialization and decompression have a few differences. Marsupialization is a surgical technique of fenestration of the cystic wall and it can interconnect the cyst cavity with the oral cavity by suturing the inner cystic lumen with the oral mucosa. On the other hand, decompression means opening in the cystic wall for keeping the opening patent by using tube or stent.¹⁹ The term was unified with decompression in this study because there was no case of only marsupialization.

Marsupialization has been regarded as a conservative treatment for OKC,^{20,21} although the exact mechanism that can reduce the size of the OKC and repair normal bone after marsupialization is not clear.¹¹ Aggressive treatment can be the recurrence even to 0%,²² it is highly problematical whether aggressive treatment is the best choice when functional morbidity or cosmetic problems are considered. Even, the recurrence rate of decompression followed by enucleation is not significantly higher than aggressive treatment.^{8,22} So, Madras and Lapointe²³ suggested that decompression followed by enucleation is most effective treatment, marsupialization alone is not as a definitive treatment.

Shudou et al. reported that the reduction form of the OKC was like a balloon, the volume half-life was approximately 8 months and it is possible to enucleate the OKC only 1 month after marsupialization because larger OKC showed a stronger effect on marsupialization.¹¹ This study was shown similar results such as average 8.5 months decompression periods, 56% average decreasing rate.

Histopathologically, the OKC has regular parakeratinized stratified squamous epithelium with little or no evidence of rete ridges, and well-defined palisaded basal layer of columnar or cuboidal cells. The parakeratotic layers often have a corrugated surface.^{1,8} Major histopathologic features that can be considered to recurrences in OKC are as follows;⁶ 1) higher level of cell proliferative activity in the epithelium, 2) budding in the basal layer of the epithelium, 3) parakeratinization, 4) supraepithelial and subepithelial split of the epithelial lining, 5) presence of remnants, daughter cysts. Decompression results in considerable reduction in the cystic lumen, histologic change of the thin, fragile epithelium into thick, solid epithelium with no adhesion to the adjacent structures.²⁴ August et al. reported that epithelial dedifferentiation was observed in 64% of 14 patients treated by decompression/irrigation after 9 months.²⁵ Nakamura et al.¹³ even reported the histologic changes from a parakeratinized epithelium into a hyperplastic, stratified, non-keratinizing squamous epithelium after decompression. The inflammation may be closely related to the transformation of the classic epithelial cyst lining.²⁶

Because the OKCs are not common lesions, this study has been limited with a relative small number of the samples. Although decompression followed by enucleation cannot be generalized, this study has worth that present clinical and histomorphometric evidence to explain low recurrence rate of the decompression followed by enucleation.

Ethics statement/confirmation of patients' permission

This study was approved by Institutional Review Board of Chosun University Dental Hospital (CDMDIRB-1323-128).

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

This study was supported by research fund from Chosun University Dental Hospital, 2018.

References

- Philipsen HP. Keratocystic odontogenic tumour. In: Barnes L EJ, Reichart P, Sidransky D, eds. *World Health Organization classification of tumours. Pathology and genetics of head and neck tumours*. Lyon: International Agency for Research on Cancer, 2005:306–7.
- Speight PM, Takata T. New tumour entities in the 4th edition of the World Health Organization Classification of Head and Neck tumours: odontogenic and maxillofacial bone tumours. *Virchows Arch* 2017;3 [Epub ahead of print].
- Siwach P, Joy T, Tupkari J, Thakur A. Controversies in odontogenic tumours: Review. *Sultan Qaboos Univ Med J* 2017;17:e268–76.
- Suluk-Tekkeşin M, Wright JM. *The World health organization classification of odontogenic lesions: a summary of the changes of the 2017 (4th) Edition*. Turk Patoloji Derg, 2018:34.
- Wright JM, Vered M. Update from the 4th edition of the World health organization classification of head and neck tumours: odontogenic and maxillofacial bone tumors. *Head Neck Pathol* 2017;11:68–77.
- Li TJ. The odontogenic keratocyst: a cyst, or a cystic neoplasm? *J Dent Res* 2011;90:133–42.
- Nayak MT, Singh A, Singhvi A, Sharma R. Odontogenic keratocyst: what is in the name? *J Nat Sci Biol Med* 2013;4:282–5.
- Jafaripozve N, Jafaripozve S, Khorasgani MA. Keratocyst odontogenic tumor: importance of selection the best treatment modality and a periodical follow-up to prevent from recurrence: a case report and literature review. *Int J Prev Med* 2013;4:967–70.
- Ebenezer V, Ramalingam B. Importance of different modalities of treatment for the management of keratocystic odontogenic tumour with five year follow-up. *J Clin Diagn Res* 2014;8:225–8.
- Zhao Y, Liu B, Han QB, Wang SP, Wang YN. Changes in bone density and cyst volume after marsupialization of mandibular odontogenic keratocysts (keratocystic odontogenic tumors). *J Oral Maxillofac Surg* 2011;69:1361–6.
- Shudou H, Sasaki M, Yamashiro T, et al. Marsupialisation for keratocystic odontogenic tumours in the mandible: longitudinal image analysis of tumour size using 3D visualised CT scans. *Int J Oral Maxillofac Surg* 2012;41:290–6.
- Wushou A, Zhao YJ, Shao ZM. Marsupialization is the optimal treatment approach for keratocystic odontogenic tumour. *J Cranio-Maxillo-Fac Surg* 2014;42:1540–4.
- Nakamura N, Mitsuyasu T, Mitsuyasu Y, Taketomi T, Higuchi Y, Ohishi M. Marsupialization for odontogenic keratocysts: long-term follow-up analysis of the effects and changes in growth characteristics. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;94:543–53.
- Telles DC, Castro WH, Gomez RS, Souto GR, Mesquita RA. Morphometric evaluation of keratocystic odontogenic tumor before and after marsupialization. *Braz Oral Res* 2013;27:496–502.
- Brannon RB. The odontogenic keratocyst. A clinicopathologic study of 312 cases. Part I. Clinical features. *Oral Surg Oral Med Oral Pathol* 1976;42:54–72.
- Woolgar JA, Rippin JW, Browne RM. A comparative study of the clinical and histological features of recurrent and non-recurrent odontogenic keratocysts. *J Oral Pathol* 1987;16:124–8.
- Forsell K, Forsell H, Kahnberg KE. Recurrence of keratocysts. A long-term follow-up study. *Int J Oral Maxillofac Surg* 1988;17:25–8.
- Kaczmarzyk T, Mojsa I, Stypulkowska J. A systematic review of the recurrence rate for keratocystic odontogenic tumour in relation to treatment modalities. *Int J Oral Maxillofac Surg* 2012;41:756–67.
- Allon DM, Allon I, Anavi Y, Kaplan I, Chaushu G. Decompression as a treatment of odontogenic cystic lesions in children. *J Oral Maxillofac Surg* 2015;73:649–54.
- Morgan TA, Burton CC, Qian F. A retrospective review of treatment of the odontogenic keratocyst. *J Oral Maxillofac Surg* 2005;63:635–9.
- Pogrel MA, Jordan RC. Marsupialization as a definitive treatment for the odontogenic keratocyst. *J Oral Maxillofac Surg* 2004;62:651–5. discussion 655–656.
- Marker P, Brondum N, Clausen PP, Bastian HL. Treatment of large odontogenic keratocysts by decompression and later cystectomy: a long-term follow-up and a histologic study of 23 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:122–31.
- Madras J, Lapointe H. Keratocystic odontogenic tumour: reclassification of the odontogenic keratocyst from cyst to tumour. *J Can Dent Assoc* 2008;74: 165–5.
- Brondum N, Jensen VJ. Recurrence of keratocysts and decompression treatment. A long-term follow-up of forty-four cases. *Oral Surg Oral Med Oral Pathol* 1991;72:265–9.
- August M, Faquin WC, Troulis MJ, Kaban LB. Dedifferentiation of odontogenic keratocyst epithelium after cyst decompression. *J Oral Maxillofac Surg* 2003;61:678–83. discussion 683–684.
- Rodu B, Tate AL, Martinez Jr MG. The implications of inflammation in odontogenic keratocysts. *J Oral Pathol* 1987;16:518–21.