DECOMPRESSION EFFECT ON MORPHOLOGICAL AND HISTOLOGICAL CHANGES OF ODONTOGENIC KERATOCYST

Original Article

Khaled I. Barakat*, Hamed M. Gad * Ahmed A. Elhawaty**

*Professor of Oral and Maxillofacial Surgery Faculty of Dentistry, Minia University *, Candidate of Master Degree Oral and Maxillofacial Department, Faculty of Dentistry, Minia University ***

ABSTRACT

Odontogenic Keratocyst (OKC) is a benign cystic lesion characterized with aggressive behavior and relatively high recurrence rate. Most of the current suggested therapeutic surgical approaches are jeopardizing vital structures and integrity of the mandible ending with unjustified resections. We aim to evaluate the validity of decompression as a curative treatment for OKC

Patients and Methods: Prospective case series studies of 10 patients were diagnosed with OKC through clinical, radiographical and pathological examination. All patients were treated with decompression. Histopathological features and volumetric changes were evaluated during follow up periods at 3, 6 and 9 months postoperatively.

Results: All OKC lesions showed positive response to decompression. Age ranged from 8 to 45 with mean age of 25.9 years. Lesions' size ranged from 47478.6 mm3 to 4615.52 mm3 with mean size of 20949.5 mm3. Reduction rate percentage in a period of 9 months follow up was 80.36% (P-value=0.002)

Conclusion: Decompression is a noninvasive preliminary curative approach for treating OKC.

Key Words: Odontogenic Keratocyst, Decompression, Histopathological changes, volumetric changes, CBCT

Received: 1 August 2023, **Accepted:** 8 August 2023.

Corresponding Author: Khaled I. Barakat ,Professor of Oral and Maxillofacial Surgery Faculty of Dentistry, Minia University , **Tel :** 22677077, **Mobile:** +201222324596 , **E-mail:** send2barakat@yahoo.com

ISSN: 2090-097X, July 2023, Vol. 14, No. 3

INTRODUCTION:

Odontogenic Keratocyst (OKC) is a developmental odontogenic benign lesion of epithelial origin that affects both genders with wide age range. It is mostly presented in the posterior mandible as lytic expansile mass that may induce facial deformity and even pathological fractures[1].

Despite their benign nature, theses lesions are characterized with aggressiveness, invasiveness and high recurrence rate [2, 3] . Diverse theories and explanations were given for the understanding the etiopathogenesis of such lesions. However, evidence is still lacking full explanation [4].

OKC maybe manifested as single lesion (sporadic) or multiple lesions in patients suffering Gorlin Syndrome[5].

Numerous therapeutic approaches are introduced to treat such lesions. However, the least rate of recurrence is associated with the approaches of the highest morbidity rate. Additionally, less invasive techniques as enucleation also suffer morbidity when they are adjacent to vital structures; Inferior Alveolar nerve, Maxillary sinus, Orbital floor and involved dental structures. Moreover, it is associated with a relatively high recurrence rate.[6 -10]

On the other hand, Marsupialization is the conversion of the cyst into an open pouch to be in continuity with the oral cavity as suggested by Partsch.

Several modifications had been added to the technique to overcome complications as food accumulation and possible infection. Modifications had been added to this technique such as decompression, suggested by Thomas, which is an application of a soft metal or polyethylene tube through a small opening and attached to adjacent tooth for drainage. Similarly, Neaverth and Burg added a tube that was inserted inside the cystic cavity.

This tube was reduced in length as the lesion decreased in size. Later on, Kruger modified the technique to an acrylic button traversed by metal or plastic tube to maintain opening the wound and facilitate irrigation and drainage of cystic cavity [11]. Decompression is intent to relieve osmotic pressure produced by cystic fluid into surrounding bony walls allowing diminishing of the cyst, deposition of new bone, minimizing risk of pathological fracture, preserving adjacent vital structures and allowing eruption of involved teeth[11, 12]. Decompression has not been entrusted to treat OKC as it was thought that the remnants of pathological tissues will keep proliferating. However, there is no evidence supporting this theory [13].

Cone Beam Computed Tomography (CBCT) allows the creation in "real time" of images not only in the axial plane but also 2-dimensional (2D) images in the coronal, sagittal and even oblique or curved image planes a process referred to as multiplanar reformation (MPR). In addition, CBCT

 DOI: 10.21608/OMX.2023.226577.1199

data are amenable to reformation in a volume, rather than a slice, providing 3-dimensional (3D) information [14]. The purpose of the present study was to assess the validity of decompression as a therapeutic approach for treating OKC through volumetric and histopathological changes.

MATERIALS AND METHODS:

This study was conducted in compliance with the principles of the Declaration of Helsinki, and approval of the ethics committee required for the study was obtained from the Ethics Committee of the Faculty of Dentistry, Minia University. An informed consent was obtained from all individual participants included in the study. To address the research purpose, this prospective study was conducted as a Case Series Study.

10 Patients were enrolled from outpatient clinic of Oral and Maxillofacial Surgery Department, Minia University Dental Hospital (MUDH) on the basis of the following inclusion criteria: (1) Confirmation of OKC histological diagnosis according to the WHO recommendation, (2) Patient's age ranging from 8 to 52 years old, (3) Both genders, (4) Maxillary and Mandibular lesions, (5) Systemic healthy patient. Patients were excluded if they presented any of the following criteria: (1) patients who refused to participate in the study after reading the informed consent form, (2) Patients who are not responding to Decompression; showing aggressive changes that require differing of treatment plan, (3) Cases of recurrent OKC (4) Patients with autoimmune diseases. (5) Patients with active bone diseases, (6) Patients treated from malignant or benign tumors, (7) Uncontrolled periodontal diseases.

Medical and dental histories were recorded for each patient. Additionally, Clinic examination and radiographical evaluation through preoperative panorama x-ray and CBCT were done.

Under local anesthesia with vasoconstrictor an incision was made at mucoperiosteum of the alveolar mucosa not less than 1cm in diameter. Creation of bone window for exposure of lesion's lumen by means osteotomes or round surgical burs in case of no cortical perforation. Evacuation of lesion's lumen content and partial removal of cystic wall for incisional biopsy was taken. Biopsies were transferred into labeled and coded plastic containers filled with 10% buffered formalin for formalin-fixed, paraffin-embedded (FFPE) block of tissue fabrication. Sections were prepared for Hematoxylin and Eosin Stain (H&E) for microscopic diagnosis.

A rubber base impression was taken for fabrication of acrylic plug. A silastic suction tip was stitched to the mucoperiostem using 3-0 prolene blue as a temporization to prevent closure of the opening into the cystic cavity till fabrication of the acrylic plug. Wounds were followed up of for inspection regarding; inflammation, infection, swelling and sutures fail every 2 days for first 10 days and then monthly for the next 9 months. CBCT imaging and incisional biopsies were retaken 3, 6 and 9 months postoperative.

Volumetric analysis was done using OnDemand3DApp version 1.0.10.5385 software. Profile tool was used to obtain threshold values of the lesions. After selecting Object Mask Tool, Sculpt icon was used on 3D View to mark the lesion. The obtained threshold values were inserted in the Pick box to estimate the lesion volume. Volumes were recorded in mm3. Reduction rate was calculated according to the following (R/X %). X is the preoperative lesion volume. X1 is the lesion volume in the first follow up. X2 is the lesion volume in the second follow up.X3 is the lesion volume in the third follow up. R1 is the difference between X and X1. R2 is the difference between X and X2. R3 is the difference between X and X3. Follow up H&E slides were compared to preoperative ones for reconfirmation of the initial diagnosis and detection of any histopatholgical changes.

Table1 showing demographic data, chief complain, lesion diagnosis and location

Case #	Age	Gender	Chief complain	DIAGNOSIS	lesion location
1	8	M	Extra oral swelling	OKC	Left mandibular body
2	22	M	Extra oral swelling	OKC	Left mandibular body
3	13	F	Found through x-ray	OKC(syndromic)	Right Mandibular Ramus
4	13	F	Found through x-ray	OKC(syndromic)	Left mandibular body
5	37	M	mouth opening limitation	OKC(syndromic)	Left Mandibular Ramus
6	37	M	Found through x-ray	OKC(syndromic)	Right Mandibular body
7	14	M	Extra oral swelling	OKC	Right Mandibular body
8	35	M	Found through x-ray	OKC(syndromic)	Right Posterior Maxilla
9	35	M	Found through x-ray	OKC(syndromic)	Left Posterior Maxilla
10	45	M	Tooth mobility	OKC	Anterior Maxilla

Statistical analysis:

The statistical analysis was conducted using IBM SPSS Statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA). The results were recorded as the mean and standard deviation values (mean ± SD). P-values of 0.05 or less were considered statistically significant

RESULTS:

The current study was conducted on 7 patients with diagnosed 10 OKC lesions; a female patient and nine male patients. Three male patients were excluded from the results for inability to attend follow ups as prescheduled. Four patients were diagnosed with single OKC lesion per each .Two male patients and a female patient with multiple OKC lesions with Gorlin syndrome manifestations. Five lesions were located in the mandibular body, two lesions were located in the posterior maxilla, one lesion was located in the anterior maxilla and two lesions were located in the ramus of the mandible

Table 2 showing preoperative lesions' volume, first second and third follows up volume in mm3 and reduction rate in percentage

Case #	Preoperative Volume (mm3)	1st follow up Volume (mm3)	1st follow Reduction rate (%)	2nd follow up Volume (mm3)	2nd follow Reduction rate (%)	3rd follow Volume (mm3)	3rd follow Reduction rate (%)
1	35993.5	24580.3	31.71%	17639.2	50.99%	9120.3	74.66%
2	18266	6440.57	64.74%	5900.07	67.70%	1218.6	93.33%
3	47478.6	35335.3	25.58%	16102.1	66.09%	8000.6	83.15%
4	5865.83	9210.68	-57.02%	2336.92	60.16%	600.7	89.76%
5	22548.9	15441.9	31.52%	10241.1	54.58%	5823.9	74.17%
6	4615.52	3278.01	28.98%	2237.09	51.53%	1215.9	73.66%
7	32218.5	22519.3	30.10%	10391.8	67.75%	987.3	91.03%
8	11003.4	4514.03	58.98%	3685.5	66.51%	9206.7	52.89%
9	19544.1	16895.6	13.55%	14514.8	25.73%	725.6	93.93%
10	11960.7	6490.99	45.73%	3341.75	72.06%	4236.8	86.85%

All lesions showed reduction in size. Reduction rate was calculated according to the following (R/X %). The preoperative lesions' volume ranged from 47478.6 mm3 to 4615.52 mm3. The postoperative lesion's volumes ranged from 9206.7 mm3 to 600.7 mm3. The mean of the volumetric reduction in the third follow up was 80.36%. Student T-test was done to compare the X3 to X. **Table 3** showing Preoperative and Postoperative volumes, range, mean, SD, t and P-values.

	Volume(mm3)						% of change	T-test	
	Range			Mean	±	SD		t	P-value
Preoperative	4615.52	-	47478.6	20949.5	±	13915.9	80.36%	4.197	0.002*
3rd follow	600.7	-	9206.7	4113.64	±	3642.74			

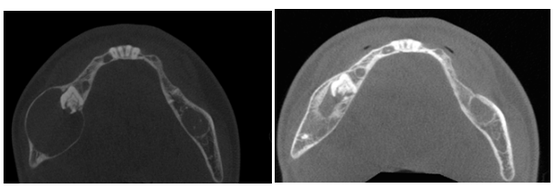

Figure 1. Preoperative and follow up Axial CBCT cuts showing lesion is reduced in size and new bone formation

Figure 2 . Preopaerative and follow up 3D views showing new remolded bone

All follow up sections reconfirmed the initial diagnosis. All of the OKC samples demonstrated typical characteristics of histopathological findings with no signs of inflammation. The wall of the cystic cavity was constructed of fibrous tissue covered by very thin regular parakeratinized stratified squamous epithelium that had eight to eleven layers. The basal cells showed palisading columnar cells with vertically oriented nuclei. Many epitheliums were separated from the fibrous capsule, very loose connection between epithelium and connective tissue without rete pegs. In follow up histological examination revealed a change of the cyst wall resembling the parakeratinized stratified squamous epithelium was changed to the hyperplastic stratified squamous epithelium and dense connective tissue. Loss of columnar shape of cells into more flattened and nuclei showed normal orientation were also noted.

Figure 3. Preoperative and follow ups sagittal CBCT cuts showing lesion is reduced in volume and new bone formation till almost resolving of the lesion.A preoperative, B first follow up; new bone formation only in the distal portion of the cyst C second follow up & D third follow up; new bone formation after extraction of the involved molar. Yellow arrow pointing at the incompelte septa. Blue arrow poinitng at new borders of the lesion. Red arrow pointing at new alovolar ridge formation

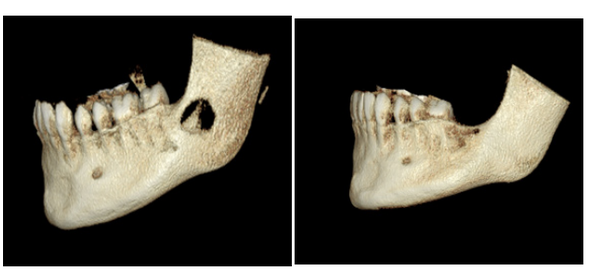

Figure 4 . Preoperative and follow up 3D models showing new remolded bone

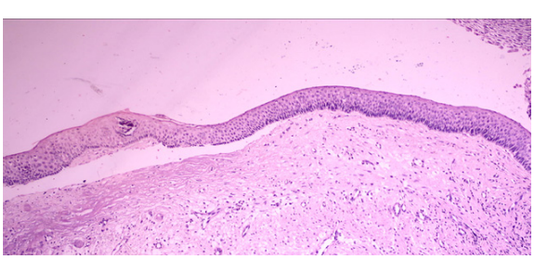

Figure 5. H&E preoperative section showing characteristic features of OKC)

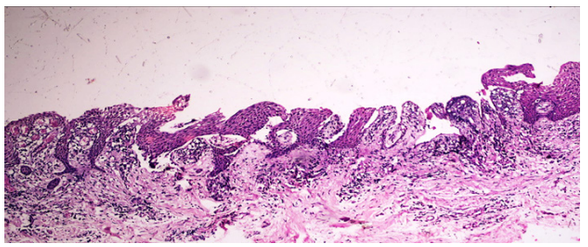

Figure 6 . H&E postoperative section showing loss of palisading nuclei of the basal layer, rete pegs and hyperplastic squamous epithelium

DISCUSSION:

Nonetheless the benign origin of OKC; its clinical behavior, local invasiveness and different presentations indicate its aggressive behavior. Complete removal of the pathological tissues was thought to be the definitive treatment for OKC. However, tissue morbidity subsequent to resections and the rate of recurrence following enucleation is relatively high.

Decompression is a minimum invasive procedure that allows reduction of odontogenic cysts volume prior to enucleation. The biological and morphgenic effect of Decompression over the pathological tissues is not clearly understood. The ongoing proliferation of the remaining pathological tissues is thought to be one of the limitations.

From our results; Decompression changed the histological and morphological characteristics of Sporadic and Syndromic OKC lesions. The volumetric analysis through CBCT imaging showed reduction in size. Histological analysis revealed loss of palisading and flattening of cuboidal cells in follow up sections. Moreover, follow up sections showed transitions of OKC lining epithelium to normal mucosal epithelium.

Marsupialization and decompression are two different modalities that share the same concept, i.e., relieving the intra-luminal osmotic pressure either completely or partially consecutively [12, 15]. Through literature both terms are used separately or as synonyms. The reduced osmotic pressure produced by cystic fluid into surrounding bony walls allowed diminishing of the cyst, deposition of new bone, minimizing risk of pathological fracture, lowering rate of recurrence, preserving adjacent vital structures and allowing eruption of involved teeth [16] . Moreover, the reduction of osmotic pressure affects the biological behavior of cells regarding proliferation, migration and apoptosis [17].

Pogrel and Jordan, [13] observed that the epithelial lining of OKC after marsupialization displayed similar characteristics of normal oral epithelium.

The lining epithelium of OKC after the marsupialization, showed increased thickness of epithelium and the keratinized epithelium was changed to a hyperplasic and non-keratinized stratified squamous epithelium and lacking of bcl-2 expressions in postoperative sections in 10 OKC lesions suggesting that marsupialization is a definitve treatment for OKC. It was also suggested that a dedifferentiation process of the epithelium as a result of the exposure of OKC's lining epithelial to the oral environment. Tabrizi, Reza, et al.[18]

reviewed the reccurence rate (RT) of OKC following marsupialization and decompression with or without adjuvant procedures. In their first analysis, the RT was higher in the marsupialization group without any adjuvant treatments. In the second analysis, there was no statistical difference for the RT between marsupialization and decompression with further enucleation or cystectomy. De Castro et al.[19] stated that RT in OKCs treated with decompression, followed by enucleation is lower than OKCs treated with enucleation only. Wushou and Zhao [20] stated that marsupialization decreases the recurrence of OKCs more than enucleation and surgical resection and it may be the ideal treatment for OKCs.

Wiesmann et al [21] stated that the differentiation of mesenchymal stem cells towards osteoblast-like cells can be influenced by different mechanical loading. In contrast, prior to mineralization the effects of the mechanical stimulation become obvious by analysis of the extracellular matrix. The collagen type I expression that was analysed by immunfluorescence. The expression of this protein is upregulated in the early phase of osteoblastic differentiation. Additionally, Sun et al, [22] in examined the efficacy of decompression on stemness and osteogenic potential of alveolar bone marrow stromal cells (BMSCs) around the cysts. BMSCs have the characteristics of self-proliferation and multi-differentiation potential. It has been previously confirmed that orofacial (maxilla and mandible) BMSCs had the same proliferative and osteogenic potentials as that isolated from the iliac crest [23] .

The higher expression of CFU-F, OCT4, Nanog and SOX2 after decompression indicates its crucial role in regulating the pluripotency of BMSCs around cysts tissues [22]. Sodnom-Ish, Buyanbileg, et al.[24] analyzed the effectiveness of decompression in an Osteomyelitis jaw model of mandibles of fourteen Sprague–Dawley rats. Decompression drains induced advanced bone healing compared to that of curettage alone.

CONFLICT OF INTEREST

This clinical study was self-funded by the authors, with no conflict of interest.

CONCLUSIONS:

Decompression is considered to be the least invasive treatment of choice for OKC. The reduction in lesions size has a positive effect in reducing aggressive behavior of such lesions.

REFERENCES

1. Rajendra Santosh AB. Odontogenic Cysts. Dental clinics of North America. 2020;64(1):105-19.

2. 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 and neck pathology. 2017;11(1):68-77.

3. Stoelinga PJW. Keratocystic odontogenic tumour (KCOT) has again been renamed odontogenic keratocyst (OKC). International journal of oral and maxillofacial surgery. 2019;48(3):415-6.

4. Ghafouri-Fard S, Atarbashi-Moghadam S, Taheri M. Genetic factors in the pathogenesis of ameloblastoma, dentigerous cyst and odontogenic keratocyst. Gene. 2021;771:145369.

5. Giovacchini F, Bensi C, Paradiso D, Belli S, Mitro V, Tullio A. Factors influencing the recurrence of keratocysts: monocentric study. Journal of Oral Medicine and Oral Surgery. 2020;26(1):1.

6. Kaczmarzyk T, Mojsa I, Stypulkowska J. A systematic review of the recurrence rate for keratocystic odontogenic tumour in relation to treatment modalities. International journal of oral and maxillofacial surgery.
2012;41(6):756-67.

7. Leung YY, Lau SL, Tsoi KY, Ma HL, Ng CL. Results of the treatment of keratocystic odontogenic tumours using enucleation and treatment of the residual bony defect with Carnoy's solution. International journal of oral and maxillofacial surgery. 2016;45(9):1154-8.

8. Journal of oral pathology & medicine : official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology.

9. Kiwilsza M, Sporniak-Tutak K. Gorlin-Goltz syndrome--a medical condition requiring a multidisciplinary approach. Medical science monitor : international medical journal of experimental and clinical research.
2012;18(9):Ra145-53.

10. Giuliani M, Grossi GB, Lajolo C, Bisceglia M, Herb KE. Conservative management of a large odontogenic keratocyst: report of a case and review of the literature. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2006;64(2):308-16.

11. AL-Omar AF, Elmorsy KA. Treatment of a large maxillary cyst with marsupialization. 2017.

12. Briki S, Elleuch W, Karray F, Abdelmoula M, Tanoubi I. Cysts and tumors of the jaws treated by marsupialization: A description of 4 clinical cases. Journal of Clinical and Experimental Dentistry. 2019;11(6):e565.

13. Pogrel MA, Jordan RC. Marsupialization as a definitive treatment for the odontogenic keratocyst. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons.
2004;62(6):651-5; discussion 5-6.

14. Scarfe WC, Farman AG, Sukovic P. Clinical applications of cone-beam computed tomography in dental practice. Journal-Canadian Dental Association. 2006;72(1):75.

15. Abdullah WA. Surgical treatment of keratocystic odontogenic tumour: A review article. The Saudi dental journal. 2011;23(2):61-5.

16. Briki S, Elleuch W, Karray F, Abdelmoula M, Tanoubi I. Cysts and tumors of the jaws treated by marsupialization: A description of 4 clinical cases. J Clin Exp Dent. 2019;11(6):e565-e9.

17. Taïeb HM, Garske DS, Contzen J, Gossen M, Bertinetti L, Robinson T, et al. Osmotic pressure modulates single cell cycle dynamics inducing reversible growth arrest and reactivation of human metastatic cells. Scientific reports. 2021;11(1):13455.

18. Tabrizi R, Hosseini Kordkheili MR, Jafarian M, Aghdashi F. Decompression or Marsupialization; Which Conservative Treatment is Associated with Low Recurrence Rate in Keratocystic Odontogenic Tumors? A Systematic Review. Journal of dentistry (Shiraz, Iran). 2019;20(3):145-51.

19.de Castro MS, Caixeta CA, de Carli ML, Ribeiro Júnior NV, Miyazawa M, Pereira AAC, et al. Conservative surgical treatments for nonsyndromic odontogenic keratocysts: a systematic review and meta-analysis. Clinical oral investigations. 2018;22(5):2089-101.

20. Wushou A, Zhao YJ, Shao ZM. Marsupialization is the optimal treatment approach for keratocystic odontogenic tumour. Journal of cranio-maxillo-facial surgery : official publication of the European Association for Cranio-Maxillo-Facial Surgery. 2014;42(7):1540-4.

21. Wiesmann A, Bühring HJ, Mentrup C, Wiesmann HP. Decreased CD90 expression in human mesenchymal stem cells by applying mechanical stimulation. Head & face medicine. 2006;2:8.

22. Sun Y, Zhang J, Qian N, Sima G, Zhang J, Zhong J, et al. Comparison of the osteogenic differentiation of orofacial bone marrow stromal cells prior to and following marsupialization in patients with odontogenic cyst. Molecular medicine reports. 2018;17(1):988-94.
osteomyelitis. Scientific reports. 2021;11(1):1-12.

23. Matsubara T, Suardita K, Ishii M, Sugiyama M, Igarashi A, Oda R, et al. Alveolar bone marrow as a cell source for regenerative medicine: differences between alveolar and iliac bone marrow stromal cells. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research.
2005;20(3):399-409.

24. Sodnom-Ish B, Eo MY, Oh JH, Seo MH, Yang HJ, Lee JH, et al. Decompression effects on bone healing in rat mandible osteomyelitis. Scientific reports.
2021;11(1):1-12.