



Topical 5-Fluorouracil as an Adjuvant in Odontogenic Keratocyst –A Case Report

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ABSTRACT:

Odontogenic keratocyst (OKC) is a developmental odontogenic cyst that arises from remnants of dental lamina. It is an aggressive lesion. In the recent year's attention is given to new adjunctive procedures in the treatment of OKC. 5-Fluorouracil (5-FU) is an antimetabolite used in the treatment of various malignant diseases like Basal cell carcinoma. OKC is found to respond to 5-FU as it shares similar molecular etiopathogenesis with Basal cell carcinoma. A case of Odontogenic keratocyst in maxilla treated with 5-FU is presented in the paper. The ease of availability, technically simple application with reduced operative time and no local or systemic adverse effect is the advantage over Carnoy's solution especially in OKC occurring in maxilla. The available literature is showing normal healing with no recurrence and neurosensory deficits with 5-FU application.

1. Introduction

Odontogenic keratocyst (OKC) is a developmental odontogenic cyst arising from remnants of dental lamina and basal cells of oral epithelium. The term odontogenic keratocyst was coined by Philipsen in 1956^{1,2,3}. OKC is an aggressive lesion of jaw, presents 1.8 to 21.5% of odontogenic cysts². It is seen in the age group from 7 to 83, years with peak incidence in 2nd and 4th decade of life¹. There is a male predominance with male to female ratio is 16:1². The most predominant site of occurrence being posterior mandible followed by posterior maxilla, anterior maxilla and anterior mandible^{1,2,3}. OKC is often asymptomatic and is accidentally detected during routine radiologic examination³. OKC presents as a well-defined unilocular or multilocular radiolucent lesion with scalloped border^{3,4}. The OKC grows Antero-posteriorly in the marrow with little or no cortical expansion and displacement of teeth. In maxilla OKC is rare, presence of cancellous bone and thin cortical bone allows extension and perforation into the maxillary sinus, nasal cavity. The patients usually present with swelling, pain, facial asymmetry^{4,5}. Pinborg and Hansen described the classical histopathological features for the diagnosis of OKC. The cyst has a thin, friable epithelial lining with satellite cysts in the connective tissue wall and overlying oral mucosa predisposing to recurrence. Management of

OKC involves marsupialization, enucleation, peripheral ostectomy and resection⁶. The various adjunctive therapies are chemical cauterization using Carnoy's solution, peripheral osteotomy with excision of overlying mucosa in cases of cortical perforation of cysts and cryotherapy are employed to reduce the recurrence rate. A newer targeted therapy 5 Fluorouracil (5-FU) is being used as an adjunctive in the treatment of OKC. It is an antimetabolite drug used in the treatment of malignant diseases. It is used as a topical agent in the treatment of superficial Basal Cell Carcinomas(BCC)⁴. In OKC, PTCH gene mutation leads to activation of smoothed receptor (SMO) and sonic hedgehog (SHH) signaling leading to neoplastic growth. 5-FU induces apoptosis by preventing SHH and SMO activation in hepatocellular carcinoma. It inhibits thymidylate synthetase an enzyme required for DNA synthesis, there by actively proliferating cells are prevented from DNA synthesis leading to cell death^{2,5,6,7}. The efficacy of 5-FU in OKC may be because of its similarities to BCC in molecular etiopathogenesis.

Case Report

A 24-year-old male patient reported to a private clinic with a chief complaint of pain in the left upper back teeth region for the past 2 months. The pain was dull aching kind present throughout the day. His medical history was



noncontributory. On examination there was no gross facial asymmetry, mouth opening was slightly reduced with full Complement of teeth present. The buccal vestibule in relation to left 2nd and 3rd molar region was obliterated extending from distal surface of first molar to the tuberosity and from the mucogingival junction to depth of the vestibule, swelling extending buccally interfering with the movement of coronoid process during opening. The molars were periodontally sound and were vital. On Palpation, pain was elicited in the buccal vestibule in relation to the molars. The bone was eroded and the oral mucosa was depressible. Provisional diagnosis of a cyst in relation to posterior maxilla was made. The CBCT showed complete opacification of the left maxillary sinus with perforation of posterolateral wall of maxillary sinus. The cyst extended into the maxillary sinus and measured 36mm Superio-inferiorly, 34mm Antero posteriorly, 29mm mesiodistally. There was blunting of palatal root apices of second and third molars. On aspiration white cheesy mixed with purulent material was obtained, incisional biopsy reported as infected OKC. The treatment plan was enucleation of the cyst and topical application of 5 Fluorouracil as an adjunctive modality. Through buccal approach the cyst was enucleated it was combined with endoscopic approach which provided better visualization and aided complete removal of cyst from maxillary sinus. The Posterio-lateral wall of maxilla was completely eroded. The cavity was packed with sterile ¼ inch gauze coated with 5% 5-FU and the end was brought out through the nasal antrostomy. The pack was removed after 24 hours and wound was irrigated. The wound healing was uneventful. The follow up at 2 years with CBCT showed regeneration of posterolateral wall with no signs of recurrence.

Discussion :

In the year 2005 OKC was renamed by WHO as Keratocystic odontogenic tumour (KCOT) due to its aggressive potential, slow growth and high recurrence rate. The two subtypes the orthokeratinized and parakeratinized variety were classified as independent types depending upon their tendency to recur under the category of epithelial tumour of odontogenic origin. In 2017, KCOT was again reclassified as odontogenic keratocyst^{1,2,7}.

The OKC has an active epithelial lining with high proliferation rate reflecting a potential aggressive growth

pattern^{2,3,5}. The Goal of the treatment is to develop a method of treatment that will minimize the morbidity and reduce recurrence^{5,6}. The treatment modality depends upon the size of lesion, location, proximity of lesion to vital structures like inferior alveolar nerve, maxillary sinus and nasal cavity⁵.

Enucleation alone has shown very high recurrence up to 56%. Application of adjunctive therapies like cryotherapy and Carnoy's solution showed almost similar recurrence rate of 11.5%. The peripheral osteotomy with 5mm margin of healthy bone has shown least recurrence rate^{7,8}. The Carnoy's solution is not advised in maxilla, because of the cancellous nature of the bone and proximity to the vital structures as it causes necrosis and postoperative neurosensory deficits. The use of modified Carnoy's solution in which the chloroform is excluded due to its carcinogenic potential has yielded high recurrence rate in the recent studies^{2,7,8}.

5 Fluorouracil a targeted approach in the management of OKC was first proposed by Ledderhoff et al understanding of molecular genetics of OKC^{1,2}. In a study conducted by them on Keratocystic odontogenic tumors compared the modified Carnoy's solution and 5-FU. It was observed that there was no recurrence and relatively very low inferior alveolar nerve paresthesia in 5 FU group. In a prospective study by Lone P A et al, comparison was done between three treatment modalities, modified Carnoy's solution, 5-FU and segmental resection. It was observed there was 66.6% recurrence in modified Carnoy's solution group with no recurrence in 5-FU and segmental resection group². In a retrospective study on 70 patients, no recurrence was found in 5-FU group compared to 9 recurrences in modified Carnoy's solution group⁸. In a case of large OKC in mandible treated with marsupialization and topical application of 5-FU, after 4 months, it was observed there was well defined new bone formation observed at the lower border⁹. The application of 5-FU for Keratocystic odontogenic tumor in a Gorlin-Goltz syndrome case, has produced a favorable response with new bone formation in the follow up¹⁰. The application of 5-FU twice a week for four weeks after medial maxillectomy, sphenoidectomy for Adenocarcinoma has shown no local adverse effects on periorbital connective tissue and it is not neurotoxic. It is particularly useful in maxillary keratocyst as it enlarges and extends to the surrounding area and usually presents late. In the case



discussed here, the lesion was in the maxilla with erosion of posterolateral surface of maxilla, after enucleation with combined transoral and endoscopic approach the novel topical application of 5-FU was advantageous to place as it is readily available, low cost with reduced postoperative morbidity in comparison to Carnoy's solution. At 3 years follow up CBCT revealed gradual amount of bone formation and no recurrence.

CONCLUSION

Odontogenic keratocyst is an aggressive lesion. There is no uniform treatment protocol followed. Surgical management protocols with multi-modal therapeutic approach which may reduce the recurrence, morbidity should be adopted. The literature available is showing promising results with topical application of 5-FU in comparison with Carnoy's solution. However larger number of studies with follow up are required.



FIG 2: Exposure of the lesion

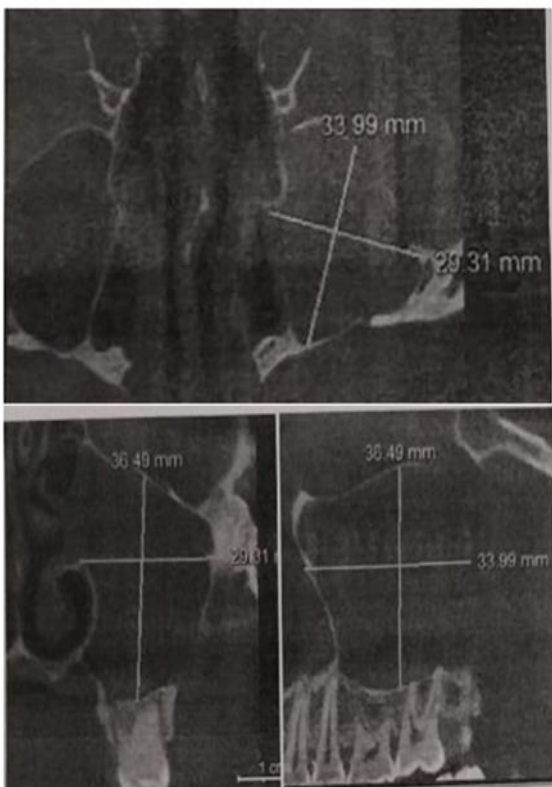


FIG 1 : Pre-operative CBCT



FIG 3: Endoscopic view of the cavity



FIG 4: Excised specimen after enucleation of the cyst

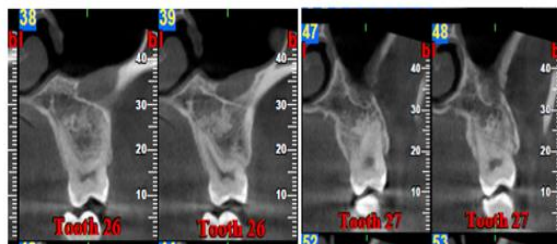


FIG 5: Post-operative CBCT

Radiology. Volume 129, Issue 1, January 2020, Page e94

10. Shiran H, et al. Use of Topical 5-Fluorouracil for Keratocystic Odontogenic Tumors of Gorlin-Goltz Syndrome as a New Targeted Therapy: A Case Report and Review of Literature. *J Res Dentomaxillofac Sci* 2019;4(4):43-48.

References:

1. Balamurugan R, 5 Fluorouracil: Trend Setter in the Management of Odontogenic Keratocyst. *Journal of Case Studies and Clinical Trials*, 2019, 1
2. Lone Akhter P, et al., Topical 5-fluorouracil application in management of odontogenic keratocysts. *J Oral Biol Craniofac Res*. 2020 Oct-Dec; 10(4): 404-406 .
3. Hadziabdic N, Dzinovic E, Udovicic Gagula D, Sulej Managic, Osmanovic A, Halilovic S, Kurtovic Kozaric A, Non syndromic examples of odontogenic keratocyst' *Case Reports in Dentistry Vol* 2019
4. Slusarenka DaSilva Y, Nacleio Homem MG, Conservative Treatment of Primary and Non Syndromic OKC : An Overview of the Practice. *International Journal of Oral Dental Health* 2018, 4:070.
5. Belgal PG, Pathak B, Shastri L, Updates in the surgical management of odontogenic keratocyst. *J Adv Clin Res Insight* 2019;6:116-118.
6. Lone PA, Singh M, Johar HS. Treatment modalities of odontogenic keratocyst of maxilla and mandible. Our experience *World J Dent* 2015;6(4); 208-12.
7. Ledderhof J.N. Topical 5-Fluorouracil is a Novel targeted therapy for the keratocystic odontogenic tumor. *J Oral Maxillofac Surg* 75:514-524, 2017.
8. Caminti M F, El -Rabbany M, Jeon J, Bradley G. Review of 5 Fluorouracil is associated with decreased recurrence risk in odontogenic Keratocyst management; A retrospective cohort study. *Journal of oral and maxillofacial surgery* vol79(4) Apr2021, 814-821.
9. Caldas RPO et al Therapy for odontogenic lesions with 5-Fluorouracil topical: A case report. *Oral Surgery, Oral Medicine, Oral Pathology and Oral*