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Surgical Management of Odontogenic Keratocyst: A Case Series of seven patients

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ABSTRACT: Odontogenic keratocyst (OKC) is a common developmental odontogenic cyst affecting the maxillofacial region that arises from the dental lamina. The OKC is distinctive among jaw cysts and has tendency toward recurrence along with aggressive clinical behavior and high conversion rate into ameloblastoma. Odontogenic keratocyst was named as keratocystic odontogenic tumor (KCOT) in the WHO classification of head and neck tumors in 2005 due to its aggressive nature, high recurrence rates and specific histological characteristics and reclassified in to the cystic category in WHO classification of head and neck pathology in 2017. In this study, 7 cases of OKC over a period of 6 year from the year 2012 to 2018 are reported. Diagnosis of all patients was made by histopathological investigation obtained by biopsy. (FNAC and or excisional biopsy). Treatment plan for 5 patients included enucleation and chemical cauterization by applying carnoy's solution and for remaining 2 patients only enucleation was done becauses of neural involvement. Out of 7 cases, 1 case has recurrence and another 1 case was converted into ameloblastoma.

KEYWORD: Odontogenic keratocyst, mandible, maxilla, enucleation, chemical cauterization.

I. INTRODUCTION

Odontogenic keratocyst was first described by Phillipsen in 1956 and confirmed by Browne in 1970 and 1971[1]. It is named keratocyst because the cyst epithelium produces so much keratin that it fills the cyst lumen[29]. Odontogenic keratocyst is benign unicystic or multicystic, intraosseous tumor of odontogenic origin with a characteristic lining of parakeratinized (86.2%) or orthokeratinized (12.2%) stratified squamous epithelium[5]. This pathological lesion represents about 11% of all odontogenic cysts, being considered the third most common cyst of the jaw. OKCs most often occur in the second and third decades of life and show a slight predilection for males (male to female ratio 1.6:1)[5]. The mandible is invariably affected more frequently than the maxilla. (65 to 70 percent of cases)[6]. In the mandible, the majority of the cysts occur in the ramus-third molar area, followed by the first and second molar area and then the anterior mandible[6, 7]. In the maxilla, the most common site is the third molar area followed by the cuspid region[2]. Long standing odontogenic keratocyst have been reported to transform in to primary intraosseous carcinoma or an ameloblastoma.

Radiographically, odontogenic keratocyst presents predominantly as a multilocular radiolucency with a ratio of unilocular to multilocular varying from 3:112 to 1:1.3[2]. Multilocular keratocyst are occasionally associated with basal cell nevus syndrome (also called Gorlin syndrome or Gorlin-Goltz syndrome) is an autosomal-dominant inheritance condition that includes a triad of multiple OKC of the jaws, other skeletal abnormalities (often including bifid ribs, abnormalities in the length of the fingers and toes, frontal bossing, and calcification of the falx cerebri), as well as cutaneous manifestations such as basal cell carcinomas, palmar pitting of the hands, and other skin abnormalities[11, 13].

Various treatment strategies have been devised on the basis of extensive reviews of

literature suggesting the modalities with reduced possibility of recurrence. Blanas et al. have founded a recurrence rate of around 17% to 56%. When treated by simple enucleation in their systematic review. They have also suggested that addition of Carnoy's solution to the cystic cavity for 3minutes after enucleation reduces the recurrence to 1.6% which is comparable to resection, without associated morbidity.

The line of management in our cases was influenced by these classic systemic review who had demonstrated that enucleation and curettage followed by application of carnoy's solution can be considered as a definitive treatment modality for OKCs.

II. CASE REPORT

Here, we are presenting the total 7 cases of OKC who were operated in the department of Oral and Maxillofacial surgery, Ahmedabad Dental College and Hospital, Gandhinagar (Gujarat). We included child and adult patients approximately age between 11- 60 year and the ratio was 4:3 (Male to female), the diagnosis was confirmed by FNAC and or excisional biopsy and all patients have common chief complain of swelling with no history of any trauma, pus discharge or adjoining systemic illness. Primarily, Panoramic radiograph (OPG) were done for all the cases. We have also done with the CBCT and CT- Face for some cases as it required.

CASE NO. 1

60 year old male patient came with intraoral swelling on right side of mandible. On intraoral inspection, swelling was present on right lower buccal vestibule with obliteration. On palpation, swelling was bony hard, non-compressible, non-fluctuant, non- tender.

The OPG showed large, single unilocular, oval shaped radiolucency with sclerotic border in relation to 44, 45 and extending up to molar region antero-posteriorly in partially edentulous arch and crestal bone to lower border of mandible supero-inferiorly.

CASE NO. 2

45 year old male patient came with facial asymmetry due to extraoral swelling on right side of the mandible, antero-posteriorly started from 2 cm behind the corner of mouth and extending up to the posterior border of ramus. Supero-inferiorly, 3 cm below the ala-tragus line to the lower border of mandible. An intraoral examination revealed a remarkable swelling, which was non- tender, bony hard, non-compressible, non- fluctuant and associated with grade-1 mobility of 47.

The OPG (Fig.1) and CBCT (Fig.2, 3) showed unilocular radiolucency from distal root of the 46 and extended up to the sigmoid notch of the right side of mandible. It is associated with impacted 48. The coronal section of the CBCT showed thinning of the buccal and lingual cortical bone and inferior alveolar nerve was passing from the inferior- lingual aspect of the lesion.

On the basis of aspirated whitish creamy material (Fig. 4) provisional diagnosis was OKC and dentigerous cyst based on CBCT.

CASE NO. 3

44 year female Patient noticed intraoral swelling on right side, which was gradually increasing. She had no history of pain and pus discharge.

On extraorally inspection, patient face was bilaterally symmetrical. On intraoral inspection, swelling was single, diffuse, and oval with inflamed overlying skin on right side of the buccal vestibule in relation to body of mandible. On intraoral palpation, swelling was non-tender, non-compressible, non- fluctuant associated vestibular obliteration.

The panoramic radiograph showed well defined unilocular radiolucency in relation to lower right third molar region extending from distal root of 1st molar up to anterior border of ramus around 2-4 cm in size, which was surrounded by radiopaque border and horizontally impacted third molar was also present superiorly in relation with lesion.

CASE NO. 4

15 year old male patient came to dept. with intraoral swelling which was present in right buccal vestibule with obliteration. On intraoral palpation, Swelling was non-compressible, fluctuant, non-tender and eggshell crackling was present.

The OPG (Fig. 8) and PNS x-ray view confirmed that a large unilocular single, well defined, oval shaped swelling was present from 11 to 16 with root resorption and displacement of 11, 12, C, 14, 15 and impacted canine was embedded in to right maxillary sinus. Coronal section of the CT-Face revealed that buccal cortical plate expansion with radiolucency enclosed within the right maxillary sinus, superiorly extending up to floor of orbit, medially up to inferior nasal concha and inferiorly up to maxilla (Fig. 9).

We performed an FNAC and aspirated whitish colored fluid. On the basis of aspiration biopsy provisional diagnosis was given OKC and dentigerous cyst based radiographic investigation.

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CASE NO. 5

11 year old female patient came to dept. with extraoral swelling on lower right side of the face which was bony hard with normal overlying skin. Antero-posteriorly, extending from corner of the mouth to lower border of mandible in front of angle of mandible. Superiorly it extended from 2cm below the zygomatic arch and inferiorly up to lower border of mandible. On extraoral palpation, Swelling was non- tender, non-fluctuant, non-compressible with no sign of extraoral bleeding or pus discharge.

The Intraoral examination of the patient revealed buccal vestibular obliteration in relation to carious primary right mandibular 1st molar and 2nd molar. Surrounding mucosa was normal in color. On palpation, it was hard in consistency, non-tender and non-fluctuant on palpation. Reddish- brown colored fluid was aspirated from lower right buccal vestibule. Bilateral buccal vestibular obliteration present in relation to right and left upper primary canine and 1st primary molar. On palpation, swelling was hard in consistency, non- tender, non-compressible and no pus discharge on right side of upper vestibule. On palpation, swelling was soft in consistency, compressible, eggshell crackling present on left side of upper vestibule. On aspiration, whitish cheesy creamy colored fluid was present on right side of the buccal vestibule and reddish-brown colored on left side of the buccal vestibule

We advised OPG and 3D reconstructed CT-Face. It showed multiple cystic lesion, a well-defined unilocular radiolucency extending from apex of the 42 to mesial root of 46. Root resorption was seen in relation to right and left primary 1st and 2nd molar and erupting canine, 1st and 2nd premolar was embedded in unilocular lesion. It was also revealed that bilateral upper erupting canine and bilateral radiolucency in relation to upper primary canine and 1st molar. Then, we also advised patient to done P-A skull, P-A cervical and P-A chest x-ray to rule out syndromic condition associated multiple OKC but we did not find any abnormalities in the x-rays.

With above clinical finding, provisional diagnosis was radicular cyst and dentigerous cyst in relation to primary mandibular 1st molar and primary 2nd molar based on aspiration and radiographic investigation respectively. In maxilla, provisional diagnosis was odontogenic keratocyst and dentigerous cyst in relation to right upper primary canine and primary 1st molar and radicular and dentigerous cyst in relation to left upper primary canine and primary 1st molar based on aspiration and radiographic investigation respectively.

CASE NO. 6

60 year old female patient came to dept. with chief complain of pain in lower right back teeth region since last 1.5 year. Pain was intermittent in nature and had swelling at right side of the face.

On extraoral inspection, swelling was present 2cm below the ala-tragus line and extended up to lower border of mandible and 3cm posterior to right side of corner of the mouth and extended up to angle of mandible. On intraoral inspection, labial and buccal vestibular obliteration were seen in lower right side of the mandible with normal overlying mucosa. On intraoral palpation, Swelling was soft, tender, and compressible on palpation.

The OPG and CT-Scan revealed that lytic mildly expansile lesion was involving the body of mandible on right side. Two other lytic lesions were also involving the symphysis menti and body of mandible on left side of total segment of mandibular is approx. 6.5×1.6 cm.

Differential diagnosis was ameloblastoma, odontogenic keratocyst, odontogenic myxoma based on CT-Scan and OPG.

CASE NO. 7

18 year old male patient came with swelling which was extending from 26 to 28 tooth region with obliterated buccal vestibule on intraoral examination. On palpation, it was firm, non-tender, non- reducible, non-compressible, non- fluctuant swelling on left upper labial and buccal vestibule with normal overlying skin.

CT scan showed well defined hypodense expansile cystic lesion involving left maxillary alveolar arch. Lesion bulged into left maxillary sinus and adjacent to left nasal cavity. Superiorly, lesion extended up to inferior wall of left orbit and showed marked thinning of antero-lateral and medial left maxillary sinus with deviated nasal septum toward right side.

III. MATERIALS AND METHODS

Routine blood and other pre-operative investigation were done for all patients. Medical and anesthetist fitness were taken for all patients to operate under general anesthesia.

In operating room, pre-anesthetic medication were given to patients and they were intubated with RAE tube through left or right nostril. Extraoral and intraoral painting (5% betadine and 70% alcohol) and draping was done after achieving the general anesthesia. Then, 5ml 2% lignocaine with adrenaline (1:80,000) was infiltered intraoral to achieved hemostasis at operated site.

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The Full thickness mucoperiostel flap were taken for removal of cystic lesion in maxilla as well as in mandible. The extent of flap was depending up on size and site of involvement of lesion. After reflecting the flaps, we were gently removed the bone at the site of the involvement with help of the round bur and separated the cystic lining from the inner bony wall of the cystic cavity to removed whole cyst in single piece. (Fig.5) Curettage was also done with using curette after cystic enucleation and irrigation was done with normal saline.

At last, carnoy's solution (60% ethanol, 10% glacial acetic acid and 1g ferric chloride) was applied in cystic cavity for 3 minute to eliminate the remaining lining of cyst in all cases except case no. 3 and 6 because the lesion was nearer to the inferior alveolar nerve so there is chances of axonal damage after direct application of carnoy's solution. The removed lesion was immersed in 10% formalin and sent to oral pathology department in Ahmedabad Dental College and Hospital, Gandhinagar for confirmation of final diagnosis.

IV. RESULTS

The Final diagnosis of all cases was confirmed by the excisional biopsy followed by cystic enucleation. OKC was confirmed as final diagnosis for all 7 cases by their histopathological feature included keratin flecks, Para-keratinized/ orthokeratinized thick epithelial layer, palisaded basal cell layer and inflammatory cell infiltration. (Fig.11)

Clinical and imaging follow ups at 1month, 3month, and 5month showed good bone trabecution in all cases (Fig. 6, 7). The 7 OKC included 1 recurrences of a lesion after 1.5 year (Case No. 3) and 1 de novo lesion after 3 year (ameloblastoma) (Case No. 6).

Fig. 1 OPG

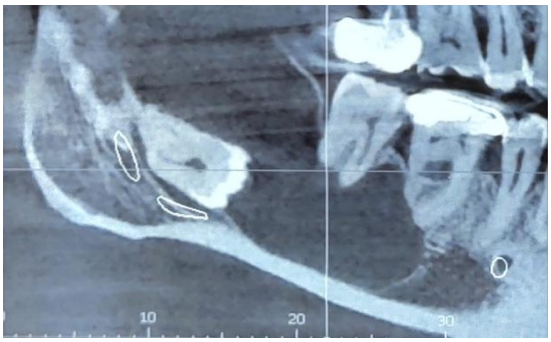

Fig. 2 Sagittal view of CBCT

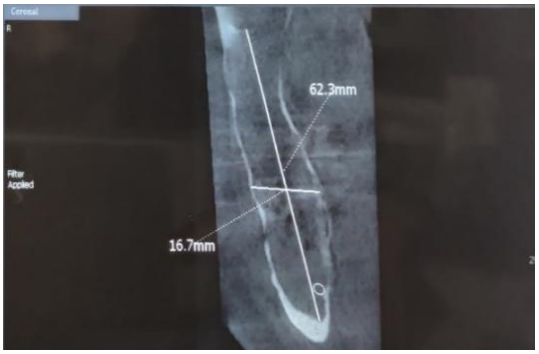

Fig. 3 Coronal view of CBCT

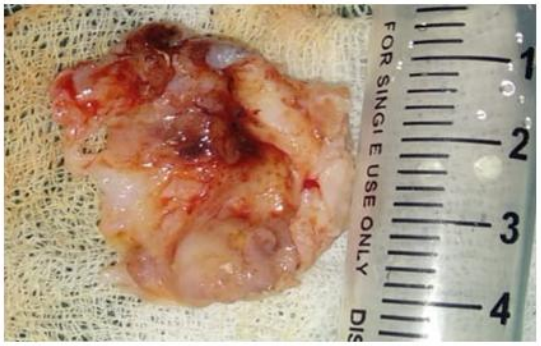

Fig. 4 aspiration biopsy

Fig.5 Cystic lesion

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Fig. 6 Follow up of 3 month

Fig. 7 Follow up of 5 month

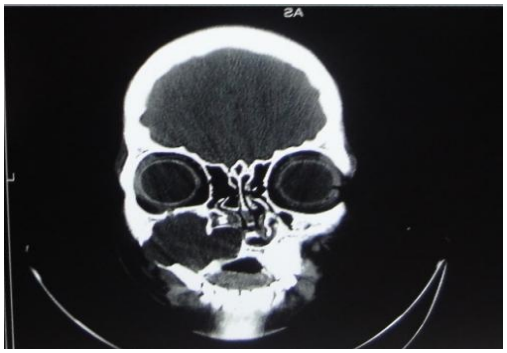

Fig. 8 OPG

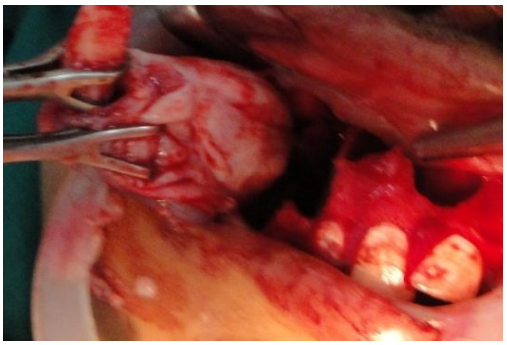

Fig. 9 CT face

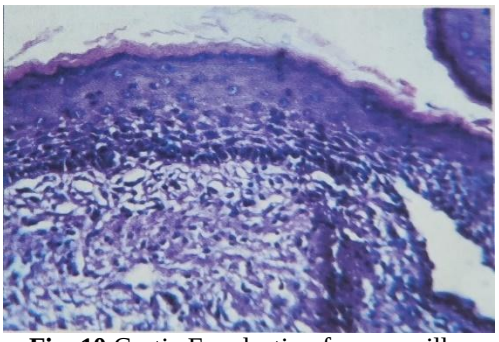

Fig. 10 Cystic Enucleation from maxilla

Fig.11 Photomicrograph showing Palisaded

Layer of low columnar basal cell with few cells Showing hyperchromatic nuclei (H&E, original Magnification 40x)

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SR. NO	AGE	SEX	PAIN	ASSOCIATED TEETH	SITE	BIOPSY	TRETMENT	FOLLOW UP	RE
1	69	MALE	NO	44, 45 and extending up to molar region	Right side of mandible	YES	Enucleation and curettage following chemical cauterization	5 month	NO
2	45	MALE	NO	46, 47, impacted 48 extended up to sigmoid notch on	Right side of mandible	YES	Enucleation and curettage following chemical cauterization	5 month	NO
3	44	FEMALE	NO	46, 47, impacted 48	Right side of mandible	YES	Enucleation and curettage	5 month	YE
4	15	MALE	NO	11, 12, right primary C, impacted 13, 14, 15, 16	Right side of maxilla	YES	Enucleation and curettage following chemical cauterization	5 month	NO
5	11	FEMALE	NO	12, right primary C, impacted 13, right primary D, right primary E, 14, 15 22, left primary C 43, left primary D, left primary E 44, 45	Bilateral maxilla and right side of mandible	YES	Enucleation and curettage following chemical cauterization	5 month	NO
6	60	FEMALE	YES	31, 32, 33, 34, 35, 36, 45, 46	Right, left and symphysis menti of mandible	YES	Enucleation and curettage	5 month	YE
7	18	MALE	NO	26, 27, 28	Left side of mandible	YES	Enucleation and curettage following chemical cauterization	5 month	NO

V. DISCUSSION

In most cases (78.6%) the lesion was a predominance in males representing 57.1% with age group of adults being the highest (mean of 28, 1 ± 18, 3)[7, 14, 15]. The literature review showed that the mandible was the most affected bone covering about 71.4% of cases [16, 17, 18] . The ramus and angle was the most affected site and the most frequent the radiological aspect was unilocular, which was present in 71.4% of reviewed cases [18, 19, 20].

One of the characteristic features of the growth of this pathology is the tendency to grow along the cancellous channels with very little cortical expansion. Various theories of expansion of KCOT have been proposed to explain this. These include intraluminal hyperosmolality, active epithelial proliferation, collagenolytic activity of the cyst wall and synthesis of interleukin 1 and 6 by keratinocytes. High proliferation rate, over expression of anti-apoptotic proteins (bcl-2) and expression of matrix metalloproteinase (MMPs 2 and 9) also favor growth and expansion of OKCs. Mutation in PTCH 1 ("patched") gene has also been considered as responsible for the pathogenesis of this cyst [21]. PTCH (Patched) is a tumor suppressor gene involved in both nevoid basal cell carcinoma syndrome and odontogenic keratocyst; mutations occur on chromosome, 9q22.3–q31[22]. Usually PTCH forms a receptor complex with the oncogene SMO for the SHH (Sonic hedgehog) ligand. SHH binding to PTCH releases the inhibition of growth signal transduction seen in PTCH binding to SMO. Thus the proliferating–stimulating effects of SMO are then predominant as seen in these conditions. The neoplastic capability and high recurrence have been attributed to a higher frequency of occurrence of proliferating nuclear antigen Ki67, p53 and bcl-2 positivity [23]. The odontogenic keratocyst can occur anywhere within the jaws.

Treatment of OKC is very challenging because of its high recurrence rate, these include curettage, marsupialization, enucleation alone, enucleation with Carnoy's solution before enucleation or to the bony cavity after enucleation, enucleation with cryotherapy, enucleation with peripheral ostectomy, and resection[9].

Our chosen treatment option was enucleation followed by a secondary procedure involving chemical cauterization using carnoy's solution (60% ethanol, 10% glacial acetic acid and 1g ferric chloride). This is a common and acknowledged procedure that carries low morbidity. Carnoy's solution acts by penetrating superficial cancellous spaces in the defect and thus devitalizes and fixes the remaining tumor cells. According to Stoelinga (2005), a mildly penetrating agent such as this should suffice in eliminating possible vital cells left behind in the defect and therefore reducing recurrence. Thus, we applied carnoy's solution after encleation in 5 cases out of 7 cases and other 2 cases were treated with only encleation and curettage because the lesion was nearer to the inferior alveolar nerve so to prevent axonal damage after direct application of carnoy's solution.

Recurrence rates with this technique are variable in the literature. In the systematic review by Kaczmarzyk et al (2012), enucleation with Carnoy's application resulted in a 50% recurrence rate. However, this outcome is questionable as it is based on just 2 patients with a mean follow-up of 5.25 years, one of whom developed a recurrence. Stoelinga (2001) reported a recurrence rate of 7.8% in 80 patients and Zhao et al. (2002) reported 6.7% recurrence in 29 patients. Follow-up periods of these 2 studies range from 1 to 29 years.

The effect of carnoy's solution on the inferior alveloer nerve were first reported by Frerich et al. (1994). The authors did not observe axonal damage during the first three minutes of direct application. In contrast, another important study, Wolgen et al. (1999), noted that the alteration in neural conductivity developed after 2 min of direct application. We did not find permanent functional damage of nerve followed by application of cornoy's solution in any cases out of 7 cases.

VI. CONCLUSION

In conclusion, any cystic lesion should be evaluated and treated cautiously. Odontogenic keratocysts may occur in any part of the upper and lower jaw with the majority occurring in the mandible, most commonly in the angle of the mandible and ramus. The maxillary sinus is a frequent site for pathologies of odontogenic origin due to its close anatomical relationship with teeth and periodontal tissues. We found that recurrence occurred in 2 patients out of 7 cases in which, we did not applied carnoy's solution after cystic enucleation and curettage. We believed that okc recurs from remaining cystic lining or epithelial remnants that should be removed by chemical cauterization after enucleation and curettage.

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