Treatment of Keratocystic Odontogenic Tumours: A Prospective Study of 30 Cases

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Abstract

Aim This prospective study aimed at presenting different treatment modalities and its association with the recurrence rate of KCOT.

Material and Method The study was conducted on 30 patients diagnosed with KCOT between March 2009 and 2012. The patients were followed up for a period of at least 1 year. The clinical, radiographic and demographic data were recorded and four different treatment modalities were followed to assess the recurrence of the tumour.

Results In the study, KCOT showed male predominance with a male: female ratio of 23:7. Of the total cases, 26 (86.67 %) patients had parakeratinised KCOT and the rest 4 (13.3 %) patients had orthokeratinised KCOT. Nine (30 %) patients were reported with recurrence of the tumour within 1–2 years of surgery—all these patients had parakeratinised cyst. Recurrence was observed in four (50 %) out of eight cases of marsupialisation and four (44.44 %) out of nine cases of treatment using the enucleation process. No recurrence was seen in patients treated with resection; however only one out of three patients treated with enucleation, followed by fixation with Carnoy's solution showed signs of

recurrence. The histopathological examination determined the aggressive nature of KCOT and its association with the recurrence rate as well. The findings of our study indicate that more aggressive treatment can aid in reducing the chances of recurrence.

Keywords KCOT · Treatment modalities · Recurrence · Orthokeratinized · Parakeratinized

Introduction

Odontogenic keratocyst (OKC), developmental epithelial cyst of jaw [1], was first described by Philipsen in 1956 [2]. Later, WHO reclassified OKC as keratocystic odontogenic tumour (KCOT) and defined it as “a benign uni or multicystic, intrasosseoustumour of odontogenic origin, with a characteristic lining of parakeratinised stratified squamous epithelium with a potential for aggressive, infiltrative behavior” [3]. Therefore, the term KCOT reflects the neoplastic nature of the keratocyst. Due to its reclassification, it is important to examine the salient features of this commonly occurring odontogenic lesion and its association with treatment modalities. Since the 1960's, the nature and possible histological types of keratocysts have been under discussion for finding the most appropriate treatment plan and clinical management of KCOT.

Many treatment modalities, ranging from the use of simple surgical techniques such as enucleation to advanced techniques such as cryotherapy, have been recommended for the treatment of KCOT, but its recurrence rates have always been the point of interest. Although, many studies are available on KCOT, only a few amongst them can be considered reliable. This is because the past studies were based on the written notes of the clinicians and lacked details on the actual surgical procedure carried during the

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retrospective analysis. This prospective study aimed at presenting a clinical experience of 30 cases of KCOT based on different treatment modalities and its association with the recurrence rate of KCOT.

Materials and Methods

Thirty patients diagnosed with KCOT were presented to the outpatient clinic of Oral and Maxillofacial Surgery Department of Sudha Rustagi College of Dental Sciences and Research, Faridabad, Haryana, India, between March 2009 and 2012. The diagnosis of KCOT was based on the clinical and histopathological examinations of the patients. The study was approved by the Research and Ethical Committee of the institution.

Patients suffering from nevoid basal cell carcinoma syndrome (NBCCS), i.e. having multiple KCOTs, were excluded from the study. Demographic details including age and sex of the patients and the site of occurrence of KCOT were recorded for all patients. Written informed consent of the patients was taken before starting the surgery. The patients were followed up for a minimum period of 1 year post surgery to assess the recurrence rate of the keratocyst. The histopathological diagnosis was based on the histochemical and histological features of lining and the type of keratin produced by the keratocyst [4], that were accordingly classified as parakeratinised or orthokeratinised variants.

Orthopantomogram and CT scans were performed to assess and correlate the findings with the histopathological examination for narrowing the differential diagnosis.

Radiographic presentation was categorized into four types [5]:

1. Unilateral KCOT surrounded by thin smooth or scalloped radiopaque border.
2. Multilocular KCOT showing at least two round or ovoid lesions that may be uniform or different in size and overlap each other. Interior may be divided by two kinds of septa – bony or fibrous.
3. Multiple KCOT's (excluding NBCCS): Separate cystic images distributed in the jaws.
4. NBCCS or Gorlin–Goltz Syndrome: Images showing five main components—multiple nevoid basal cell carcinomas, jaw cysts, congenital skeletal anomalies, ectopic calcifications, and palmar and plantar pits.

The KCOT's were further classified according to the type of cysts by correlating the radiographic and clinical findings [6], which are as follows:

1. No relation with a tooth existed.
2. KCOT appeared as a true dentigerous cyst.
3. KCOT was partially attached to the follicle of the tooth and sometimes to the periodontium as well.

4. KCOT appeared as a lateral periodontal cyst attached to the periodontium but not apically located.

The prior lab diagnostic measure was performed to examine the cystic fluid by aspiration using an 18-G needle under local anaesthesia. Aspiration biopsy represented yellow fluid aspirate revealing the keratin flakes.

The treatment rendered to the patients and the incidences of recurrence in the follow-up period were also noted. The patient's age, size of the lesion, previous recurrence history, soft tissue involvement, and histological variants were the criteria followed before proceeding with the choice of treatment. The treatment modalities availed in our institution for the 30 KCOT cases include enucleation, marsupialisation or decompression (Figs. 1, 2), excision of the overlying mucosa in conjunction with enucleation of cyst, followed by fixation with Carnoy's solution, and resection (Figs. 3, 4, 5). Lesions in young patients and involving the vital structures nearby underwent marsupialization. Well defined lesions were treated using enucleation and in recent cases to avoid recurrence even the Carnoy's solution was also used followed by enucleation. Aggressive lesions in adults were treated using resection. The data obtained were analysed to assess the efficacy of different treatment modalities. The patients were then followed up every 6 months and were asked to undergo clinical and radiographic examination for the assessment of recurrence.

Results

The review of the 30 cases (Table 1) showed that KCOT occurred in patients belonging to the age group of 8–47 years, with a mean age of 29 years. The number of KCOT occurrences was observed to be more in males than in females with a male to female ratio of 23:7. Of the total cases, 22 cases presented with cyst in the mandible region and the rest 8 cases presented with cyst in the maxillary posterior region.

Fig. 1 Case 1-Treatment with marsupialization. Preoperative OPG

Fig. 2 Case 1-Treatment with marsupialization. 5 years follow up

Fig. 3 Case 2-Subtotal mandibulectomy with graft replacement. Resected mandible

Fig. 4 Case 2-Subtotal mandibulectomy with graft replacement. Postoperative OPG

After the histopathological examination, KCOT's were classified as parakeratotic and orthokeratotic. Four (13.3 %) patients were found to have orthokeratinised KCOTs whereas the remaining 26 (86.67 %) patients had parakeratinised KCOT. Out of 30 patients, nine patients presented with recurrence of the cyst: all these patients had parakeratinised KCOT. None of the patients with the orthokeratinised variant showed recurrence of KCOT within 1 year. One patient with orthokeratinised variant did

not respond to the follow-ups. One out of nine patients showed recurrence in an area other than the operated site (previously the lesion was in angle region but the recurrence occurred in body region of mandible adjacent to the previously operated site). Recurrence was seen in four out of eight (50 %) patients treated with marsupialisation and four out of nine (44.44 %) patients treated with enucleation. Among the ten patients treated with resection one underwent reconstruction with bone implants (Figs. 6, 7); however, none of them reported with recurrence. Three patients were treated with enucleation followed by fixation with Carnoy's solution; one of these three patients showed recurrence of KCOT. One patient who underwent marsupialisation did not respond for the follow-up.

Discussion

The results of our study indicate that KCOT occurred in patients belonging to the age group of 8–47 years, with a mean age of 29 years and a male predominance ratio of 23:7. This is similar to Woolgar et al.'s [7] study in which they compared the ages of patients with sporadic KCOTs with those occurring in the NBCCS. They observed a single peak at 10–30 years of age with a mean age of 26.2 years in syndromic cases. In sporadic cases, they observed the first peak at 15–45 years and the second smaller peak at 55–65 years of age.

Generally, the most common features associated with KCOT include pain, soft tissue swelling, expansion of bones, and paraesthesia of the lip or teeth. Pathological fractures are seen when the KCOT extends into the medullary cavity and expands at a later period. Voorsmit [8] and Lund [9] described the occurrence of large KCOTs involving the maxillary sinus that led to the displacement and destruction of the floor of orbit and proptosis of the eyeballs. Vencio et al. [10] also reported a case that showed extension of KCOT into the maxillary sinus, destroying the floor. Eight of our cases were presented with occurrence of KCOT in the maxillary posterior region; however, none encroached into the sinus.

Stoelinga et al. [6] have also demonstrated the accumulations of epithelial islands in the mucosa superficial to the excised keratocyst, especially in the ascending ramus (dropping off phenomenon). The clinical implication of this phenomenon might be the removal of KCOT, due to which some of the epithelial residues left behind may later cause recurrence of the cyst. Many evidences show that a majority of the epithelial islands, as found in the wall of KCOTs, are attached to the mucosa that covers the pathological tissue. Thus, the offshoots of basal layer of epithelium might be involved in the aetiology of KCOTs [11]. In the study, all 30 patients had a common complaint

Fig. 5 Case 2-Subtotal mandibulectomy with graft replacement. Graft placement

of swelling. The cyst classically grew within the medullary spaces of the bone in an anteroposterior direction, causing expansion that was minimal at first. Buccal expansion was noted in approximately 30 % of maxillary and 50 % of mandibular lesions [12]. Donof et al. [13] demonstrated that the collagenase activity in the cyst's epithelium with its resorptive properties was responsible for the expansive growth of lesion in the bone. In a study of mathematical model analysis on the dynamics of odontogenic keratocystic growth, Landini [14] explained the degradation of central cells in the cyst that resulted in an increased osmotic pressure in the surrounding stroma, and the created gradient retracting water into the cavity.

Thus, the KCOT fibroblasts are expected to be involved in the bone resorption process via interaction with the precursor cells of osteoclasts leading to enhanced osteoclastogenesis [15].

For the diagnosis of KCOT, imaging and histopathological examination along with aspiration biopsy was performed. It was also found in a study that the proliferating cell nuclear antigen was responsible for the aggressive behaviour of KCOTs and thus, monoclonal antibody PC10 like tests were used for detection of the higher rate of epithelial proliferation. IL-1 α levels in intracystic fluid and cytokine concentration was significantly higher in KCOTs [16]. Presence of lactoferrin concentrates in keratocystic fluid might be a useful preoperative diagnostic marker for KCOTs [17]. Immunohistochemical analysis and blood antigens (tumorigenesis in KCOT) may also serve as one of the diagnostic criteria in future.

Parakeratotic variants accounted for 83–97 % of KCOTs and had greater potential for localised destruction, extension into the adjoining tissues, rapid growth, recurrence, and multiplicity. The orthokeratinised odontogenic cyst was found to be a less aggressive variant that had low recurrence rate ranging from 3.3 to 12.2 % [18]. In our study, 86.67 % patients presented with parakeratinised variant whereas 13.3 % patients had orthokeratinised variants. Haring and

Van Dis [19] reported epithelial separation in 98 % of the cases they reviewed and also observed satellite cyst in 33.3 % of KCOTs cases.

In our study, 25 % of the patients showed satellite cysts. All the clinical features along with radiographic features, and histopathological and demographic details, were taken into consideration before proceeding with the choice of treatment. Four different treatment modalities were used for the 30 cases. Resection can be further categorised into marginal or segmental type [20]. Bataineh and Al Qudah [21] reported the treatment of OKCs by marginal resection, with a 1 cm margin of the surrounding bone and a 0 % recurrence rate for that period. The only major complication from the resections was mild transient inferior alveolar nerve paresthesia. In our study, none of the patients who underwent resection reported recurrence of the cyst. Schmidt and Pogrel [22] found that 85.5 % of the patients showed no evidence of the clinical or radiographic recurrence after they were treated with enucleation and cryosurgery. In our study, four out of nine cases of treatment using the enucleation process showed recurrence and only one out of three patients treated with enucleation followed by fixation with Carnoy's solution showed signs of recurrence. The rationale behind the use of Carnoy's solution was similar to that of cryosurgery. It killed the epithelial remnants and dental lamina within the osseous margin. Voorsmit et al. [8] found that the recurrence rate of OKCs was 2.5 % when the overlying mucosa was excised, and the cyst cavity was treated with Carnoy's solution. Despite the aggressive and the recurrent nature as well as the immunohistochemical studies of OKC, it was noted in 1970s that OKCs responded to marsupialisation. However, the recommended treatment was unpredictable, as the pathological tissue could be left in situ. Decompression was reported to be performed for treatment of the cysts and enucleation was performed later with a lesser risk to the adjacent structures [23]. As the recurrence is seen higher in patients treated with enucleation, peripheral ostectomy has

Table 1 Details of 30 patients with the site of operation and follow up findings

S. no	Age/sex	Region	Histopathology	Treatment	Follow-up	Result
1	8 years/M	Right mandibular molar region	Orthokeratinized	Marsupialization	5 years	No recurrence
2	37 years/M	Lower anterior region	Parakeratinized	Enucleation	3 years	No recurrence
3	30 years/M	Left mandibular posterior region	Parakeratinized	Enucleation	3 years	Recurrence in some other area (adjacent area)
4	12 years/F	Right mandibular body region	Parakeratinized	Enucleation	2 years	No recurrence
5	28 years/M	Left mandibular posterior region	Parakeratinized	Resection	2 years	No recurrence
6	13 years/F	Right maxillary molar region	Parakeratinized	Enucleation	2 years	No recurrence
7	47 years/M	Left Mandibular body region	Parakeratinized	Resection	1–1.5 years	No recurrence
8	12 years/M	Left mandibular premolar region	Orthokeratinized	Marsupialization	1 year	No recurrence
9	34 years/M	Right maxillary posterior region	Parakeratinized	Enucleation	1 year	Recurrence after 1 year
10	28 years/M	Mandibular from left angle to right angle region	Parakeratinized	Resection	1.5 years	No recurrence
11	23 years/F	Left maxillary posterior region	Parakeratinized	Marsupialization	2 years	Recurrence in 2 years
12	18 years/M	Left mandibular premolar region	Parakeratinized	Marsupialization	1 year	No recurrence
13	30 years/M	Left Maxillary posterior region	Parakeratinized	Enucleation	1 year	Recurrence after 1 year
14	28 years/M	Mandibular from left angle to right angle region	Parakeratinized	Resection	1 year	No recurrence
15	40 years/F	Left mandibular posterior region	Parakeratinized	Marsupialization	1.5 years	Recurrence
16	45 years/F	Left mandibular premolar region	Parakeratinized	Resection and bone grafting with implants	1 year	No recurrence
17	30 years/F	Right maxillary posterior region	Parakeratinized	Enucleation	1 year	Recurrence after 1 year
18	25 years/M	Mandibular posterior region	Parakeratinized	Resection	1 year	No recurrence
19	27 years/F	Right maxillary posterior region	Orthokeratinized	Marsupialization	6 months	Not responded
20	45 years/M	Right mandibular posterior region	Orthokeratinized	Enucleation	1 year	No recurrence
21	27 years/M	Right mandibular premolar region	Parakeratinized	Resection	1.5 years	No recurrence
22	38 years/M	Right mandibular anterior region	Parakeratinized	Resection	2 years	No recurrence
23	47 years/M	Right maxillary posterior region	Parakeratinized	Marsupialization	1.5 years	Recurrence after 1.5 years
24	33 years/M	Right mandibular premolar region	Parakeratinized	Enucleation followed by Carnoy's solution	1.5 years	No recurrence
25	30 years/M	Right mandibular body region	Parakeratinized	Enucleation	1 year	Recurrence after 1 year
26	25 years/M	Left mandibular posterior region	Parakeratinized	Resection	1 year	No recurrence
27	29 years/M	Right mandibular premolar region	Parakeratinized	Enucleation followed by Carnoy's solution	1 year	No recurrence
28	15 years/M	Left maxillary posterior region	Parakeratinized	Marsupialization	1 year	Recurrence after 1 year

Table 1 continued

S. no	Age/sex	Region	Histopathology	Treatment	Follow-up	Result
29	43 years/M	Mandibular anterior region	Parakeratinized	Enucleation followed by Carnoy's solution	1 year	Recurrence after 1 year
30	28 years/M	Right mandibular posterior region	Parakeratinized	Resection	1 year	No recurrence

Fig. 6 Case 3-Resection and reconstruction with bone grafts and implants. Preoperative OPG **Fig. 7** Case 3-Resection and reconstruction with bone grafts and implants. Graft

been seen as an emerging trend these days in which after enucleation, 1–2 mm of bone is removed beyond visible margin, which is expected to improve the cure rate. In addition, vital staining using methylene blue is needed and around 2 mm of bone from marrow and 1 mm from cortical bone is removed. However, this practice requires high precision. Therefore, in our study wherever aggressive form of treatment was needed, we followed resection for such patients to avoid any chance of recurrence.

Madras et al. [24] suggested that the recurrence rate was relatively slow with aggressive treatment whereas more conservative methods tend to result in more recurrences. Recurrence rate ranged from 0 to 62 % [21]. Woolgar et al. [7] described three different theories for the recurrence.

First theory stated that the incomplete removal of cystic lining could be a cause for recurrence. The second theory described the small satellite cysts or odontogenic epithelial rests left behind after the surgical treatment. The third theory involved the development of an unrelated KCOT in an adjacent region of the jaws that was considered to be recurrent. Our findings could be correlated to a study by Morgan et al. [25], in which incidence of recurrence with enucleation was found to be 54.5 %, and patients treated with resection did not show any recurrence at all.

Our results suggested that more aggressive treatment could aid in reducing the chances of recurrence postoperatively, and also the variant type may determine the aggressive nature of KCOTs along with the recurrence incidence.

Compliance with Ethical Standards

This study is in compliance with the World Medical Association Declaration of Helsinki on medical research protocols and ethics.

Conflict of interest None.

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