Original Article

A Rare Entity of Multiple Odontogenic Keratocysts in Non-syndromic Patient: A Case Report

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Abstract

Odontogenic keratocyst (OKC) is a common developmental non-inflammatory odontogenic cyst affecting the maxillofacial region that arises from the dental lamina. It can occur anywhere in the jaws but are most commonly seen in the posterior part of the mandible. OKCs may occur in two different forms, either as solitary (non-syndromic OKCs) or as multiple OKCs (syndromic OKCs). The OKC is distinctive among jaw cysts and has a tendency toward recurrence along with aggressive clinical behavior. The recurrent rate of OKC is 25–30%. Multiple OKCs are usually seen in association with Gorlin-Goltz syndrome or Nevoid basal cell carcinoma syndrome, but approximately 5% of patients with OKC have multiple cysts without concomitant syndromic presentation. The following is an article on a case report of a 23-year-old male who presented with multiple cysts. The cysts were initially diagnosed as multiple dentigerous cysts based on the clinical and radiographic features. Later, it was confirmed as multiple OKCs with no clinical signs of the syndrome based on a histopathological examination of the excised specimen.

Keywords: Carnoy's solution, Multiple odontogenic keratocyst, Recurrence OKC, Topical 5-fluorouracil.

Introduction

Odontogenic keratocyst (OKC) was first explained by Phillipsen in 1956,[1] while Pindborg and Hansen, in 1963, described the essential features of this type of cyst.[2,3] It is the cyst arising from the cell rests of the dental lamina, very aggressive due to its high recurrence rate, and tendency to invade the surrounding structure.[4] The World Health Organization (WHO) reclassified this lesion in 2005 as a keratocystic odontogenic tumor (KCOT) and defined it as"a benign uni- or multicystic intraosseous tumor of odontogenic origin, with a characteristic lining of parakeratinized stratified squamous epithelium and potentially aggressive, infiltrative behavior".[5-8] In the new revision by the WHO in 2017, the name "OKC" was reinstituted.[9] OKCs appear most frequently in the third molar area of the mandible, in the 2–4th decade of life, with a slight predominance in males.[9-11] Typically, multiple KCOTs have been known to occur in association with Nevoid basal cell carcinoma syndrome (NBCCS), but rarely they may be seen without concomitant syndromic manifestations.[12] Studies reveal that 5.8% of multiple OKCs presented without any features of a syndrome, 8.1% were associated with NBCCS, and 7.6% of them had recurrences.[13] Various treatment modalities have been suggested in the literature for multiple OKCs. For small lesions, enucleation is preferred and marsupialization for larger lesions. The application of Carnoy's solution has been suggested after surgical enucleation to prevent recurrences. A periodic follow-up is recommended for these lesions due to their high recurrence rates.[14]

Case Report

A 23-year-old male patient reported to the department of oral medicine and radiology, with a complaint of pain and swelling in the 46 and 47 teeth region with intraoral and extraoral yellowish pus discharge since 3 months. His past dental history revealed that he underwent extraction of 46 teeth 1 month back. There was associated pus discharge during extraction and 1 week after extraction. Even after tooth extraction, pain persists and swelling was not reduced. Pain is intermittent, dull, with no diurnal variations, and aggravates on chewing food, which decreases on taking medication. Medical history was

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non-contributory. Right and left submandibular lymph nodes were palpable, and tender, each one in number, round in shape, and firm in consistency. Right level II A lymph nodes were palpable, non-tender, and soft to firm in consistency, three in number, measuring approximately 1.5 cm, 0.5 cm, and 1cm in their diameter, respectively.

Extraoral examination reveals that face is grossly asymmetrical due to swelling on the right side of face in the lower third measuring approximately 3 × 2 cm, extending anterioposteriorly 2 cm away from the corner of the mouth to 0.5 cm away from angle of the mandible on the right side; superioinferiorly, 2.5 cm below the ala-tragus line to 0.2 cm below the inferior border of mandible, oval in shape, and surface shows a sinus tract with evident pus discharge. On palpation swelling is tender & hard in consistency [Figure 1].

Intraoral examination revealed swelling from distal aspect of 45–47 tooth region, measuring approximately 2 cm × 1.5 cm in its size, extending anterioposteriorly, obliterating the buccal vestibule of root stump 46, and partially erupted 47 teeth and was tender and hard in consistency on palpation [Figure 2].

On the right upper back teeth region, swelling measuring approximately 3 cm × 1 cm in its size, extended buccopalatally was seen in relation to 15, 16, and 17 teeth region, oval in shape, and the crowns of 15 and 17 were submerged. No secondary changes were seen. Swelling was non-tender and hard in consistency on palpation [Figure 3].

FNAC procedure revealed straw-colored fluid with swelling right mandibular region [Figure 4].

All the required hematological and radiological investigations were performed. The hematological investigations were unremarkable. Radiographic investigations included intraoral periapical radiograph (IOPAR), orthopantomogram, and computed tomography (CT).

Intraoral periapical radiograph (IOPAR) in relation to 46 and 47 teeth region revealed partially seen cystic changes with well-corticated margin involving root stump 46 and horizontally impacted 47 [Figure 5a].

Intraoral periapical radiograph (IOPAR) in relation to 36, 37, and 38 teeth region revealed a well-defined radiolucency with a sclerotic margin, seen at the mesial aspect of 38 encapsulating its crown [Figure 5b].

Intraoral periapical radiograph (IOPAR) of relation to 14, 15, and 16 teeth region revealed a diffuse radiolucency with well-defined sclerotic margins extended from cementoenamel junction (CEJ) of 14 to apical aspect of 16 tooth region with impacted 15 [Figure 5c].

OPG [Figure 6] reveals a unilocular homogenous radiolucency with well-defined margins, corticated border, measuring approximately 5 × 3 cms in its size, is seen extending mediolaterally from apical third region at distal aspect of 46 root stump to apical aspect of mesial root of impacted 48, displacing the 47, and right mandibular canal but sparing the inferior border of mandible as intact without causing any roots resorption of involved teeth.

A unilocular homogenous radiolucency with well-defined margins and corticated border, measuring approximately 2

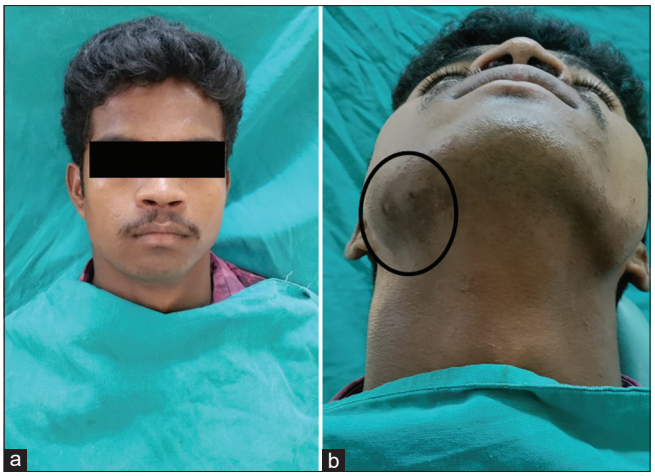

Figure 1: Extraoral view; (a) face is grossly asymmetrical due to presence of swelling on right lower third of face. (b) Snails view – sinus tract opening

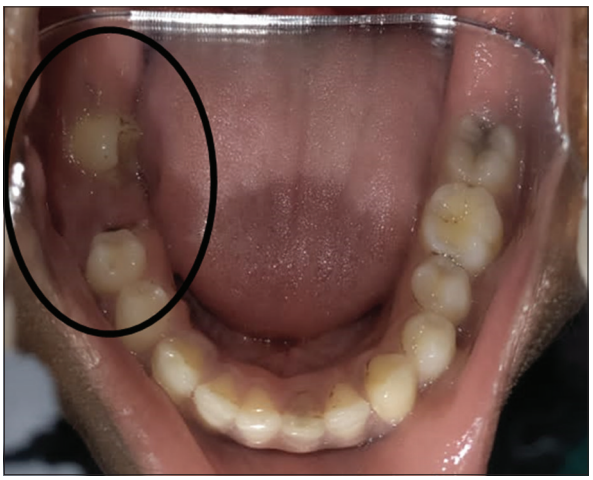

Figure 2: Presence of swelling on the right lower back tooth region

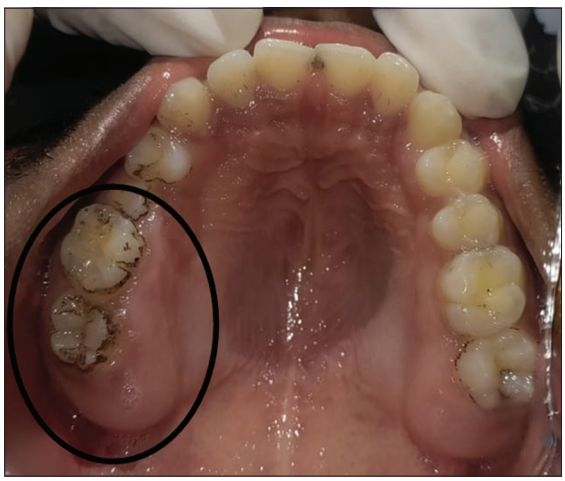

Figure 3: Presence of swelling on the right side upper back tooth region

× 1 cm in its size, seen extending from the cementoenamel junction (CEJ) at distal aspect of distal root to the distal aspect of impacted 38 encapsulating its crown.

A well-defined and unilocular homogenous radiolucency measuring 4 × 3 cm is seen extending from cementoenamel junction (CEJ) of 14 to apical third of 16 teeth region with impacted 15. Internal structure is radiolucent with a well-corticated border.

Computed tomography (CT scan) revealed multiple cystic lesions in maxillary and mandibular jaws with impacted teeth 15, 38, 47, and 48, respectively [Figure 7].

Radiologically diagnosed as multiple dentigerous cysts with differential diagnosis as Odontogenic keratocyst. Hematological investigations were within normal limits. Enucleation of the cystic lesions was planned and performed under general anesthesia. On histopathological examination of excised tissue, the multiple OKCs without syndromic features were diagnosed. The patient is under regular follow-up for any recurrence.

Discussion

Mickulizin, in 1826, first described OKC as a part of a familial condition affecting the jaws. It was referred to as "cholesteatoma" in 1926 which means cystic or "open" mass of keratin squamous with a living "matrix." Later in 1945, Robinson mentioned this cyst as a primordial cyst as they arise from remnants of the dental lamina or the enamel organs before enamel formation had taken place. However, it was not until 1956 that the cyst was named OKC by Phillipsen. TOLLER, in 1967, suggested that OKC is to be named as benign neoplasm. Shear used the term "keratocystoma" due to its aggressive nature and finally labeled it as a benign cystic neoplasm. OKC was reclassified and renamed as KCOT in the WHO classification of head and neck tumors in 2005.[10] In the new revision by the WHO in 2017, the name "OKC" was reinstituted.[9]

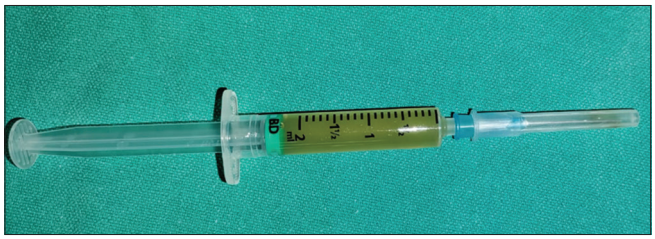

Figure 4: Straw-colored fluid on fine-needle aspiration

There are a few factors that led to the re-characterization of the keratocyst as KCOT.[5]

1. The KCOT exhibits locally destructive and highly recurrent behavior.
2. KCOTs are characterized by parakeratinized epithelium, in contrast to the orthokeratinized variant seen in orthokeratinized odontogenic cysts (OOC). KCOT reveals the budding of the basal layer into the connective tissue and is frequent mitotic.
3. KCOTs are associated with the inactivation of protein patched homolog (PTCH), the tumor suppressor gene.
4. Multiple KCOTs may present as one of the stigmata of the inherited NBCCS. It is also known as Gorlin syndrome.

KCOT arises from odontogenic epithelium. The available evidence points to two main sources of epithelium, the dental lamina, or the remnants and extensions of basal cells from the overlying oral epithelium. Recent studies have demonstrated the role of the PTCH gene in the etiology of KCOTs.[7]

The OKC is derived from the remnants of the dental lamina. It is noted to be third most common odontogenic cyst after radicular and dentigerous cysts. Most commonly occurs in third and fifth decades. Several authors have also noted a 2nd peak between the 5th and 8th decades. According to Chow et al, 32.1–37.8 years is the mean age for the occurrence of OKC at the time of his diagnosis.[6] In all series, there is a predilection for occurrence in males, ranging from 1.44:1 (Brannon), 1.46:1 (Browne), to 1.79:1 (Forssell).[2,4] KCOTs may occur in any part of the jaws, cysts of the jaws, with the majority occurring in the mandible, most commonly occurring at the angle of the mandible and ramus.[4,6] However, our patient had a relatively rare localization in the maxilla. This lesion can be associated, with an impacted tooth and is most frequently located within the jaws. However, some rare cases have been reported in the gingiva. This form has been chosen as peripheral OKC. Such lesions are often misdiagnosed as gingival cyst of the adult, lateral radicular cyst, or lateral periodontal cysts. Peripheral OKC is clinically aggressive and has likely to recur as the classical OKC.[6] OKC is mostly an intraosseous lesion, though peripheral counterparts also

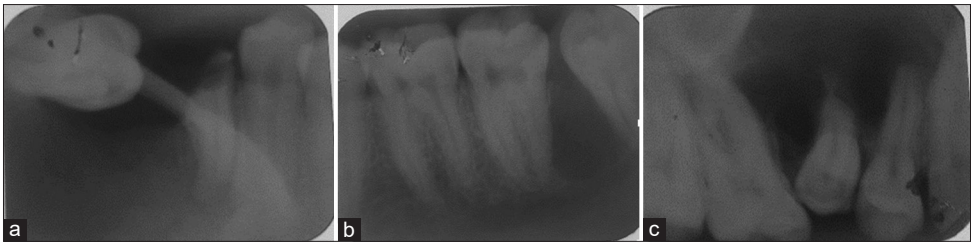

Figure 5: (a) Intraoral periapical radiograph of 46 and 47. (b) Intraoral periapical radiograph of 36, 37, and 38. (c) Intraoral periapical radiograph of 14, 15, and 16 teeth region

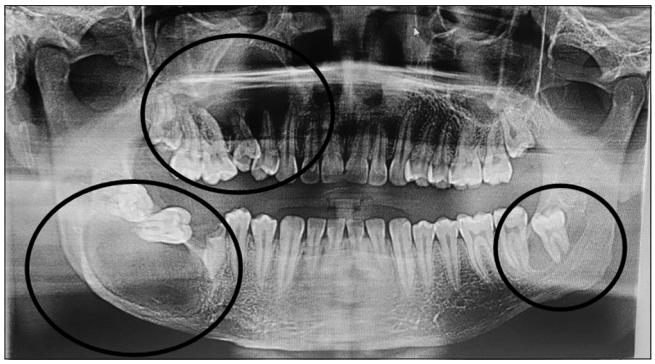

Figure 6: Orthopantamogram (OPG) showing multiple cystic lesions

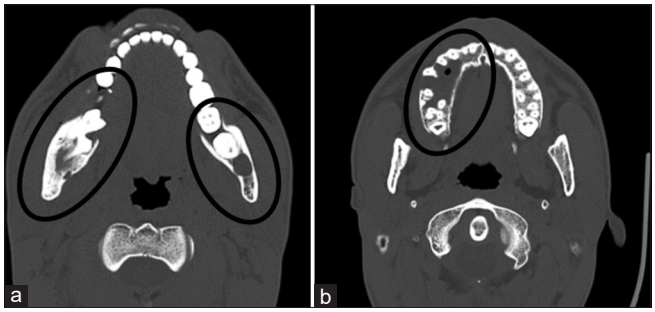

Figure 7: Computed tomography – axial sections of facial bones. (a) Well-defined unilocular homogenously hypodense lesions on the right and left sides body of the mandible with impacted 47, 48, and 38, respectively. (b) Unicystic appearance from the right maxillary posterior teeth region

have been reported in buccal gingival in the canine region of mandible. According to Chirapathomsakul *et al*., in 2006, peripheral OKCs have female predominance with a male: female ratio of 2.2:1.[3]

The aspiration from the lesion mostly contains cheesy material suggestive of keratin. The aspiration may also contain a straw-colored fluid.[2]

Radiographically, OKC presents as well-defined unilocular or multilocular (25–40%) radiolucent lesion with a smooth margin (corticated margin in secondarily infected cases), displacement of adjacent teeth without root resorption, a lesion may contain impacted tooth (25–40% cases), and expansion of cortical plates (buccal > lingual) with or without perforation. Cyst grows in medullary spaces of bone in an anteroposterior direction, so bony expansion is minimal in the initial stages (Chirapathomsakul *et al.*, 2006; Philipsen, 2005; and Sciubba *et al.*, 1999).[3]

Radiological types of Odontogenic keratocyst (main,1970) [Figures 8-11].[3,7]

Differential diagnosis includes dentigerous cyst (in OKC, the cyst is connected to the tooth at a point apical to cementoenamel junction), ameloblastoma (usually multilocular, no straw-colored fluid on aspiration), traumatic cyst (unilocular with scalloped margins, rarely show cortical expansion), giant cell granuloma (usually in anterior region of jaw), and odontogenic myxoma.[8]

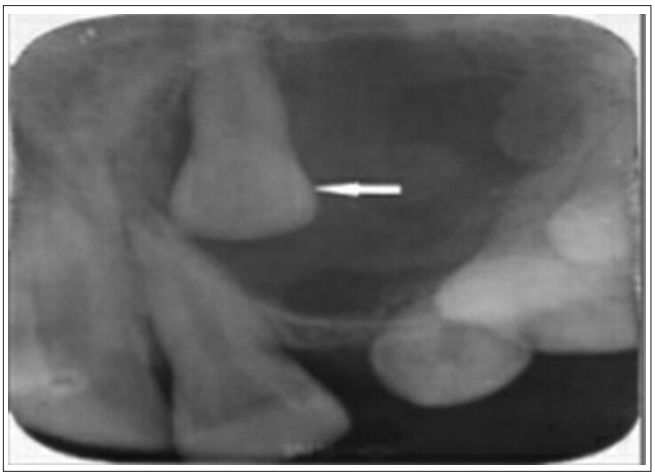

Figure 8: Replacement type: Cyst which forms in the place of normal teeth

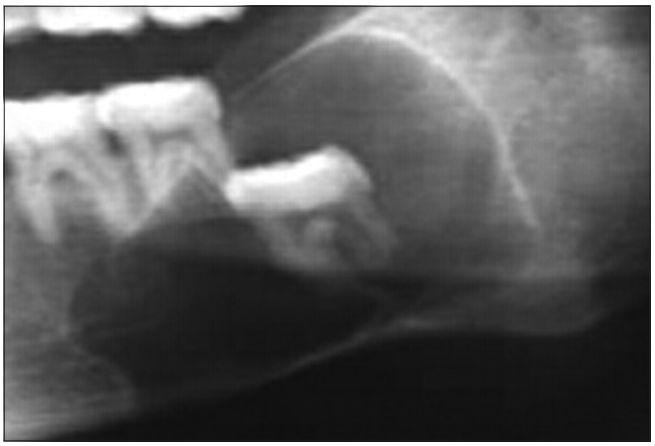

Figure 9: Envelop mental type: Cyst which embraces an adjacent unerupted tooth

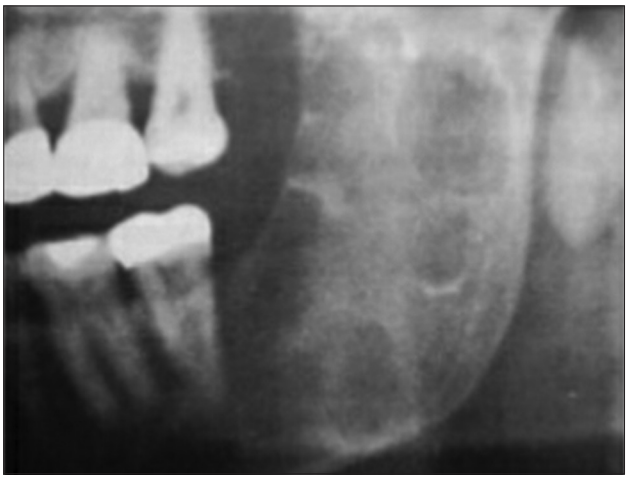

Figure 10: Extraneous type: Cyst which occurs in ascending ramus away from the teeth

On histopathology, the epithelium is distinctive with uniformity of thin epithelial lining of six to eight cell layers and does not demonstrate rete ridges. A prominent palisaded basal layer of hyperchromatic columnar to cuboidal cells is often described

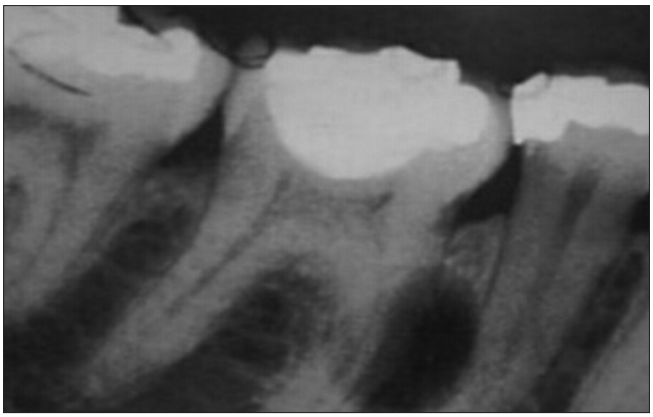

Figure 11: Collateral type: Cyst which occurs adjacent to the root of teeth which are indistinguishable radiologically from a lateral periodontal cyst

Table 1: Recurrence rates with different treatment modalities

Enucleation	30%
Enucleation + Carnoy's solution	9%
Enucleation + peripheral ostectomy	18%
Enucleation + Carnoy's solution + peripheral ostectomy	8%
Enucleation + cryotherapy	38%
Marsupialization	33%
Marsupialization + cystectomy	13%
Resection	0%

as having a "picket fence" or "tombstone" appearance. The superficial luminal surface of the epithelium demonstrates a parakeratinized surface; hence, the epithelium is usually described as corrugated, rippled, or wrinkled parakeratinized epithelium. Epithelial islands, daughter cysts or small satellite epithelial budding of the basal layer, and dystrophic calcification have been reported in OKC and KCOT. The lumen of the cyst may be filled with a thin straw-colored fluid. Cholesterol, as well as hyaline bodies at the site of inflammation, may also be present.[2,5]

According to Bakaeen *et al.*, 2004 and Gonzalez-Alva *et al.*, 2008, syndromes associated with multiple OKC are NBCCS, Gorlin-Goltz syndrome, Marfan's syndrome, Ehlers-Danlos syndrome, Noonan's syndrome, Orofacial digital syndrome, and Simpson-Golabi-Behmel syndrome.

However, except for the presence of KCOTs, our patient was healthy in clinical examinations, and suggestive features of these syndromes such as basal cell carcinoma, skeletal or orofacial defects, stunted growth, bleeding diathesis, hyper-extensible skin, and hypermobile joints, and other features were not present.[12] Auluck *et al.* discussed a 22-year-old patient with multiple recurrent KCOTs in all four quadrants with a complaint of pus drainage from the left maxillary posterior gums over the previous week without pain, facial swelling, or foul odor. The patient had no other features associated with NBCCS.[15] Parikh reported a 19-year-old case with two KCOTs in both jaws without any other concomitant syndromic features. The complaint was swelling in the lower left side of face since I year and pain for 3 months in the right upper anterior teeth. A panoramic radiograph revealed two radiolucencies with corticated borders.[16] Bartake *et al.* reported a 20-year-old case with multiple recurrent KCOTs without any other manifestation of the Gorlin syndrome. No recurrence occurred after 3- a year of follow-up.[17] Guruprasad *et al.* discussed a 16-year-old patient with multiple KCOTs without any other features of the syndrome. The patient complained of swelling on the left upper jaw for 2 months with slow progressing swelling. Orthopantomogram reveals multiple cysts with impacted teeth.[18]

The treatment options include enucleation, marsupialization, decompression, combined with adjuvant cryotherapy with Carnoy's solution, and marginal or radical resection.[1,4,10] The treatment modality depends on the size of the lesion, location, and proximity of lesion to vital structures such as inferior alveolar nerve, maxillary sinus, and nasal cavity.[19] According to Minami *et al.* (1996), smaller KCOT should be treated by curettage, enucleation, and peripheral osteotomy. Larger KCOT should be treated by marginal or segmental resection.[7,11] Blanchard introduced a new method using ultrasonic debridement of the cystic cavity in an attempt to remove any possible epithelial remnants. He monitored his cases for 5 years and reported no incidence of recurrence.[7] Balamurugan also reported 5-FU as a trendsetter treatment modality in OKC. 5-FU has been considered more useful in the treatment of OKC than Carnoy's solution due to its short operating time, availability, technical simplicity, reduced morbidity, and low cost, with low or no recurrence, thereby decreasing the need for a second surgery.[19]

Recurrence of OKC

It has a high recurrence rate ranging from 25 to 60%,[3] follow-up of any case of OKC with annual radiographs is essential for at least 5 years after the surgery.[1] Table showing Recurrence rates with different treatment modalities (Madras and Lapointe, 2008) [Table 1].

Conclusion

With the above discussion, we conclude that the present case of multiple odontogenic keratocytes (OKCs) in the non-syndromic patient. Odontogenic keratocytes (OKCs) is a unique entity among developmental non-inflammatory odontogenic cysts, due to varied, clinical, radiological, and histological features. In any patient with the presence of multiple OKCs, a careful histological examination should be done and should correlate with clinical and radiological features, which is paramount important to achieve a definitive diagnosis. Moreover, a long-term follow-up must be performed to detect any recurrence or any other defects with NBCCS.

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