EVALUATION OF THE EFFICACY OF CARNOY'S SOLUTION IN THE MANAGEMENT OF ODONTOGENIC KERATOCYST

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ABSTRACT

BACKGROUND

Odontogenic keratocyst is a locally aggressive cystic lesion of the jaw with high recurrence characteristics, frequently found to be associated with naevoid basal cell carcinoma syndrome (NBCCS).

METHODS

This retrospective study evaluates the effects of enucleation with chemical cauterisation (Carnoy's solution) in 10 patients (16 lesions) with odontogenic keratocyst associated with and without NBCCS in a follow up period of three years.

RESULTS

The recurrence rate was 6.25% with no statistically significant difference between syndromic and non-syndromic individuals. The incidence of postoperative paraesthesia and wound dehiscence were minimal.

CONCLUSION

Enucleation with chemical cauterisation is an effective method in the management of odontogenic keratocyst both in syndromic and non-syndromic cases. And hence, radical surgical treatments like resection should be reserved only for recurrent and large multilocular cystic lesions of the jaw.

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BACKGROUND

Odontogenic keratocyst is a developmental cyst of epithelial origin. It is a locally aggressive, cystic lesion of the jaw with a putative high-growth potential and propensity for recurrence. Hence, the world health organisation (WHO) has previously classified it under the head of odontogenic tumours and re-designated it as keratocystic odontogenic tumour. Odontogenic keratocyst (OKC) is a (KCOT). The cyst is found to be frequently associated with Nevoid Basal Cell Carcinoma syndrome (NBCCS) / Gorlin Goltz syndrome.

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NBCC syndrome is an autosomal dominant inherited disorder[1] characterized by the presence of multiple odontogenic keratocysts along with various cutaneous, dental, osseous, ophthalmic, neurological, and sex organ abnormalities.[2,3]

A wide range of treatment modalities have been tried over decades in the management of this cystic lesion including aggressive resection, simple enucleation, enucleation with peripheral ostectomy, chemical cauterisation (Carnoy's solution) and cryotherapy.

Carnoy's solution is a cauterizing agent with fixative properties. When applied over the surgical bed it produces superficial necrosis, thereby providing a safety margin in the treatment of invasive neoplasm. However, the possible complications associated with the use of Carnoy's solution includes infection, dehiscence, bone sequestrum formation and neuropathy.[4]

This study aims at the evaluation of the effects of Carnoy's solution in patients of south Indian origin with

odontogenic keratocyst associated with and without syndromic manifestations.

METHODS

This retrospective study included 10 patients (16 cystic lesions) treated at the Department of oral and maxillofacial surgery, Tamilnadu Government Dental college and Hospital between Jan 2014 to Mar 2016 with histopathological proven diagnosis of odontogenic keratocyst (Pindborg et al., 1962). The cases were divided in to two groups, Group I - Syndromic and Group II - Non-syndromic, based on the major and minor criteria given by Evans et al (discussed later). Group I consisted of 3 patients and Group II consisted of 7 patients.

Owing to the occurrence of multiple OKCs in patients with NBCCS (fig 1), a total of 16 cystic lesions were treated in the above mentioned 10 patients. Accordingly, Group I had 9 lesions and Group II had 7 lesions totally.

Figure 1. A Case of NBCCS in Group I

Huge cystic lesions with thinned out mandible (lower border less than 5 mm), requiring resection and reconstruction of the jaw were excluded from the study.

Enucleation with peripheral osteotomy along with 3 min application of Carnoy's solution is the standard modality of treatment. Carnoy's solution was freshly prepared on the morning of surgery containing 6 ml of 95% ethanol, 3 ml of chloroform, 1 ml of glacial acetic acid, and 1 g of ferric chloride for each 10 ml of solution.[5]

Surgical Procedure (Figure 2, 3)

Figure 2. Management of The Case Shown in Figure 1

Figure 3. Cases of Group II at Various Stages of Surgery

The patients were treated either under general anaesthesia or local anaesthesia depending upon the site and the extent of the lesion. The approaches were usually intra oral. Mucoperiosteal flaps were raised. Bony windows were created, and the cyst lining was slowly separated from the bony walls. Due care was given to remove entire lining in toto without fragmentation. The nerves, if involved by the cyst were carefully dissected out without much manipulation. The overlying soft tissues attached to the cyst were excised.[6] A rotary instrument and a powered hand piece were used to remove a margin of peripheral bone all along the walls of the cyst.

The cystic cavities were rinsed with saline and then packed with a gauze soaked in Carnoy's solution and left in place for 3 minutes. In cases were the inferior alveolar nerve is directly exposed due to fenestrations in the mandibular canal the nerve was pre protected by the application of white petroleum jelly. The cystic lumen is re rinsed with saline and wound closure was done in layers.

The patients were followed up postoperatively, once a week for first 1 month and then once a month for next 6 months and biannually thereafter. The minimum total follow-up period was 3 yrs. Follow-up consisted of clinical and radiographic evaluation (panoramic radiography for all cases and computed tomography, as necessary). Patients were assessed for recurrence, occurrence of nerve paraesthesia and wound dehiscence.

Recurrence

Lesion recurrence was defined as appearance of an osteolytic area in the region of previous treatment. Any image observed in panoramic radiography was re-evaluated using computerized tomography. This radiological data was subsequently compared with a new surgical intervention and the histological evaluation.

Since the majority of the recurrences are expected to be detected before the third postoperative year,[7] the minimum total follow-up period was kept as 3 yrs. Recurrence frequency was compared among syndromic and

non-syndromic OKC lesions. The results obtained were subjected to chi-square test with Yate's correction and p-value was arrived.

Nerve Paraesthesia

Nerve testing for the evaluation of paraesthesia was carried out at the end of 1 month, 6 months and third year postoperatively. In order to assess the direct effect of Carnoy's solution on the inferior alveolar nerve, and to avoid the interference arising from surgical trauma, retraction and manipulation of the nerve, only those cases where cystic lesions were present in the molar ramus area of the mandible were included for the assessment of nerve paraesthesia. This consisted of 10 lesions totally.

A 1-cm area of the intermediate portion of the lip skin just below the vermillion was chosen for evaluation. The methods used were static light touch, two-point discrimination, brush directional discrimination and pin pressure. The degree of paraesthesia was assessed using a visual analog scale (VAS) ranging from 0 to 10 (0 = insensitive, 1-9 = paraesthesia and 10 = normal). The unaffected side was used as a control with an equivalent value of 10. Paraesthesia was subdivided into mild (7–9); moderate (4-6); and severe (1-3) based on the values of VAS.

Wound Dehiscence

The incidences of wound dehiscence were recorded retrospectively from the patients' case sheets and comparison were made between syndromic and non-syndromic cases.

RESULTS

Of the total 10 patients included in the study, 6 were male and 4 were female. They were of age ranging from 10 years to 42 years. The common site of occurrence was mandibular molar ramus region.

The only registered recurrence was observed in a large multilocular mandibular ramus lesion of a patient with NBCC syndrome (Group I) at the 2nd year of follow up. The recurrence rate was 6.25% (1/16 lesions). If only syndromic cases were considered the recurrence rate increased to 11.11% (1/9 lesions). There was no registered case of recurrence among non-syndromic patients (0/ 7 lesions) and the difference was not statistically significant (p = 0.38).

Out of the 10 lesions in the mandibular molar ramus area, only 3 cases reported with post-operative paraesthesia. The results of nerve conduction studies carried out at the end of 1 month, 6 months and 3 years were tabulated as follows

	1 Month	6 Months	3 Years
Mild	0	2	3
Moderate	2	1	0
Severe	1	0	0

Table 1

3 out of total 16 lesions (18.75%) developed post-operative wound dehiscence. It occurred in 1 of total 9 lesions in group I (syndromic) and 2 of the total 7 lesions in group II (non-syndromic).

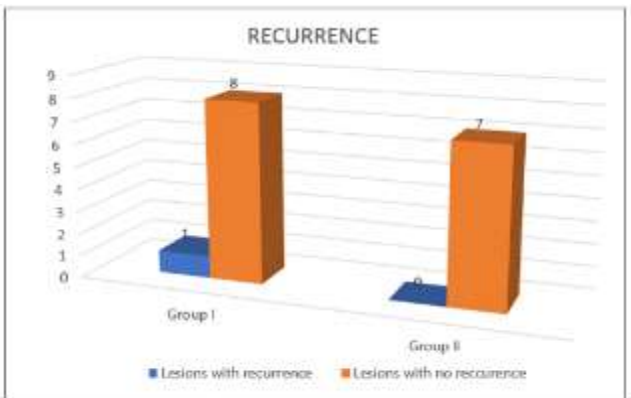

Figure 4. Recurrence

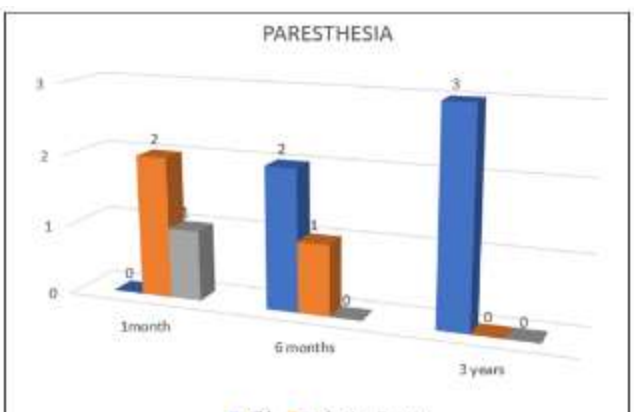

Figure 5. Paraesthesia

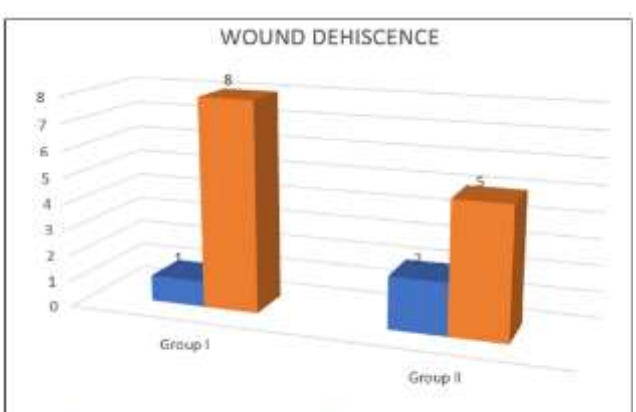

Figure 6. Wound Dehiscence

DISCUSSION

World health organisation (WHO) has defined OKC as "a benign uni or multicystic intraosseous tumour of odontogenic origin (dental lamina and its remnants) with characteristic lining of para keratinised stratified squamous epithelium and potential for aggressive and infiltrative behaviour."

Previously classified under developmental odontogenic cyst of jaw by WHO in 1971 & 1992, OKC has been reclassified and renamed as keratocystic odontogenic tumour (KCOT) in the WHO classifications of head and neck tumours in 2005 due to its aggressive behaviour, high recurrence rates and specific histological characteristics. However, In 2017, the new WHO classification of Head and Neck pathology re-classified OKC back into the cystic category.

The causes for high rate of recurrence of OKC includes-

1. Presence of satellite cyst /daughter cyst/epithelial islands in the walls of the cyst.
2. Incomplete removal of cystic lining.
3. Thin and friable nature of epithelial lining.
4. Higher level of cell proliferative activity in the epithelium.
5. Budding in the basal layer of the epithelium.
6. Bony perforation.
7. Adherence to adjacent soft tissue.
8. Supra-epithelial and Subepithelial split of the epithelial lining.
9. Parakeratinization of the surface layer.
10. Remnants of dental lamina epithelium not associated with original OKC and development of new OKC in the adjacent area.

The presence of multiple OKC of the jaws must alert a clinician as to the possibility of NBCC syndrome. The syndrome was 1st reported by Jarisch and White in 1894, and later in detail by Gorlin and Goltz. The pathogenesis of the syndrome is attributed to abnormalities in the long arm of chromosome 9(q22.3–q31) and loss of / mutations of human patched gene (PTCH1 gene).

Diagnosis of NBCC/ Gorlin-Goltz syndrome can be established when two major or one major and two minor criteria are present.[8]

Major Criteria

- Multiple basal cell carcinomas or one occurring under the age of 20 years.
- Histologically proven OKCs of the jaws.
- Palmar or plantar pits (three or more).
- Bi-lamellar calcification of the falx cerebri.
- Bifid, fused or markedly splayed ribs.
- First-degree relative with Nevoid Basal Cell Carcinoma syndrome.

Minor Criteria

- Macrocephaly (adjusted for height).
- Congenital malformation: cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism.
- Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
- Radiological abnormalities: bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modelling defects of the hands and feet or flame shaped hands or feet.
- Ovarian fibroma. - Medulloblastoma.

Management of OKC has been a topic of great debate over decades with some surgeons like Forssell, 1988;[9] Madras & Lapointe, 2008;[10] and Apajalahti et al, 2011[11] advocating more aggressive techniques like resection and reconstruction, while others recommending conservative methods like enucleation, peripheral ostectomy, cryotherapy and chemical cauterisation. Researches over years have shown that enucleation with peripheral ostectomy and chemical cauterisation have yielded better results with minimal morbidity to the patients.

Carnoy's solution is a cauterizing agent with moderate tissue penetration, rapid local fixation, and haemostatic action. The solution is usually applied over the surgical bony bed after enucleation and is found to produce a superficial necrosis of about 1.5 mm deep,[12] thereby providing a safety margin in the treatment of invasive neoplasm. Clinical application of Carnoy's solution came in the year 1973, after a land mark study by Stoelinga and Peters[13] demonstrating lower recurrence rates (2.5%) in patients treated by enucleation with chemical cauterisation than the patients who were treated by enucleation alone (13.5%).

Recurrence

As mentioned previously the majority of the recurrences are expected to be detected before the third postoperative year, based on a yearly mean growth of 7 mm in recurrent OKC and an average of 2.2 years for radiographic manifestation (Forssell, 1980; Apajalahti et al, 2011). However, the reports of recurrence even after decades of follow-up (Forssell, 1980; Oi; Zhao et al, 2002) emphasis need for long term follow up of these patients.

In the present study, recurrence occurred only in 1 case belonging to group I (syndromic) of the total 16 lesions (6.25%). The results are similar to the study conducted by Morgan et al[14] in 2005 which showed a null recurrence index in 13 KOTs in a mean follow-up of 63 months. If only syndromic cases were considered the percentage of recurrence increases to 11.11% (1 out of 9 lesions).

Though the literature review suggests a higher rate of recurrence in syndromic cases, the results presented here declares that the combination of Carnoy's solution and peripheral ostectomy is efficient method in the treatment both non-syndromic and syndromic cases as well. The only recurrence which occurred in a syndromic case might be occasional, since no statistically significant difference ($p = 0.38$) was observed when compared to the nonsyndromic cases. However, it is important to highlight that syndromic OKC lesions do need lifelong follow-up for further conclusion, considering the higher recurrence characteristics.

Nerve Paraesthesia

As mentioned previously, to study the direct effects of Carnoy's solution on the inferior alveolar nerve, only those

lesions that were present in the molar ramus region of the mandible were included for the study of nerve paraesthesia. This consisted of 10 lesions totally.

Out of the ten lesions, residual paraesthesia after three years was present only in 3 cases (30%). All these 3 cases presented with fenestrations of the mandibular canal with direct exposure of the nerve in to the surgical bed at the time of surgery. Although they were protected with the application of white petroleum jelly prior to the application of Carnoy's solution, some degree of deficient nerve conduction was present postoperatively. Improvement has occurred over time with most patients reporting very minimal or even negligible VAS scores at the end of three years. Degree of paraesthesia was related to the size of the fenestrations, with smaller defects presenting with lesser VAS scores and larger ones with greater VAS scores. Similarly, cases with smaller fenestrations recovered faster than the larger ones.

The neuropathic effects of Carnoy's solution is related to the degree of neural damage and its relation to axonal integrity.[15] Frerich has reported that there is no axonal degeneration when Carnoy's solution is applied over the nerve for up to 3 min (Frerich et al, 1994).

The association between bone fenestration and paraesthesia as observed in all 3 cases is 100%. This was statistically significant when compared with the other 7 cases that did not present with fenestrations ($P < 0.01$), indicating that the solution is safe to use in cases without mandibular canal fenestration. Also, the absence of paraesthesia in cases without neural exposure suggests that direct contact between Carnoy's solution on the epineurium is responsible for such a complication.

This study also demonstrates that neuropathies secondary to the direct application of Carnoy's solution over the epineurium surface, completely or partially resolve after months when solution use is limited to a single, 3-min application. Even in cases that had a partial resolution, the residual dysfunction was considered absent or insignificant.

Wound Dehiscence

Occurrence of wound dehiscence was found to be unrelated to NBCC syndrome. In our study 3 out of total 16 lesions (18.75%) developed wound dehiscence postoperatively. It was 1 lesion in group I (syndromic) and 2 in group II (non-syndromic). This was similar to the study by Riberio junior et al[16] were 5 of the total 22 lesions developed wound dehiscence (22.7%).

In our opinion occurrence of wound dehiscence is more related to overlying tissue excision and size of the lesion. Large multilocular radiolucencies, and cases with deficient soft tissue (due to the excision of the soft tissue attached to the cyst) are more prone for post-operative wound dehiscence. Wound dehiscence was managed by wound irrigation and revision closure in two cases and by sequential iodoform packing in one case.

CONCLUSION

According to this study, based on the recurrence rate of 6.25% (1 out of 16 lesions at the end of three years) and negligible residual paraesthesia, enucleation with peripheral ostectomy along with the application of Carnoy's solution is an effective method in the management of odontogenic keratocyst.

Comparing the syndromic and non-syndromic cases, since there is no statistically significant difference in terms of recurrence, it is concluded that chemical cauterisation with Carnoy's solution is effective in the management of syndromic cases as well and hence, radical and more aggressive surgical treatments like resection and reconstruction should be reserved only to recurrent and large multilocular cystic lesions with thinned out mandible.

However, further studies with large sample size and long follow up period is recommended to ascertain the benefits of Carnoy's solution and to evaluate the recurrences, especially in cases of NBCC syndrome.

REFERENCES

[1] Jeyaraj P, Nitesh N, Srinivas V. Case report on multiple keratocystic odontogenic tumors of jaws: comparison of a non-syndromic case versus a case of Gorlin Goltz Syndrome. Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 2013;26(4):569-575.

[2] Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib. A syndrome. N Engl J Med 1960;262:908-912.

[3] McGrath CJ, Myall RW. Conservative management of recurrent keratocysts in basal-cell naevus syndrome. Aust Dent J 1997;42(6):399-403.

[4] Stoelinga PJ. Long-term follow-up on keratocysts treated according to a defined protocol. Int J Oral Maxillofac Surg 2001;30(1):14-25.

[5] Voorsmit RA, Stoelinga PJ, van Haelst UJ. The management of keratocysts. J Maxillofac Surg 1981;9(4):228-236.

[6] Stoelinga PJ. Treatment of odontogenic keratocyst by the excision of the overlying attached mucosa, enucleation and treatment of the bony defect with carnoy solution. J Oral Maxillofac Surg 2005;63(11):1662-1666.

[7] Forssell K. The primordial cyst. A clinical and radiographic study. Proc Finn Dent Soc 1980;76(3):129-174.

[8] Evans DG, Ladusans EJ, Rimmer S, et al. Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. J Med Genet 1993;30(6):460-464.

[9] Forssell K, Forssell H, Kahnberg KE. Recurrence of keratocysts. A long-term follow-up study. Int J Oral Maxillofac Surg 1988;17(1):25-28.

[10] Madras J, Lapointe H. Keratocystic odontogenic tumour: reclassification of the odontogenic keratocyst from cyst to tumour. J Can Dent Assoc 2008;74(2):165-165h.

[11] Apajalahti S, Hagstrom J, Lindqvist C, et al. Computerized tomography findings and recurrence of keratocystic odontogenic tumor of the mandible and maxillofacial region in a series of 46 patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111(3):e29-e37.
[12] Williams TP, Connor FA. Surgical management of the odontogenic keratocyst: aggressive approach. J Oral Maxillofac Surg 1994;52(9):964-966.
[13] Stoelinga PJ, Peters JH. A note on the origin of keratocysts of the jaws. Int J Oral Surg 1973;2(2):37-44.
[14] Morgan TA, Burton CC, Qian F. A retrospective review of treatment of the odontogenic keratocyst. J Oral Maxillofac Surg 2005;63(5):635-639.
[15] Frerich B, Cornelius CP, Wietholter H. Critical time of exposure of the rabbit inferior alveolar nerve to Carnoy's solution. J Oral Maxillofac Surg 1994;52(6):599-606.
[16] Ribeiro Junior O, Borba AM, Alves CA, et al. Complications of Carnoy solution in the treatment of odontogenic tumors. RGO 2007;55:263-226.