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RESEARCH

Recurrent keratocystic odontogenic tumours: report of 19 cases

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Objectives: The aim of this study was to analyse 19 recurrent keratocystic odontogenic tumours (KCOTs).

Methods: 19 patients with recurrent KCOTs were retrospectively analysed. These patients had been treated by either enucleation or a combination of enucleation and Carnoy's solution. The analyses covered major aspects of primary KCOT and/or recurrent KCOT identities, including patient profile, clinical features, histopathology, radiology, treatment and prognosis.

Results: 19 (7.4%) out of 257 primary KCOT cases recurred, with an average patient age of 30.5 years (age range 18–45 years). 15 lesions were in the mandible and the remaining 4 were in the maxilla. There were more unilocular than multilocular occurrences for the primary tumours, with a ratio of 2.2:1. These KCOTs were initially treated by simple enucleation (12 cases) or enucleation with Carnoy's solution (7 cases). After the initial surgery, 15 out of 19 (78.9%) recurred within 6 years, while 4 (21.1%) recurred after 6 years. Evidently, the recurrent lesion was involved with the roots of the teeth in three out of six cases whose teeth were preserved. In addition, the recurrent KCOTs had a tendency to be more multilocular or multifocal than the primary cases, with a unilocular-to-multilocular ratio of 1.1:1.

Conclusions: 7.4% of primary KCOTs recurred within 6 years after initial treatment with either enucleation or a combination of enucleation and Carnoy's solution. The recurrent KCOTs were more likely to be multilocular or multifocal than the primary cases and often involved the teeth. The method of operation for these recurrent lesions would be considered as a more aggressive approach.

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Keywords: keratocystic odontogenic tumour; odontogenic keratocyst; enucleation; recurrence

Introduction

Keratocystic odontogenic tumour (KCOT), formerly referred to as odontogenic keratocyst, is an aggressive benign neoplasm of the jaws with a high recurrence rate and a great tendency to invade adjacent tissue.[1] KCOT may occur in any part of the jaws, although the majority of lesions are located in the mandible, especially in the posterior body and ascending ramus.[2,3]

There is no consensus over the most appropriate treatment modality for this tumour. The common strategies include marsupialization and enucleation, which may be combined with adjuvant treatments such as application of Carnoy's solution, marginal resection or radical resection. The recurrence rate of KCOTs varies from 12% to 58%.[2–7] The real reasons for the high recurrence rate of KCOTs remain substantially unknown.

In this report, we reviewed major clinical, radiographic and histopathological features of 19 recurrent KCOT patients who underwent simple enucleation or enucleation with Carnoy's solution and analysed some factors that possibly affected the recurrence rate.

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Materials and methods

We reviewed all 257 KCOT cases treated at the Department of Oral and Maxillofacial Surgery, Hospital of Stomatology, Wuhan University, China, from January 1990 to December 2008. The data analysed in this study included patients' records, radiographs and histopathological results, together with follow-up reports of more than a year old. The treatment of the primary lesion was enucleation with or without application of Carnoy's solution,[8] with a follow-up schedule of every 3 months after surgery for the first year and every 6–12 months after that. All histopathological slides were reviewed by a pathologist to confirm the original diagnosis according to the new World Health Organization classification.[1]

Data of recurrent KCOTs were analysed, with emphasis on the aspects that potentially affect the recurrence. These aspects included clinical, radiographic and histopathological features, such as age and gender of the patients, radiographic appearance, management of the affected teeth, histopathological findings, treatment modalities and outcomes, and the surgeon's experience. The recurrence interval was defined as from the date of enucleation to the time when any radiolucent area was detected by an imaging examination at the primary site. The recurrent KCOT cases were confirmed histopathologically and were limited to the solitary KCOT, excluding the ones which were part of basal cell nevus syndrome.

The χ^2 test was used to analyse the significance of the differences in recurrence rates and imaging features between groups at a 5% significance level. In addition, the average number of years of surgeons' experience was analysed with one-way ANOVA to see whether their experiences are enough to cause significantly different recurrence rates.

Results

Patient profiles

19 recurrent KCOTs were found in 257 cases, all of which underwent surgical enucleation and follow-up from 1 to 15 years. The overall recurrence rate was 7.4%. There were 12 male and 7 female patients with an average age of 30.5 years (age range 18–45 years) at the time of the initial surgery (Table 1). The duration from the onset of the symptoms to the time of visiting the doctor varied from 2 weeks to 3 years.

Clinical features

Symptoms: Among these 19 patients with recurrent KCOTs, the symptoms for their primary lesions are different—only one case was non-symptomatic and revealed by radiographs and all other cases showed symptoms. The most frequently cited symptom was swelling (eight cases) followed by swelling with local pain (seven cases) and fistula or no healing of the wound after extraction (three cases). However, the symptoms of these recurrent KCOT patients are somewhat different from those of the primary KCOT patients (the same patient group). 12 recurrent KCOT patients cited that swelling or swelling with pain was the most pronounced symptom; 2 patients complained of a poor fit or loosening of their removable partial dentures and 5 patients without symptoms were detected radiologically in the follow-up examination.

Location of KCOTs: 15 lesions (78.9%) were in the mandible and 4 (21.1%) were in the maxilla (Figure 1).

Size of KCOTs: The size of the lesions varied from 3.5 cm to 11 cm with an average of 6.5 cm. The size of recurrent KCOTs was smaller or significantly smaller

Table 1 Clinical, radiographic findings of 19 cases of recurrent keratocystic odontogenic tumours

				Radiographic appearance			
Case	*Age (years)*	*Sex*	*Site*	*Primary*	*Recurrence*	*Initial treatment*	*Date of recurrence (months)*
1	18	M	Mn/R	Mul	Uni	Enu	10
2	21	M	Mn/L	Uni	Uni	Enu	36
3	32	M	Mn/L	Uni	Mul	Enu	120
4	22	F	Mn/R	Uni	Uni	Enu	9
5	29	M	Mn/Bi	Uni	Mul	Enu	77
6	37	M	Mn/R	Mul	Mul	Enu+CS	37
7	31	F	Mn/L	Uni	Uni	Enu	5
8	27	M	Mx/L	Uni	Uni	Enu+CS	39
9	39	M	Mn/R	Uni	Mul	Enu	66
10	29	F	Mx/R	Uni	Uni	Enu+CS	54
11	45	M	Mx/L	Mul	Mul	Enu+CS	71
12	22	F	Mn/R	Uni	Mul	Enu	56
13	37	M	Mn/L	Mul	Uni	Enu	124
14	25	F	Mn/Bi	Uni	Mul	Enu+CS	96
15	35	F	Mn/Bi	Mul	Mul	Enu	67
16	41	F	Mx/L	Uni	Uni	Enu+CS	23
17	43	M	Mn/R	Mul	Mul	Enu+CS	56
18	20	M	Mn/L	Uni	Uni	Enu	39
19	27	M	Mn/R	Uni	Uni	Enu	34

Bi, bilateral; Enu, enucleation; Enu+CS, enucleation with Carnoy's solution; F, female; L, left; M, male; Mn, mandible; Mul, multilocular; Mx, maxilla; R, right; Uni, unilocular.

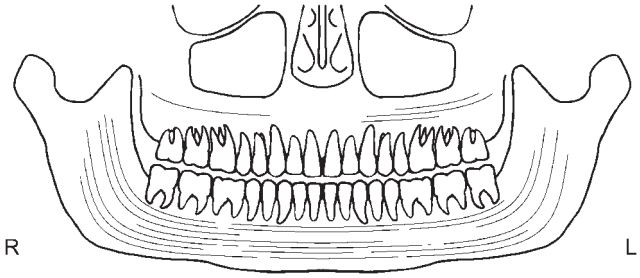


Figure 1 The sites of involvement of 19 keratocystic odontogenic tumours at the first presentation. L, left; R, right

than the primary lesion in all 12 patients who were followed up in the specified time period. However, for the seven patients who failed to comply with the follow-up schedule, their recurrent tumour sizes were similar to or bigger than the primary lesion which was most likely owing to the delay of diagnosis and treatment.

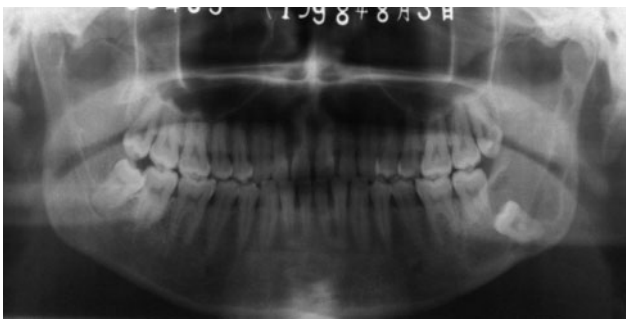
Recurrence time and recurrence rate: The recurrences took place from 5 months to 12 years after the initial treatment (Table 1). The duration from enucleation to the first recurrence was as follows: less than 3 years in six cases; 4–6 years in nine cases; and greater than 6 years in four cases.

As mentioned above, the recurrence rate was 7.4% for the total KCOT patients. However, if these patients were divided into different groups based on treatment modalities, different recurrence rates were found between these two groups: 12 recurred in 133 cases treated by simple enucleation (a recurrence rate of 9.0%) and 7 recurred in 124 cases by enucleation with Carnoy's solution (a recurrence rate of 5.6%). The recurrence rate in cases treated by enucleation plus Carnoy's solution was lower than simple enucleation, but the difference was not statistically significant ($p > 0.05$). The average experience of the surgeons was 7.9 years for the recurrent group (19 cases) and 9.5 years for the non-recurrent group (238 cases), suggesting that the surgeons' experiences were not a significant cause for the tumour recurrence ($p > 0.05$).

Radiology

Primary KCOTs: 13 out of 19 (68.4%) primary tumours were unilocular with a well-demarcated border, whereas 6 (31.6%) were multilocular and the ratio of unilocular cases to multilocular cases was 2.2:1 (Table 1). Four cases were associated with an impacted tooth and resorption of the roots was observed radiographically in five cases. The number of teeth involved by the tumour ranged from 1 to 11, excluding the third molars. Part or all of the affected teeth were extracted in 12 cases.

Recurrent KCOTs: The early recurrent lesions tended to be in single radiolucent or multiple radiolucent areas without a significant sclerotic margin (Figure 2) and the tumour grew faster than those which recurred at a longer



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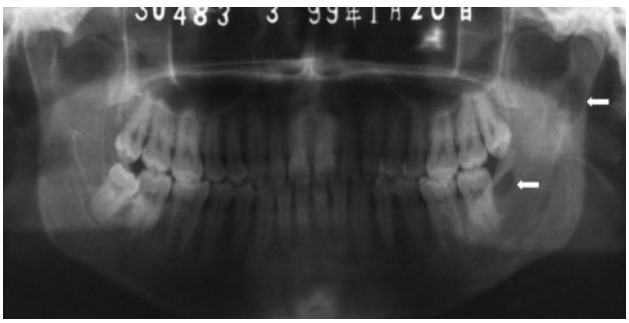

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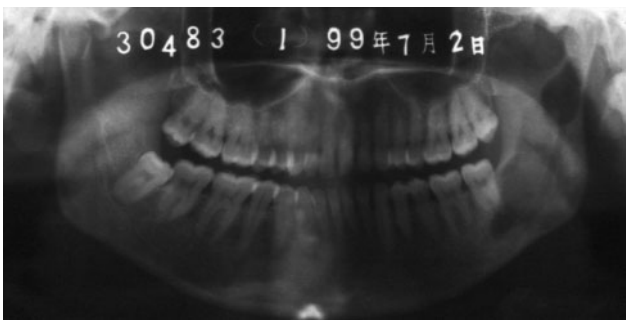

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Figure 2 (a) Panoramic radiograph showing a well-circumscribed radiolucency in the left mandibular ascending ramus, extending from the second molar area to the coronoid process and the condyle with an impacted third molar. (b) Significant bone consolidation in the operative area 5 months after enucleation, but two small radiolucencies on the third molar area and condylar neck were found (arrows), suggesting recurrence. (c) The size of recurrent lesion was remarkably increased at 11 months post-operatively

interval after initial surgery. In contrast, the later recurrent tumours displayed the radiolucency with a clear sclerotic line and grew at a slower speed (Figures 3 and 4). In the 19 recurrent tumours, there were 10 unilocular cases and 9 multilocular or multifocal (multiple separate lesions) cases (Figures 3 and 5), with a unilocular-to-multilocular ratio of 1.1:1 (Table 1). In addition, the recurrent lesions were involved with the tooth roots in three out of six cases whose teeth were preserved (Figures 3 and 4).

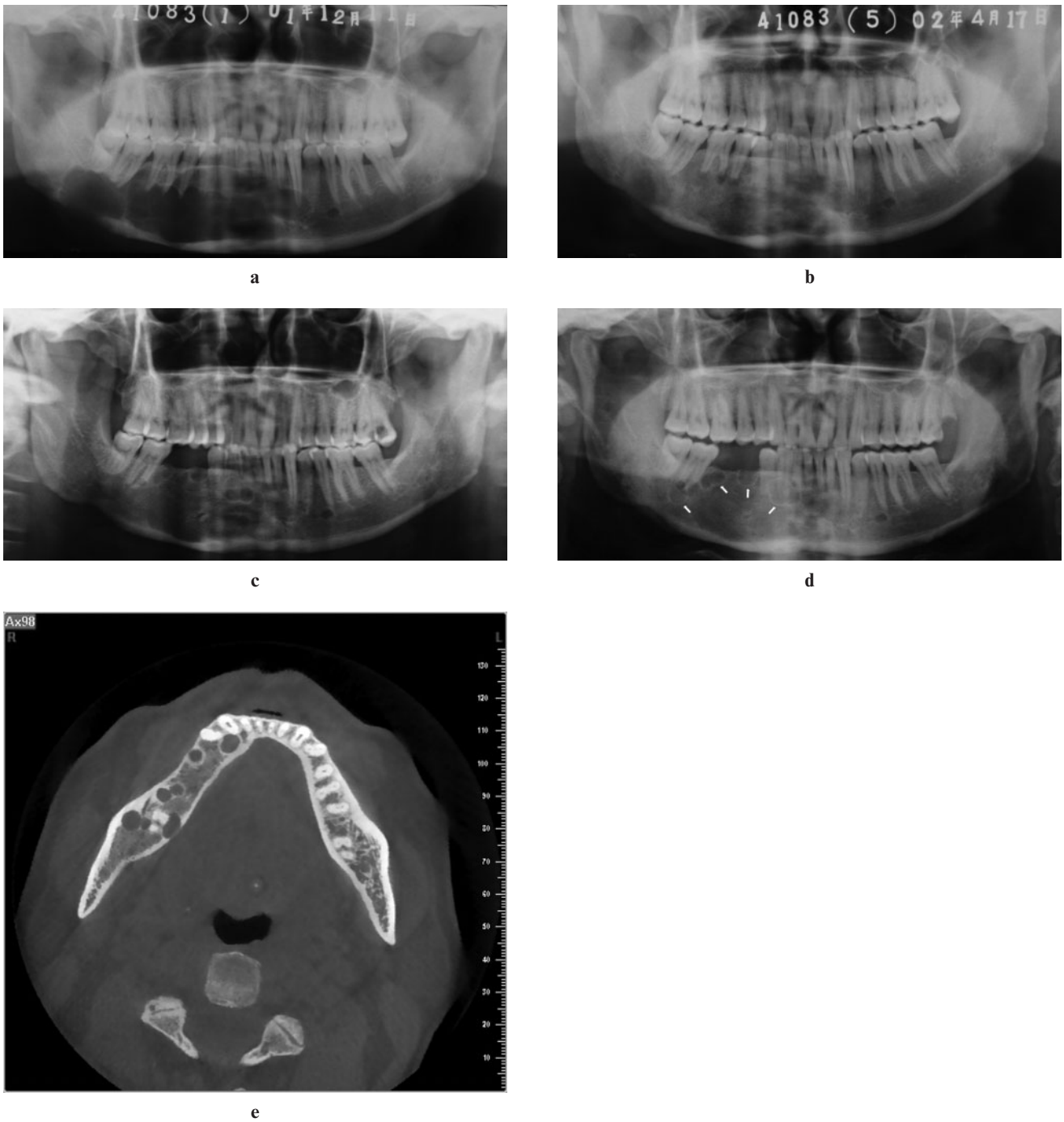

Figure 3 (a) Panoramic radiograph showing a multilocular radiolucency from the right posterior mandible to the left premolar area. (b) Significant bone regeneration 4 months after enucleation, but periapical radiolucency with symptoms of periapical periodontitis of the right first molar and second premolar, which were extracted after the patient received antibiotics therapy. (c) Radiograph 56 months after surgery showing multiple separate radiolucencies with a thin sclerotic line on the alveolar bone of the right mandibular anterior teeth, the second premolar and the first molar extraction sites, indicating recurrences. (d) The size of radiolucencies was increased and periapical radiolucency on the second molar was formed 103 months after surgery (arrows). (e) Cone beam CT scan demonstrated that these lesions were separated and associated with a tooth respectively

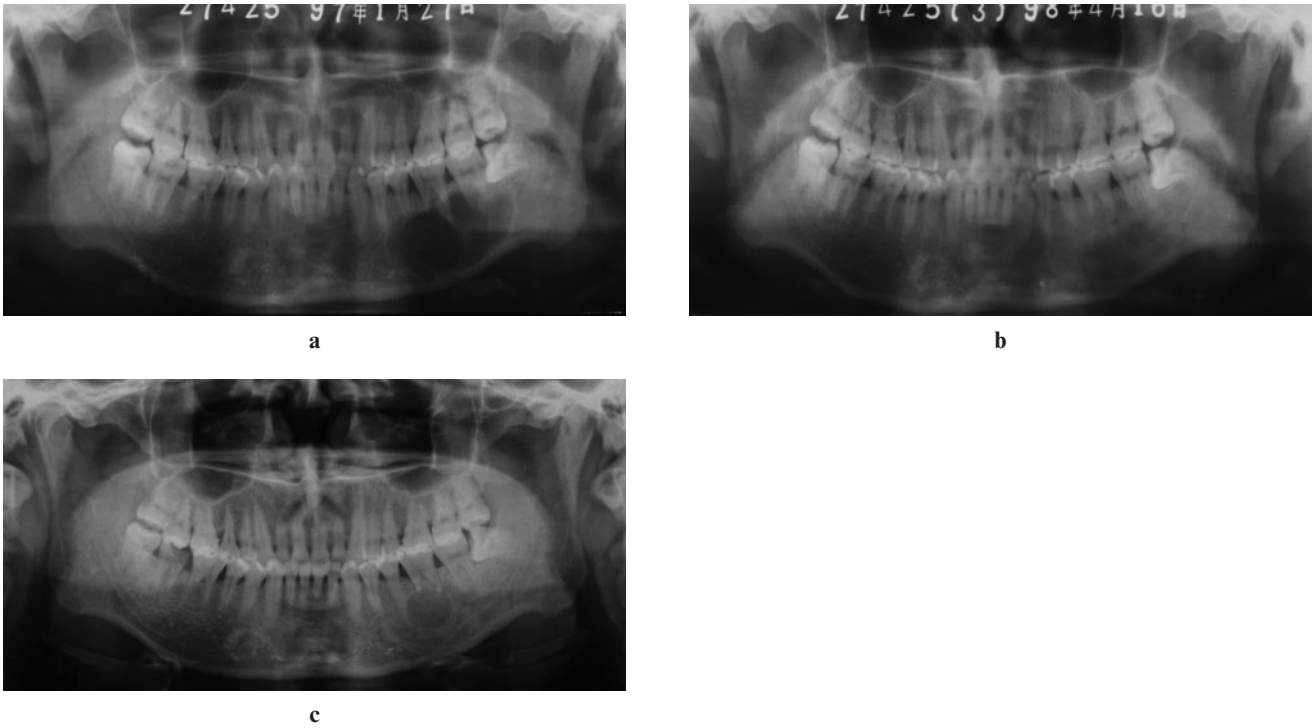

Figure 4 (a) Multilocular radiolucency with slight root resorption of the first mandibular molar. (b) Significant bone consolidation with remodelling of the mandibular canal 15 months after enucleation. (c) Unilocular radiolucency of the recurrent tumour 124 months after enucleation

Treatment and prognosis

12 recurrences were subsequently treated by enucleation with Carnoy's solution or just enucleation, 4 were treated by marginal resection and 3 by segmental resection. After the second operation, 16 patients did not show any sign of recurrence after up to 7 years' follow-up. Two patients suffered from the second recurrence after a second enucleation and were finally treated by enucleation with Carnoy's solution and segmental mandibulectomy, respectively. Only one patient, treated by enucleation the first time and enucleation with Carnoy's solution the second time, had a third recurrence and was treated with a partial maxillectomy.

Histopathology

Histopathologically, all 19 primary and recurrent KCOTs appeared as parakeratin types. The presence of daughter cysts or epithelial islands in the cyst wall was demonstrated in three primary and two recurrent lesions, respectively. No evidence of ameloblastoma-like epithelial proliferation or epithelial dysplasia was observed in either primary and recurrent lesions.

Discussion

In the current study, the KCOTs were located primarily in the posterior mandible and were found more

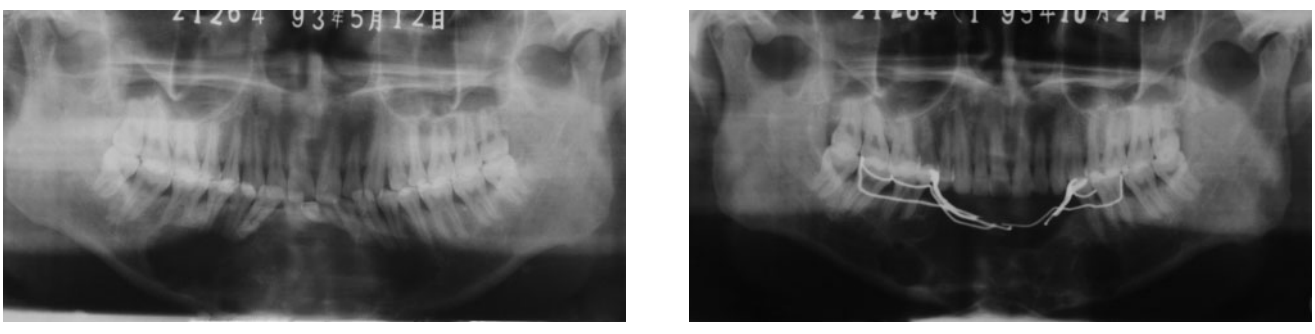

Figure 5 (a) Mandibular extensive keracystic odontogenic tumour with the involvement of the symphysis and bilateral body. (b) A recurrent tumour presented as a multilocular radiolucency approximately 77 months after enucleation

frequently in males than in females, which is consistent with other studies.[2,6]

Enucleation is a commonly used method for surgical treatment of KCOT in Europe and Asia.[6,8–13] The perceived advantages of enucleation include the complete removal of the cyst and a potentially thorough histopathological examination of the lesion. However, KCOTs treated with enucleation alone had a significantly higher recurrence rate than those treated with more aggressive methods. Blanas et al[5] reviewed the literatures pertaining to the treatment and prognosis of KCOTs and found that simple enucleation had a recurrence rate of 17–56%, and enucleation combined with adjunctive therapy, such as the application of Carnoy's solution or decompression before enucleation, had a low recurrence rate (1–8.7%). Recurrence may result from residual epithelial islands and possibly microcysts left behind; therefore, some research recommends treatment of the cyst cavity or bone defect around the cyst with Carnoy's solution to destroy these epithelial rests in the cyst wall.[8,14–16] Our report also showed that the application of Carnoy's solution reduced the recurrence rate, which is in agreement with earlier reports.[10,14]

It was reported that KCOTs in the mandibular molar region, angle or ascending ramus had a higher recurrence rate.[6,17] The logical explanation is that there is more chance for the epithelial rests of the cyst wall to be left behind after surgery, owing to the limited surgical access to the posterior part of the mandible. Some clinicians believed that the histopathological presence of daughter cysts or epithelial islands in the cyst wall may result in higher recurrence of KCOT, which was shown in a report by Myoung et al[6] where the presence of one or more daughter cysts showed a statistically significant higher recurrence rate. However, their study included some patients with nevoid basal cell carcinoma syndrome which has a significantly higher occurrence of epithelial islands and/or microcysts in the cyst wall and thus has a higher recurrence rate than the non-syndromatic KCOT. On the contrary, our report here, together with the study from Ahfors et al,[4] demonstrated that there was no correlation between daughter cysts or epithelial islands and the recurrence of KCOT.

The impacted or displaced tooth or teeth in the tumour site should be removed with enucleation. However, there is still no consensus about whether standing teeth involved need to be extracted. Chirpathomsakut et al[7] found that recurrent lesions were associated with the remaining teeth. Therefore, they suggested that if enucleation is chosen as a surgical treatment, the clinician should give more attention to the dentate area and remove the teeth if they are not sure whether the pathological tissue can be removed completely. Three recurrences in our cases may be due to incomplete removal of the epithelium around the tooth roots which extended into the cyst cavity (Figures 3 and 4). We recommend that affected teeth be removed or treated with apicoectomy if the roots extend into the cyst lumina and interfere with the complete removal of the cyst wall.

To preserve the patients' masticatory function after surgery, Tan et al[18] reported that the majority of teeth involved pre-operatively could be preserved when marsupialization in combination with secondary enucleation was performed for the treatment of mandibular KCOTs. Some research suggested that this two-stage surgery minimized the damage to adjacent structures and reduced the recurrence rate when used for large or extensive KCOTs.[8,19,20] Therefore, it seems appropriate to perform marsupialization or decompression at the first stage followed by enucleation if multiple teeth are involved by KCOT.

Radiographic follow-up showed that bone condensation in the residual cavity was progressively increased after enucleation of KCOT. The radiographic appearance of recurrent tumours was affected by the post-operative time interval and KCOT location. We found that the lesions recurring within 1 year post-operatively appeared as radiolucency without a markedly sclerotic margin and that the lesions which presented after a longer post-operative interval, when regenerated bone had been remodelled, had radiolucency with a clear sclerotic border of bone. With regard to the location, radiolucency in the maxilla usually presents no significant sclerotic border owing to the thinness of bone and image superimposition on the plain radiographs.

We also demonstrated that recurrence often occurred at the periphery of the original bone cavity or around the tooth roots affected by the tumour. Small recurrent lesions may separate each other and appear as multifocal if they are identified early, and they may possibly coalesce to eventually form a multilocular or multicystic tumour in the primary site if no intervention is performed; our results revealed that there is a higher frequency of multilocularity in recurrent KCOTs than in the primary lesions. Currently, panoramic radiography is the chief imaging method for follow-up after enucleation of the jaw cystic lesions. However, in real practice CT is a superior imaging tool given the fact that it can assess bone healing of the residual cavity, the exact location of the recurrent lesion and the relationship between the tumour and its adjacent anatomical structures.

In our study, the average length for the first recurrence was 53.2 months and 78.9% of tumours recurred within the first 6 years after surgery, roughly in line with other reports.[2,7,12] We recommend a follow-up schedule of every 3 months within the first year after initial treatment owing to the rapid growth of recurrent tumours found at this period; every 6–12 months from 2 years to 6 years, which is in line with the guidelines suggested by most clinicians; and annually for the rest of the patient's life since recurrence has been reported up to 40 years after initial surgical treatment.[21,22] CT should be used if recurrence is suspected based upon the result of the panoramic radiograph.

The recurrent KCOTs after enucleation should be addressed more aggressively than the primary counterpart.[23] To minimize the risk of future recurrence, a radical approach such as marginal or segmental resection could be justified in the cases of multiple recurrences, poor compliance with follow-up appointments or large multilocular cysts.[24–26] If there is a cortical perforation, the periosteum should be removed as well. In cases in which the tumour invades the alveolus and perforates through the alveolar bone, the overlying mucosa should be included in the resection. Consequently, this aggressive treatment has two major disadvantages: the resulting facial deformity and the loss of masticatory function usually necessitate reconstructive surgery. Therefore, a strict follow-up protocol for KCOT will allow for early surgical intervention in cases of recurrence and could minimize the need for second surgery.[12]

In conclusion, the keratocystic odontogenic tumours recurred from 5 months to 124 months after enucleation, with the majority of them being diagnosed within the first 6 years after the initial surgery. Recurrent tumours usually displayed multilocular or multifocal radiolucency and were associated with teeth preserved in the sites of involvement. KCOTs recurrence is associated with many factors and the clear link between clinical or radiological findings and recurrence after enucleation remains elusive.

Acknowledgments

Y Zhao and B Liu contributed equally to this work.

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