A 10-year study on the incidence of Oral Maxillofacial lesions in Department of Oral Maxillofacial Surgery, Mahidol University: Keratocystic odontogenic tumor

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Abstract

Introduction: Keratocystic odontogenic tumor (KCOT) is one of the most aggressive odontogenic cysts due to its relatively high recurrence rate, fast growth, and its tendency to invade adjacent tissues.

Objective: The aim of the study was to retrospectively analyze the clinico-pathological characteristics of 109 KCOT cases.

Materials and methods: <describe the study protocol in short>

Results: The study comprised of 46 male and 63 female patients with an age range of 3-87 years with an average age of 32 years. The posterior mandible (48.4%) was the most frequent site of KCOT. Most of the patients were asymptomatic (41%), where as some noted associated swelling, pain, discharge, and paraesthesia. On pathological analysis, 45% of the cystic cavity content was noted to be keratin. On radiologic findings, KCOT appeared as unilocular (83%) as well as multilocular lesions (14%). KCOT was associated with the displacement of impacted teeth; the mandibular third molars (40.37%) were the most frequent impacted teeth. Three patients were confirmed to be associated with nevoid basal cell carcinoma syndrome.

Conclusion: Almost all of the lesions were diagnosed histologically as stratified squamous parakeratinized epithelium (90.82%).

Key words: Keratocystic odontogenic tumor, odontogenic tumor, odontogenic cysts, impacted teeth, incidence, retrospective study

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Introduction

Odontogenic keratocyst (OKC) was first reported in 1956 by Philipsento as an epithelial keratinized jaw bone cyst.[1] In 1963 Pindborg, Philipsen, and Hansen reported the histopathological features that were characteristic of OKC.[2] Then, in 1998 Chow HT reported that parakeratinized epithelium can be found more frequently than an orthokeratinized epithelium.[3] In 2005 WHO established a new classification for odontogenic tumors. Formerly known as OKC, keratocystic odontogenic tumor (KCOT) is defined as a benign unicystic or multicystic, intraosseous tumor of odontogenic origin, with a characteristic lining of parakeratinized stratified squamous epithelium and potential for aggressive, infiltrative behavior. Orthokeratinized epithelium is not part of KCOT.[4] Among the main reasons for this change are its potentially aggressive biological behavior, high recurrence rates, presence of daughter cysts in the capsule, budding of the epithelium basal layer, increase of the mitotic activity, and the influence of genetic alterations, such as mutations of the PTCH gene and loss of heterozygosis of the 9q22 chromosome (Agaram et al., 2004; Madras & Lapointe, 2008; Vered et al., 2009).[5-8]

There is a general agreement that OKCs develop from dental lamina remnants in the mandible and maxilla. However, origin of this cyst from extension of basal cells of the overlying oral epithelium has also been reported.[9,10] It is characterized by histology and behavior differences from other odontogenic cyst because of growth and expansion of the osmotic pressure within the lumen and the releasing of substances, such as growth factor proteins.[11,12]

The pathogenesis mechanism involved in the growth and expansion of KCOT are many - proteins p53, PCNA and Ki-67 volumes in the suprabasal layer represents the proliferation of lesions as well as an increase in the antiapoptotic protein (BCL-2), where as transforming growth factor and matrix metalloproteinases interleukin are associated with osteolytic activity. [13-15] Other genes that can be correlated to OKC/KCOT are PTCH2 and SUFU. Few authors also have demonstrated loss of heterozygosity in p16, MCC, TSLC1, LTAS2, and FHIT genes.[14] These findings are helpful to explain the aggressive behavior of KCOT.[13,15]

KCOT is found in approximately 3-11 % of odontogenic cysts.[16-19] They may occur in any part of jaws with the majority of lesions occurring in the posterior region of the mandible, most commonly in the posterior body and ascending ramus.[17,18] KCOT may occur at any age range, with peaks between the second and third decades of life with a slight male predilection. OKCs are solitary lesions, unless they are associated with nevoid basal cell carcinoma syndrome. [20-27]

Distinctive clinical features include a potential for local destruction and a tendency for multiplicity.[28] Clinically, KCOT generally presents as a swelling, with or without pain.[29-30] The tumor classically grows within the medullary spaces of the bone in an anterioposterior direction, causing expansion that is minimal at first.[15] Buccal expansion is noted in approximately 30% of maxillary and 50% of mandibular lesions.[29] According to Brannon et al, 50% of the patients were symptomatic before seeking treatment, and the most common features were pain, soft tissue swelling, and expansion of bone. These lesions are also associated with drainage and neural manifestations, such as paraesthesia of lip.[31] Aspirated content usually is curd or thick creamy material that contains a lot of keratin debris and has a low protein content, below 4 g/100 ml from electrophoresis.[32]

Radiographically, KCOTs present as well-defined radiolucent unilocular or multiloculars with corticated or scalloped margins, unless they have been secondarily infected.[33] In 25-40% of cases, there is an unerupted tooth involved in the lesion. Adjacent teeth may be displaced, but root resorption is rarely seen.[27] Larger lesions can cause bony expansion with or without perforation of the cortical plates.[34]

KCOTs are histologically composed of a parakeratinized stratified squamous epithelium without rete ridges. Surface keratinization is corrugated. The basal layer is classically well-defined with columnar or cubical cells in palisade. There may be daughter cysts and epithelial islands in the capsule, and budding of the basal layer. Loss of characteristic cellular and architectural features may be in the presence of inflammatory infiltrates.[30-35] The incidence of daughter cysts in the wall is reported to range from 7% to 30.1%.[36]

The recurrence rates of KCOT range from 2.5% to 62%, but the rate of recurrence of KCOT with nevoid basal cell carcinoma syndrome (NBCCS) is as high as 82%.[37] Recurrence of KCOT occurs for several reasons. Incomplete removal of the cystic lesion allows new cyst formation or epithelial islands in the wall of the original cyst remains in the surrounding bone or soft tissue. New KCOT can also develop from the basal layer of the oral epithelium.[30] Patients with NBCCS are more prone to continuous formation of new cysts.[38 39] Most recur within 5 - 7 years after treatment. However, there are reports of recurrence that occurred more than 10 years after treatment. Therefore, a long-term follow-up is necessary to maintain KCOT.[40] Malignant transformation to SCC may occur, but it is unusual and accounts for 0.1 - 1.8%.[41] KCOT can be found in NBCCS, which was described by Gorlin and Goltz in 1960. These symptoms can be transmitted by autosomal dominant genetic disorder with a prevalence ranging from 1:57,000 - 1:256,000 and found equally in male and female. NBCCS is caused by mutation of the PTCH gene. Clinical features include KCOT at multiple locations; basal cell carcinoma; palmar or plantar pits; cleft lip or cleft palate; hypertelorism; congenital skeletal anomalies such as bifid ribs, fused ribs, splayed ribs, missing ribs; ectopic calcification, such as calcification of the falxcerebri; macrocephaly, medulloblastoma; ovarian fibroma; fibrosarcoma; meningioma; and cardiac fibroma. An individual patient has different clinical manifestations and levels of severity.[42]

Peripheral KCOT results in soft tissue, such as the gingiva and buccal mucosa or muscle. It arises from the dental lamina rests that are displaced and persist in the buccal mucosa during odontogenesis. The average age of the patients is 57.8 years. Peripheral KCOT is found in female more than male with a ratio of 2.3:1. Clinical symptoms are asymptomatic fluctuant normal to blue, gray, white, or pale yellow nodule. No significant findings were noted on radiographic examination.[43]

The orthokeratinized odontogenic keratocyst had its diagnosis changed to orthokeratinized odontogenic cyst (OOC) due to WHO reclassification.[44] This cyst has different features as compared to KCOT regarding the orthokeratinized epithelium. However, it has biological behaviors such as less aggressive, and lower rate of recurrence and has not been associated with NBCCS. It has been found in 7 - 17% of all keratinizing jaw cysts. There are no clinical or radiographic features that differentiate them from other inflammatory or developmental odontogenic cysts. [45, 46]

In a review article, the surgical treatment of KCOT was divided into three groups. Conservative treatments include enucleation

and marsupialization. Enucleation can also be used to collect anatomical structures including teeth. This is good because KCOT is commonly found in younger patients. Inter conservative-aggressive treatment include enucleation with mechanical, chemical, and physical curettage. Aggressive treatment includes resection, which is often chosen for patients with NBCCS, large KCOT, or recurrent KCOT. [39 48]

The choice of treatment is based on multiple factors, such as age, size, location of the cyst, and soft tissue involvement. The goal is to choose the treatment modality that carries the lowest risk of recurrence and the least morbidity.[47] The aim of this study is to report the frequency, demographic, clinical, radiological, and histopathological features of KCOT observed in a 10-year period at the Faculty of Dentistry Mahidol University.

Materials and methods

The present study comprised of 109 patients who had been diagnosed with KCOT, and were checked at the Department of Oral and Maxillofacial Surgery, Mahidol University between the January in 2002 and April in 2012. Clinical and radiological findings, and histological data were compiled from pathologic reports. Each case was then analyzed with focus on the following factors: (1) age and gender, (2) anatomic location, (3) chief complaints, (4) radiologic finding and association with impacted teeth, and (5) histopathological finding.

Results

The age of patients at the time of diagnosis ranged from 3 to 87 years with an average of 32 years. KCOT had a peak occurrence in the third decade of life, followed by the second decade of life. The male-to-female ratio was 1:1.12 (Table 1).

According to mandible and maxilla, the overall ratio was 2.12:1. In the 109 cases of KCOT, 70 cases (64%) were found in the mandible, 33 cases (30%) occurred in the maxilla, and 2 cases (2%) occurred in the submucosa. The remaining KCOT (4%) had multiple distributions (Table 2). The posterior mandibular area was the most frequent site of KCOT in the jaws (Table 3).

Table 3 showed that 41.28% of the patients (45 cases) were asymptomatic followed by complaints of swelling, pain, pus discharge, and neurologic deficits, respectively. Forty-five percent of the cystic cavity content was keratin curd (Figure 2).

Table 1 Distribution of KCOT according to the patient age and gender

Age	Female	%	Male	%	Total
0-9	3	2.75	1	0.92	4
10-19	15	13.76	10	9.17	25
20-29	23	21.10	9	8.26	32
30-39	5	4.59	9	8.26	14
40-49	8	7.34	6	5.50	14
50-59	7	6.42	6	5.50	13
60-69	2	1.83	4	3.67	6
80-89	0	0.00	1	0.92	1
Total	63	57.80	46	42.20	109

Table 2 Distribution of KCOT according to location

Region	Total	%
Mandible	70	64.22
Maxilla	33	30.28
Maxilla-mandible	4	3.67
Submucosa	2	1.83
Total	109	100

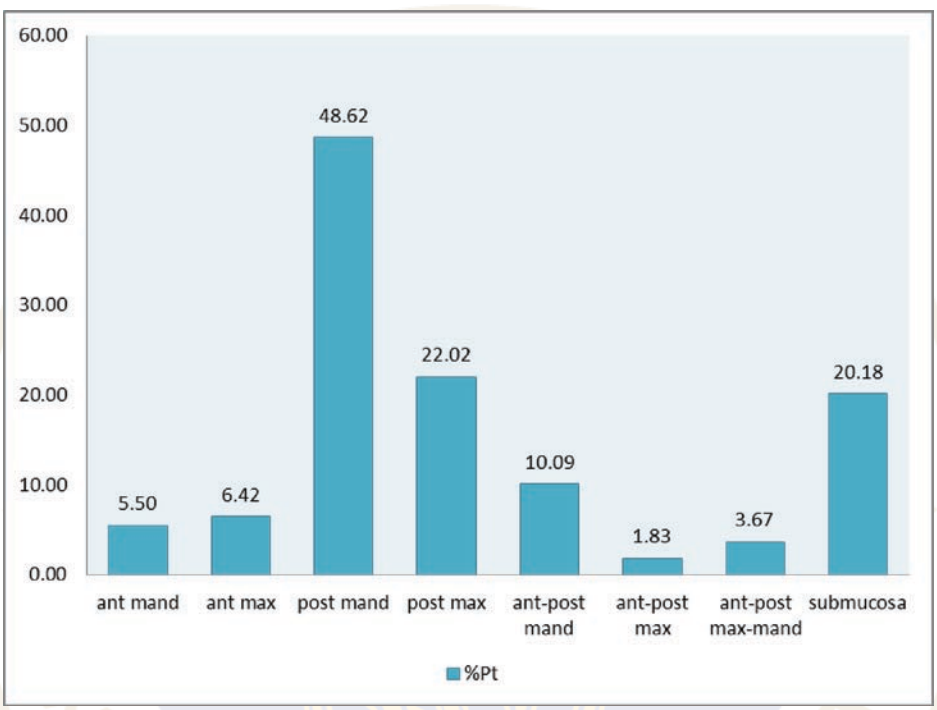

Figure 1 Percentage distribution of patients according to the occurrence of KCOT
ant : anterior
post : posterior
mand : mandible
max : maxilla

Table 3 Chief complaints observed with the occurrence of KCOT

Chief complaint	Total	%
Asymptomatic	45	41.28
Swelling	30	27.52
Swelling and pain	13	11.93
Pain	11	10.09
Swelling and discharge	4	3.67
Discharge	4	3.67
Paraesthesia	1	0.92
Pain and paraesthesia	1	0.92
Total	109	100.00

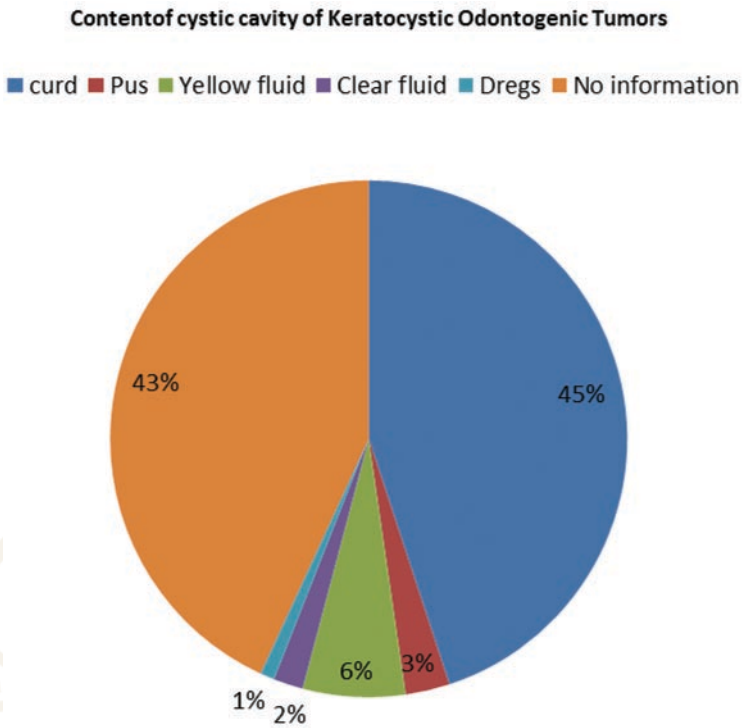

Figure 2 Contents of the cystic cavity of KCOT

The main radiographic findings were unilocular radiolucency (90/109 cases, 82.57%), followed by multilocular radiolucencies (17/109 cases, 15.60%) and mixed radiolucencies and radiopacities (2/109 cases, 1.83%). An unerupted tooth was involved in 40.37 %. The mandibular third molars were the most frequently impacted teeth associated with the KCOTs, followed by maxillary third molars (Table 4).

Almost all of the lesions were diagnosed histologically as stratified squamous parakeratinized epithelium (99/109 cases, 90.82%). Orthokeratinized epithelium was found in 1 case (0.9%), and non-keratinized epithelium was found in 9 cases (8.25%). Other histopathological finding included palisading of basal cell, keratineceous material, and daughter cysts in the capsule.

Table 4

X-ray	Total	%
Unilocular radiolucent	90	82.57
Multilocular radiolucent	17	15.60
Mixed radiolucent + radiopaque	2	1.83
Total	109	100.00

Discussion

Keratocystic odontogenic tumors may occur at virtually any age. Many studies found a mean age of 32.1 - 37.8 years at time of diagnosis.[24] In the present study, the age distribution averaged 32.2 years and the age range of the patients was 3-87 years. There appeared to be two distinct incidence peaks-between 10 and 19 years and between 20 and 29 years of age. The age distribution in our series was in agreement with those in other reports, with a peak incidence in the third decade of life, followed by the second decade.[3,17,49] Several authors have also noted a second peak between the fifth and eighth decades.[50,51]

The gender distribution may be equal or may have a male predominance (1.3 - 3:1).[13] In our study, the lesions were more commonly found in females than males with the ratio 1: 1.15. In a Thai population, Chirapathomsakul et al found that females were affected slightly more often than males (male:female = 1:1.2).[27] Similarly, Maurette et al found a male to female ratio of 1:2.1 in Brazilians cases.[52]

More KCOTs were found in the mandible than in the maxilla, varying from 65% to 83%, and the most frequent site of occurrence was at angle or ramus of the mandible. In the maxilla, posterior region was also preferentially involved.[17,19] This was quite similar to the result of our study in which the mandible was affected 64%, and the most common site was the posterior mandible. We also found multiple KCOTs; 4 cases in maxilla and mandible and were associated with NBCCS.

KCOT appears as a unilocular or multilocular radiolucency with a scalloped contour. The lesion may be single or multiple, the latter case being more common in patients with the NBCCS. Radiographically, 90 cysts (82.57%) in our study presented as unilocular, which is similar to the study by Partridge and Towers, in which 73.3% were classified as unilocular. The ratios of unilocular to multilocular radiolucent lesions in maxilla and mandible were 6:1 and 1.9:1, respectively. [14,27,53] The incidence of teeth associated with the lesion was higher than previous reports (33% and 22%-26.7%, respectively).[27] In this study, the mandibular third molars were the most frequently impacted teeth, followed by maxillary third molars.

In approximately 50% of patients, the lesions were asymptomatic. Other complaints associated with the lesions were pain, extra-and/or intraoral swelling or drainage, and neurologic involvement.[13,53]

In the present study, most of the lesions were asymptomatic and was observed in 45 cases (41.28%), followed by symptoms of swelling, pain, pus discharge, and neurologic deficit, respectively. KCOTs were coincidentally found during the treatment of other dental problems.

After histopathological analysis, our results regarding epithelial keratinization were similar to those of other authors. Three variations were significantly observed that were similar to previous studies, and included the presence of islands of odontogenic epithelium in the capsule, the presence of daughter cysts in the basal layer, and the occurrence of budding of the basal layer. These represent evidences of the neoplastic nature of the KCOT.[11,13]

In conclusion, this study retrospectively investigated 109 KCOT cases focusing on the clinical manifestations. Patient age ranged from 3 to 87 years with an average age of 32 years, and there was a female predominance (male:female = 1:1.5). The posterior areas of the mandible were the most frequent occurrence sites. Many patients (41.28%) exhibited no symptoms or complaints. On roentgenograms, most KCOTs appeared as unilocular lesions (82.57%), and mandibular

third molars were the most frequently associated impacted teeth. Most KCOTs were formed with a stratified squamous epithelium that produced par keratin.

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