A clinicopathologic review of keratocystic odontogenic tumours (KCOTs) seen at the Lagos University Teaching Hospital

***Efflom OA, **Adeyemo WL, *Akinshipo A, **Gbotolorun OM, *Ajayi OF, *Odukoya O**

*Department of Oral Pathology, Faculty of Dental Sciences, College of Medicine,
**Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences, College of Medicine, University of Lagos

Correspondence: Adeyemo WL
E-mail: lanreadeyemo@yahoo.com

Abstract

Objective: The aim of the study was to review all cases of keratocystic odontogenic tumours (KCOTs) seen over a 37-year period (1972-2008) at the Departments of Oral Pathology & Oral Biology and Oral & Maxillofacial Surgery of the Lagos University Teaching Hospital with a view to highlighting the age, sex, location of lesion, radiological and histological features of the lesion.

Method: Clinical and histological information on all cases of histologically diagnosed KCOTs seen during the period were retrieved and analysed based on the following: age, sex, site of lesion, radiographic appearance, clinical diagnosis at time of hospital presentation, radiographic features and histologic features.

Result: Fifty-four cases of KCOTs were recorded of which 39 (72.2%) were in males and 15 (27.8%) in females. The peak incidence of occurrence was in the 4th decade of life (31.5%). Forty-six (85.2%) tumours were located in the mandible and only eight (14.8%) were located in the maxilla with a mandible-maxilla ratio of 5.8: 1. The most common site of involvement was the 1st and 2nd molar region (42.6%) of both jaws. Multilocular radiolucency was the most common radiographic appearance while parakeratinised form of epithelial lining was the most common histologic form. Ameloblastoma (19 cases), followed by dentigerous cyst (13 cases) were the most common clinical diagnosis made for the KCOTs. There was no cyst associated with Gorlin - Gortz syndrome (GGS).

Conclusion: KCOTs commonly occur in the 4th decade of life and in the mandible. The most common jaw location of KCOTs is the 1st and 2nd molar region with male preponderance. No case of GGS was recorded in our study; therefore the association of KCOTs with GGS is an infrequent finding in this environment.

Key words: Clinicopathologic; review keratocyst, odontogenic tumour,

Introduction

Odontogenic keratocyst (OKC) which was first described by Philipsen in 1956[1] and is one of the most aggressive cysts of the oral cavity. It was subsequently renamed keratocystic odontogenic tumour (KCOT) by the WHO in 2005 and defined as "a benign uni- or multicystic, intraosseous tumour of odontogenic origin, with a characteristic lining of parakeratinized stratified squamous epithelium and potential for aggressive, infiltrative behavior[2]. Due to its unspecific clinical and radiographic features, KCOT may be easily misdiagnosed as ordinary cyst or ameloblastoma.

Radiographically, KCOT generally presents as a well-defined radiolucent lesion with smooth and corticated margins[3-6]. It may present as either a multilocular or unilocular radiolucent lesion[3-6]. Large unilocular KCOTs may be clinically and radiologically indistinguishable from cystic ameloblastomas[3-6], while smaller unilocular KCOTs may be peripherally located and therefore misdiagnosed as periapical cysts[3,5-11]. In addition, in 25 - 40% of KCOTs, there is an un-erupted tooth involved with the lesion[7,12]. This could lead to a radiological misdiagnosis of dentigerous cyst[5,7,8,9,12]. A diagnosis solely based on clinical information and radiological presentation could therefore pose a difficult challenge for surgeons and could result in under-diagnosis and in-appropriate treatment which would cause un-necessary recurrences of the tumour. Histologic examinations of biopsied tumours are therefore pertinent for accurate diagnosis and appropriate patient management.

Although KCOT has been shown to more commonly involve the mandible[3,7,10,13-15], there are still some inconsistencies in its predominant precise location. To the best of our knowledge there has been no study conducted to determine the most predominant precise jaw location of KCOT in Nigerians. In addition, clinicopathologic analysis of the tumour is sparse in the literature, especially from Nigeria or Africa.

The aim of the study was to review all cases of KCOTs seen over a 37-year period (1972-2008) at the Departments of Oral pathology and Oral Biology and Oral and Maxillofacial Surgery of the Lagos University Teaching Hospital with a view to highlighting the age, sex, location of lesion, radiological and histological features.

Materials and Method

Clinical information on all cases of histologically diagnosed KCOTs seen during the period from January 1972 to December 2008 was retrieved from patients biopsy records and case files of the Department of Oral Pathology & Oral Biology and Oral & Maxillofacial Surgery of the Lagos University Teaching Hospital (LUTH). Haematoxylin and eosin (H&E) stained glass slides of these cases were retrieved and re-evaluated to confirm diagnosis. Only tumours that strictly complied with the histologic features described by Pindborg and Hansen[16] for KCOTs were included in the study. These were subsequently analyzed for age, sex, site of lesion, radiographic features, information regarding clinical diagnosis, and histological features. For the assessment of the histological features, multiple celloidinized paraffin sections of each lesion were obtained and stained with H&E stain to assess the following parameters: epithelial tumour lining type, presence of daughter cysts and presence of epithelial rests within the cyst. The following criteria previously used by Ali and Baugman[5] were used to determine the precise jaw location of KCOT in the present series:

1. Anterior location of tumour (AL): From the mid line of the jaw to the distal surface of the lateral incisor
2 Canine location of tumour (CL): From the distal surface of the lateral incisor to the mesial surface of the 1st premolar.
3. Premolar location of tumour (PL): From the mesial surface of the 1st premolar to the distal surface of the 2nd premolar.
4. 1st and 2nd molar location of tumour (ML): From the distal surface of 2nd premolar to the distal surface of 2nd molar.
5. Ramus and 3rd molar location of tumour (RML): From the distal surface of 2nd molar to the distal surface of 3rd molar including the ramus.
6. Tuberosity and 3rd molar location of tumour (TML): From the distal surface of 2nd molar to the distal surface of 3rd molar including the tuberosity.

Recurrent cases, cases with inadequate history and cases with non-classical histologic features of KCOT described by Pindborg and Hansen[16] were excluded from the study.

KCOTs with either parakeratinization or orthokeratinization within its epithelium were labelled parakeratinized and orthokeratinzed respectively.

Data analysis

Data was analysed using the SPSS for Windows (version 12.0; SPSS Inc, Chicago, IL) statistical software package; and presented in descriptive and tabular forms.

Result

Fifty-four cases of histologically diagnosed KCOTs were included in the analysis. The tumour occurred in patients aged 5-45 years with a mean age of 25.1 ±10.0 years and a peak incidence in the 4th decade. A total of 39 KCOTs (72.2%) occurred in males while 15 (27.8%) cases occurred in females with a male-to-female ratio of 2. 6 : 1. **(Figure 1).** There were 46 (85.2%) cases in the mandible and 8 (14.8%) cases in the maxilla with a mandibular: maxillary ratio of 5. 8 : 1 **(Figure2).** A total of 19(35.2%) cases of KCOTs, occurred in the 1st and 2nd mandibular molar region, while a total of 4 cases (7.4%) occurred in the 1st and 2nd maxillary molar region. No tumour was observed in the maxillary canine region **(Figure 2).**

Table 1: Frequency distribution of clinical diagnosis made by clinicians

Clinical diagnosis	Mandible N(%)	Maxilla N(%)	Total N(%)
Ameloblastoma	19(35.2)	0	19(35.2)
KCOT	9(16.7)	1(1.9	10(18.5)
Dentigerous cyst	11(20.4)	2(3.7)	13(24.1)
Nasopalatine cyst	0	1(1.9)	1(1.9)
Periapical cyst	2(3.7)	3(5.6)	5(9.3)
Odontogenicmyxoma	2(3.7)	0	2(3.7)
Periodontal cyst	2(3.7)	1(1.9)	3(5.6)
Giant-cell granuloma	1(1.9)	0	1(1.9)
Total	**46(85.2)**	**8(14.8)**	**54(100.0)**

Table 2: Radiographic presentations of KCOT in relation to type of cystic epithelium

Cystic epithelium	Multilocular N(%)	Unilocular N(%)	Total N(%)
Orthokeratotic	7(13.0)	6(11.1)	13(24.1)
Parakeratotic	24(44.4)	17(31.5)	41(75.9)
Total	**31(57.4)**	**23(42.6)**	**54(100.0)**

Table 3: Site distribution of KCOT in relation to radiographic presentation

X-ray presentation	Mandible N(%)	Maxilla N(%)	Total N(%)
Multilocular	29(53.7)	2(3.7)	31(57.4)
Unilocular	17(31.5)	6(11.1)	23(42.6)
Total	**46(85.2)**	**8(14.8)**	**54(100.0)**

Observation from records showed that the most frequent clinical diagnosis(which was made prior to histological examination and diagnosis), recorded for the mandibular located tumours was ameloblastoma (19 cases/35.2%) , followed by dentigerous cyst (13cases /24.1%) whereas initial clinical diagnosis of KCOT was made only in 10(18.5%) mandibular cases . The most frequent clinical diagnosis recorded the for maxillary lesions was periapical cyst (3cases/5.6%) while initial clinical diagnosis of KCOT was recorded only in 1(1.9%) case **(Table 1).**

A total of 41 (75.9%) cases of KCOTs were lined with parakeratinzed epithelium **(Table 2).** Microcysts were observed in 15(27.8%) cases of KCOTs while epithelial islands were observed in 14(25.9%) cases. **Figure 3** shows a photomicrograph of a typical KCOT (parakeratotic type). Histologically, the lining epithelium which comprised of a palisaded and polarized basal layer of cells, generally had a uniform thickness and was devoid of rete pegs **(Figure 3).**

diagnoses were ameloblastoma and dentigerous cysts for mandibular KCOTs and periapical cysts for maxillary KCOTs. KCOTs can easily be mistaken for other benign odontogenic tumours/cysts or inflammatory lesions of the jaws[3,6,8,10,20]. In addition KCOTs have been observed as small unilocular radiolucencies adjacent to endodontically treated or non-vital teeth[6,10,21].

In the past, the tumour was regarded as a cystic lesion (odontogenic keratocyst)[1]. It is presently considered a benign cystic neoplasm,[19,22] that has a potential for aggressive and infiltrative behaviour, and a development characteristic that is related to the mutation of a suppressor tumour gene PTCH, found in sporadic and in associated basal cell nevus syndrome keratocysts.[23].

KCOTs have a tendency to recur. Average recurrent rate of between 30 -65 percent has been reported in the scientific literature[16,24]. The factors that contribute to high recurrence rate are misdiagnosis and improper management, presence of residual epithelial islands and microcysts in the cystic wall[16,24]. Although recurrent cases were excluded from this study, it is still observed that a quarter of the KCOTs obviously had residual epithelial islands and microcysts within the cystic wall. The mode of expansion of KCOTs differs from other inflammatory cysts. Its growth rate is aggressive because of its high cellular activity and rapid proliferative rate when compared to other inflammatory cysts[10]. High levels of acid phosphates and oxidative enzymes have been observed in KCOTs[14,15]. The presence of high levels of acid phosphatase and oxidative enzymes within a lesion indicates high metabolic and lysosomal activities. This invariably results in increased cell activity and rapid proliferation[14,15].

In the present study, the most common histological variant was parakeratinized epithelium. According to the new classification[2], the microscopic criterion for KCOT clearly indicates that the spectrum of this tumour consists only of jaw lesions with a characteristic lining consisting of parakeratinized stratified squamous epithelium[2]. Odontogenic keratocyst (OKC) previously included both parakeratinized and orthokeratinized variant. Designation of an OKC is currently reserved for cystic jaw lesions that are lined solely by orthokeratinizing epithelium, and they do not form a part of the range of KCOT[2]. In accordance with the current World Health Organization classification[2], the designation of KCOT and OKC are not synonymous. These two entities not only have different microscopic features but also distinct pathobiology: KCOT (previously parakeratinized variant of OKC) shows locally aggressive behavior and a high recurrence rate, whereas orthokeratinized odontogenic cyst (previously orthokeratinized variant of OKC) has a significantly lower recurrence rate[26].

Multilocular radiolucency was the most common radiographic feature in the present series, although a substantial number (23(42.6%) of cases of unilocular radiolucent lesions were observed. KCOTs typically present as multilocular radiolucent lesions[27]. This may be responsible for the most common clinical diagnosis (ameloblastoma) made by clinicians prior to histological examination. Occasionally, a KCOT may envelope an erupted tooth and be indistinguishable radiolographically from a dentigerous cyst or may present as a radiolucent lesion of the jaws[27].

Gorlin-Gortz syndrome is heritable as an autosomal dominant trait; and key features include multiple KCOTs, basal cell naevus syndrome and intracranial/skeletal anomalies[27]. None of the cases in this study was associated with the syndrome.

Conclusion

KCOTs commonly occur in the 4th decade of life and in the mandible. The most common jaw location of KCOT is the 1st and 2nd molar region with male preponderance. KCOT present both as multilocular and unilocular radiolucent lesions of the jaws. No case of GGS was recorded in this study; therefore the association of KCOTs with GGS is an infrequent finding in this environment.

References

1. Philipsen HP. On keratocysts in the jaws. Tandlaege Bladet 1956; 60:963-980.
2. Barnes L, Eveson JW, Reichart P, Sidransky D, ed. Pathology and genetics of head and neck tumours. Lyon: IARC Press; 2005. WHO classification of tumours series.
3. Oda D, Rivera V, Ghanae N, Kenny EA, Dawson KH. Odontogenic keratocyst. The NorthWestern USA experience. J Contemp Dent Prac 2000;1:1-10.
4. Hayashi K, Tozaki M, Yoshida N Fukuda K, Tanabe H. Dynamic multislice helical CT of ameloblastoma and odontogenic keratocyst: correlation between contrast enhancement and angiogenesis. J Comput Assist Tomogr 2002;26:922-926.
5. Ali M, Baughman RA. Maxillary odontogenic keratocyst. A common and serious clinical misdiagnosis. J Am Dent Assoc 2003;134:877-883.
6. Mozaffari E, Marnior DS, Alawi F. Odontogenic keratocyst with a misleading clinical and radiologic appearance. Quintessence Int 2007; 38:837-841.
7. Brannon RB. The odontogenic keratocyst: a clinincopathologic study of 312 cases. Part II-histologic features. Oral Surg Oral Med Oral Pathol 1977; 43:233-255.
8. O'Neill R, Al -Hezaimi K. Identification of an odontogenic keratocyst and treatment with guided tissue regeneration: case report. J Can Dent Assoc 2011; 77:b6.
9. Coleman A, Altini M, Ali H, Doglioni C, Favia G, Maiorano E. Use of calretinin in the differential diagnosis of unicystic ameloblastoma. Histopathology 2001; 38:312-317.
10. Veena KM, Rekha Rao, Jagadishchandra H, Prasanna Kumar Rao. Odontogenic keratocyst. Looks can be deceptive, causing endodontic misdiagnosis. Cases reports in pathology. 2011; 2011 article ID 159501, 3 pages. doi: 10.1155/2011/159501.
11. Garlock JA, Pringle GA, Hicks ML. The odontogenic keratocyst: a potential endodontic misdiagnosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85:452-456.
12. Meara JG, Li KK, Shah SS, Cunningham MJ. Odontogenic keratocysts in the pediatric population. Arch Otolaryngol Head Neck Surg 1996; 122:725-728.

13. Myoung H, Hong SP, Lee JI et al. Odontogenic keratocyst: review of 256cases for recurrence and clinicopathologic parameters. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001; 91:328-333.
14. Chow H. odontogenic keratocyst: a clinical experience in Singapore. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 86:53-57.
15. Neville BW, Dam DD, Allen CM, Bouquot J. Oral and maxillofacial pathology, W.B Saunders, Philadelphia, Pa, U.S.A, 2nd edition, 2004.
16. Pindborg JJ, Hansen J. Studies on odontogenic cyst epithelium: clinical and roentgenologic aspects of odontogenic keratocysts. Acta Pathol crobiol Scand 1963; 58:283-294.
17. Panders AK, Hadders HN. Solitary keratocysts of the jaws J Oral Surg 1969; 27:931-938.
18. Kakarantza- angelopoulou E, Nicolatou O. Odontogenic keratocyst: clinicopathologic study of 87 classes. J Oral Maxillofac Surg 1990; 48:593-599.
19. Shear M. The aggressive nature of odontogenic keratocyst; is it a benign cystic neoplasm? Part 1. Clinical and early experimental evidence of aggressive behaviour. Oral Oncol 2002; 38:219-226
20. Tsukamoto G, Sasaki A, Akiyama T, et al. A radiologic analysis of dentigerous cysts and odontogenic keratocysts associated with a mandibular third molar. Oral Surg Oral Med Oral Pathol Oral Radiol Endod2001;91:743-747.
21. Nohl FS, Gulabivala K. Odontogenic keratocyst as periradicular radiolucency in the anterior mandible: two case reports. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996; 81:103-109.
22. Henly J, Summerlin DJ, Tomich C. Zhang S, Cheng L. Molecular evidence supporting the neoplastic nature of odontogenic keratocyst: a laser capture microdissection study of 15 cases. Histopathology 2005;47:582-586.
23. Barreto DC, Gomez RS, Bale AE, Boson WL, De Marco L. PTCH gene mutations in odontogenic keratocysts. J Dent Res 2000; 79:1418-1422.
24. Zachriades N, Papanicolaou S, Triantafyllou D. Odontogenic keratocysts: review of the literature and report of sixteen cases. J Oral Maxillofac Surg 1985;43:177-182.
25. Magnusson BC. Odontogenic keratocysts: a clinical and histological study with special reference to enzyme histochemistry. J Oral Pathol 1978; 7:8-18.
26. Macdonald-jankowski DS. Orthokeratinized odontogenic cyst: A systematic review. Dentomaxillofac Radiol 2010; 39-455-460.
27. Cawson RA, Odell EW. Essentials of oral pathology and oral medicine. 6th Ed. Churchill Livingstone, UK, 1998: 97-116.