

Keratocystic Odontogenic Tumour: An Experience in the Northeast of Brazil

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SUMMARY

Introduction Keratocystic odontogenic tumours raise particular interest, because of their high recurrence rate and association with nevoid basal cell carcinoma syndrome.

Objective To analyze the clinical and histopathological features of all cases diagnosed as keratocystic odontogenic tumour in a Brazilian population.

Methods A total of 64 keratocystic odontogenic tumours, arising in forty-six patients, were evaluated using the following parameters: association with nevoid basal cell carcinoma syndrome, gender, age at first diagnosis, race, anatomical location, symptoms, radiographic features, history of recurrence, association with teeth, and treatment.

Results Keratocystic odontogenic tumours were more frequent among women than men (1:0.84). The mean patient age was 31.5 years (SD: ±16.6). Ten tumours (16.4%) involved the maxilla and 51 (83.6%) the mandible. Swelling (n=12; 46.1%), followed by pain and swelling (n=4; 15.3%), were most common clinical manifestations. A unilocular radiotransparency with well-defined margins was the main radiographic finding (n=29; 87.8%). A significant association was observed between the multilocular radiographic pattern and recurrence ($p < 0.05$, Fisher's Test). Sixty-one (95.3%) tumours were treated by surgical enucleation followed by bone curettage, and the recurrence rate was 13% (n=6). This study showed that the keratocystic odontogenic tumours relapsed within a mean period of 25-36 months.

Conclusion Despite the results of this study being similar to previous reports found in the literature, it provides an important insight about keratocystic odontogenic tumours in a Brazilian population.

Keywords: epidemiology; odontogenic tumours; Brazilian population

INTRODUCTION

Keratocystic odontogenic tumours (KOTs) are benign cystic epithelial neoplasms that affect the jaw bones [1] and arise from the dental lamina [1, 2] or its remnants and extensions of basal cells from the overlying oral epithelium [3]. Since their first description in 1956 by Philipsen [4] KOTs have raised particular interest because of their locally aggressive behaviour, high recurrence rate, specific histopathological characteristics, and tendency towards development of multiple lesions, especially when associated with nevoid basal cell carcinoma syndrome (NBCCS) [4, 5]. This syndrome is a dominant autosomal disease with complete penetrance and variable expression, which is characterized by abnormal skeletal development, ectopic calcifications and multiple KOTs, as well as a predisposition to the development of basal cell carcinomas [6].

KOTs usually affect the mandible. Radiographically, these lesions present as unilocular or multilocular radiolucent areas with uniform sclerotic borders associated or not with unerupted teeth [7, 8]. Histopathologically, these tumours are characterized by an

atrophic, parakeratinized stratified squamous epithelium exhibiting palisade-like basal cells [1]. Epithelial detachment from the cystic wall is observed in some cases [8, 9].

OBJECTIVE

Little is known about the epidemiological profile of KOTs in Brazil, especially those reported in the English literature [10]. Therefore, the aim of the present study was to investigate a Brazilian population with KOTs, diagnosed between 2002 and 2008. The following aspects were emphasized: gender, age at first diagnosis, race, anatomical location, symptoms, radiographic features, history of recurrence, association with teeth and NBCCS, histology and types of treatment.

METHODS

This study was approved by the Ethics Committee on Human Research of the Gonçalo Moniz Research Center (FIOCRUZ, Bahia). A survey

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KOT cases was performed at a surgical pathology service, in the city of Salvador, Bahia.

Forty-six patients, registered between 2002 and 2008, were identified in the archives of this laboratory, and a total of 64 lesions of KOTs were diagnosed and included in this study. All tumours were reassessed histomorphologically by an experienced oral pathologist (J.N.S) using the 2005 World Health Organization criteria [1]. Clinicopathological data, such as gender, age at first diagnosis, race, anatomical location, symptoms, radiographic features, history of recurrence, association with teeth and NBCCs and types of treatment, were retrieved from the biopsy charts and/or patient records. Only KOTs that involved the same anatomical location were included as recurrent according to Stoelinga [3].

The differences were tested using statistically Fisher's χ^2 test, as the data showed no normal distribution. The level of significance was set at 5%. All statistical calculations were performed with the Bioestat 5.0 program (Sociedade Civil Mimirauá, MCT-CNPq, Conservation International, Brasil, 2003).

RESULTS

The sample comprised 46 patients with a histopathological diagnosis of KOT between 2002 and 2008. Six (13%) of these patients had a diagnosis of NBCCS and presented multiple lesions. The clinicopathological features are summarized in Table 1.

Twenty-five (54.3%) patients were females and 21 (45.6%) were males at a proportion of 1:0.84. Patients' age at first diagnosis ranged from 6 to 73 years, with a mean of 31.5 years (SD \pm 16.6). However, considering the distribution according to decades, most patients were between 21 and 30 years old (n=14, 30.5%). With respect to race, 14 (40%) patients were of mixed origin, 13 (37.4%) were African Brazilians and 8 (22.85%) were Caucasians.

In 20 (43.5%) patients, KOTs were discovered upon routine radiographic examination. However, 26 (56.5%) patients reported some symptoms. They were represented by swelling (n=12, 46.1%), but four (15.3%) patients reported swelling followed by pain (Table 2).

In the present series, most patients (n=39; 84.8%) had only one KOT and five (10.8%) presented multiple lesions. In the latter group, all patients had the diagnosis of NBCCS.

Among the studied KOTs, 10 (16.4%) involved the maxilla and 51 (83.6%) the mandible, with the region of the corpus and ramus being most frequently affected (n=27; 44.3%)

Radiographic findings were evaluated in 33 patients. Twenty-nine (87.8%) of these patients appeared as unilocular radiotransparency with well-defined margins and four (12.1%) presented a multilocular aspect. A significant association was observed between a multilocular radiographic pattern and recurrence (p<0.05, Fisher's test). The tumours were associated with unerupted teeth in 10 (30.3%) patients and displaced teeth in eight (24.2%) (Figure 1).

Histologically, all KOTs showed a thin cystic wall exhibiting the epithelial lining of uniform thickness, as well as



Figure 1. Radiographic features of keratocystic odontogenic tumours in panoramic radiographs. **A** – Large multilocular radiolucency involving symphysis and parasymphysis bilaterally, and causing resorption and displacement of roots or teeth. **B** – Large multilocular radiolucency extending from the body until the coronoid process of right mandible; the lesion is associated with unerupted tooth. **C** – Unilocular radiolucent lesion close to the right unerupted third molar. **D** – Multiple unilocular radiolucent lesions located in the mandible of the patient with NBCCS.

Table 1. Clinical and epidemiological aspects of keratocystic odontogenic tumours (KOTs) in a Brazilian population

Patient	Age (years)	Gender	Symptoms	Location
1	60	Male	Swelling	Corpus and ramus
2	-	Female	Absent	Corpus and ramus
3	24	Male	Absent	Corpus and ramus
4	46	Female	Absent	Posterior maxilla
5	23	Male	Pain, swelling, exudation	Corpus and ramus in both
6	24	Female	Absent	-
7	13	Female	Absent	Posterior maxilla
8	16	Male	Absent	-
9	43	Female	Absent	Corpus and ramus
10	15	Female	Pain and exudation	Anterior maxilla
11	61	Male	Pain and swelling	Corpus and ramus
12	-	-	Swelling	Ramus
13	-	Male	Absent	Corpus and ramus
14	22	Female	Absent	-
15	30	Female	Swelling	Symphysis/parasymphysis
16	44	Male	Exudation	Corpus and ramus
17	60	Female	Swelling	Corpus and ramus
18	19	Female	Absent	Posterior maxilla
19	32	Female	Absent	Corpus and ramus in both
20	55	Female	Pain and swelling	Corpus; corpus and ramus; ramus; ramus
21	24	Male	Swelling, exudation, fistula	Symphysis/parasymphysis
22	19	Female	Absent	Symphysis/parasymphysis; right and left posterior maxilla; right and left corpus and ramus
23	10	Female	Swelling	Corpus
24	16	Male	Swelling	Ramus
25	37	Female	Swelling	Posterior maxilla
26	24	Female	Absent	Symphysis/parasymphysis; right and left corpus and ramus; posterior maxilla
27	32	Male	Pain and swelling	Ramus; anterior and posterior maxilla
28	12	Female	Swelling	Ramus
29	22	Male	Absent	Corpus and ramus in both
30	21	Male	Absent	Ramus
31	-	Female	Pain	Corpus and ramus
32	41	Female	Absent	Corpus
33	11	Male	Swelling	Symphysis/parasymphysis
34	46	Male	Absent	Corpus and ramus
35	31	Male	Pain and exudation	Corpus
36	27	Male	Exudation	Corpus and ramus
37	23	Female	Paresthesia	Corpus
38	31	Female	Absent	Ramus
39	58	Male	Swelling	Corpus and ramus in both
40	24	Male	Absent	Corpus and ramus
41	22	Female	Pain and swelling	Corpus and ramus in both
42	17	Male	Pain	Symphysis/parasymphysis
43	47	Male	Absent	Corpus
44	59	Female	Exudation	Corpus
45	73	Female	Swelling	Corpus
46	6	Female	Swelling	Corpus; symphysis/parasymphysis

parakeratinized and corrugated surface. Other features were also found, including satellite cysts, epithelial islands, subepithelial splits, and significant chronic inflammation which was seen in 26 (56.52 %) cases. We also observed hyperplastic epithelium, due to inflammation, in 15 (32.6%), as well as the Roushton body in only one case (Figure 2). Ameloblastoma, dysplasia, and carcinoma were not found.

Sixty-one (95.3%) tumours were treated by surgical enucleation followed by bone curettage, and three (6.5%) tumours were treated only by enucleation. Follow-up information was available for 30 patients and ranged from 12

to 48 months. Six (13.05%) patients of the present series had recurrent KOTs, with these tumours relapsing within a mean period of 25-36 months in most cases (n=4).

DISCUSSION

According to retrospective epidemiological studies, KOTs account for 7.2% to 21.5% of all odontogenic jaw cysts [11-17]. Table 2 compares the epidemiological profile of our series with those reported by other investigators over the last 10 years.

In the present study, KOTs showed a discrete predominance for females, with a female/male proportion of 1:0.84. Although most studies have reported a discrete male predominance of these tumours [4, 5, 18, 19], other demonstrated a female predominance [7, 10] or even no gender preference [8, 9]. With respect to age distribution,

Table 2. Clinical and epidemiological data of cases of keratocystic odontogenic tumours published over the last 10 years compared to present study

Author [reference]	Year	No. of patients	Gender (Male:Female)	Mean age (years)	Anatomical site	Radiographic feature	Association with unerupted tooth	Recurrence	Patients with NBCCS
Stoelinga [3]	2001	80	1:1	-	Angle and ramus	Unilocular	52.4%	10.9	0
Myoung et al. [4]	2001	256	1.42:1	30.8	Molar mandibular	-	-	58.3	4.29%
Habibi et al. [5]	2007	74	1.47:1	27.08	Corpus and ramus	-	-	8.4	6.75%
Chirapathomsakul et al. [7]	2006	51	1:1.2	36.9	Corpus and ramus	Unilocular	31.3%	22.6	-
González-Alva et al. [9]	2008	183	1.05:1	32.8	Corpus and ramus	-	-	13.1	6.01%
Maurette et al. [10]	2004	28	-	-	Angle and ramus	-	46.4%	14.3	Not included
Bataineh and Al Qudah [18]	1998	31	1.8:1	34	Angle and ramus	Multilocular	-	0	-
Morgan et al. [19]	2005	40	1.7:1	40.7	Corpus and ramus	-	-	22.5	-
Lam and Chan [20]	2000	69	1.4:1	23	Posterior mandible	-	-	24	4.34%
Oda et al. [21]	2000	393	3:2	-	Corpus	-	-	-	4.32%
Zhao et al. [22]	2002	484	1.93:1	31.2	Ramus and angle	Unilocular	35.3%	15.2	Not included
Madras and Lapointe [24]	2008	21	-	-	Corpus and ramus	-	-	29	-
Chow [25]	1998	70	1.68:1	32.8	Posterior mandible	-	52.8%	20	1.42%
Yagyu et al. [26]	2008	74	1.96:1	41.1	Corpus	Unilocular	27.1%	14.3	Not included
Pogrel and Jordan [29]	2004	10	1.5:1	-	-	-	-	-	0%
Present study	2011	46	0.84:1	31.5	Corpus and ramus	Unilocular	30.3%	13	13%

NBCCS – nevoid basal cell carcinoma syndrome

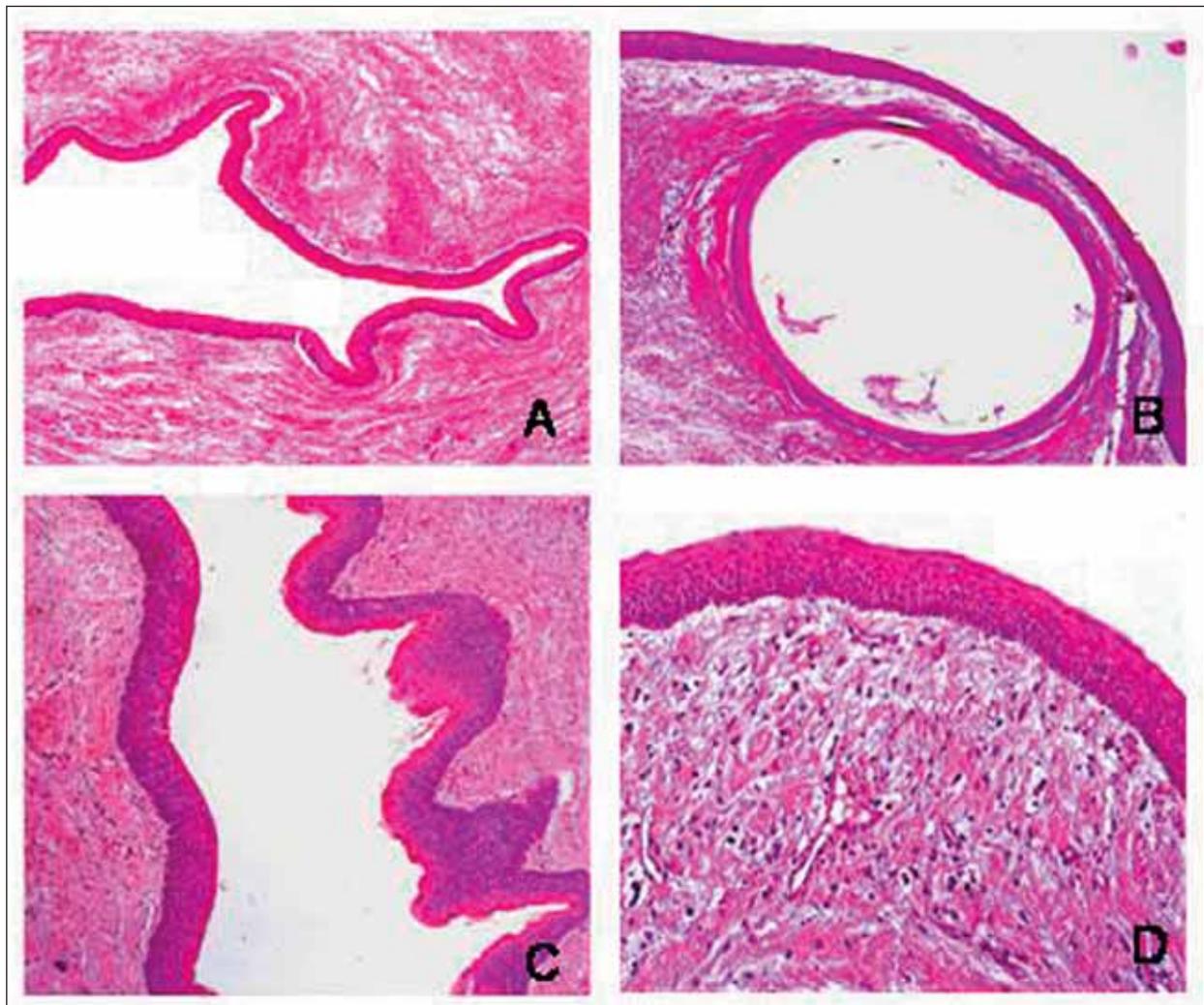


Figure 2. Keratocystic odontogenic tumour. **A** – cystic wall covered by atrophic, stratified squamous epithelium (H/E, $\times 40$). **B** – cystic wall with satellite cyst (H/E, $\times 40$). **C** – parakeratinized and corrugated surface exhibiting palisade-like basal cells (H/E, $\times 100$). **D** – epithelial lining with palisade-like basal cells and slight chronic inflammation (H/E, $\times 200$).

KOTs were more frequent among patients in the third decade of life, with a mean age around 30 years. Therefore, as observed in this series, KOTs are more common in young adults [4, 9, 20, 21, 22]. However, only one case was diagnosed in a paediatric patient group. [1, 4, 7, 18]. It is important to state that although the inclusion of syndromic or non-syndromic patients with multiple KOTs may reduce the age distribution when studying groups of patients [1], in the present study the inclusion of five syndromic patients with more than two lesions does not seem to have influenced this distribution.

According to Oda et al. [21], Maurette et al. [10], Morgan et al. [19], KOTs are more common in Caucasian individuals. This finding is in contrast to the present series in which 40% and 37.4% patients were of mixed origin and African Brazilians, respectively. This result might be explained by the racial profile of the population of the city of Salvador (Bahia, Brazil), which is characterized by a predominance of African Brazilians and miscegenation [23].

This study showed that 26 (56.5%) patients reported some symptoms, especially swelling and pain, in agreement with other investigators who reported that KOTs can be symptomatic at the time of diagnosis and, when present, these symptoms are most common [4, 5, 7].

In the present study, KOTs more frequently affected the mandible (83.6%) than the maxilla (16.4%), with the body and the ramus being the main anatomical sites involved. Similar results have been reported in previous studies [7, 8, 20, 22, 24]. As observed in the present investigation, other studies also demonstrated that the posterior region of the mandible showed a high rate of recurrence [4, 7]. In our series, KOTs were detected upon routine radiographic examination in 20 (43.5%) patients. This result agrees with Chow [25] who reported that this tumour may infiltrate bone tissue in the anteroposterior direction without causing cortical bone expansion, thus being identified incidentally during a routine radiographic examination.

A unilocular radiopacity with well-defined margins was the most frequent finding in the present series. This presentation is the most characteristic of KOTs [7, 8, 21] and seems to be indistinguishable from other odontogenic lesions. A multilocular aspect of KOTs was found in only four patients, with a significant association between this radiographic feature and recurrence ($p < 0.05$, Fisher's test). According to Stoeltinga [3], the multilocular presentation of KOTs impairs surgical treatment; this occurs due to the difficult approach and, consequently, incomplete removal of the whole tumour. KOTs were associated with unerupted teeth in 30.3% patients and displaced teeth in 24.2%. Similar findings have been found in other countries like Singapore [25], Japan [26] and China [22].

NBCCS presents a low prevalence and affects one in 56,000 live born individuals [9]. Recent genetic studies have demonstrated that alterations in the Sonic Hedgehog signalling pathway are related to the phenotype of these patients [6]. Multiple KOTs are frequent in patients with the syndrome and are one of the main criteria for the diagnosis of this disease [27]. Although some investigators [8, 19] excluded syndromic patients from their series

based on the assumption that the tumours present distinct biological characteristics and a more aggressive biological behaviour in these patients, in the present series six (13%) patients were syndromic. This percentage is higher than that reported by Chow [25] and Habibi et al. [5] who observed rates of 1% and 6.75%, respectively. According to Shear [8], the presence or absence of multiple KOTs might be associated with the variable expression of NBCCS. Thus, patients with recurrent KOTs should be investigated regarding the presence of the syndrome even in the absence of other clinical features, especially conducting genetic studies.

Histologically, our cases fulfil the criteria adopted by the World Health Organization. The lesions disclosed a cystic wall with parakeratinized stratified squamous epithelium and a well-defined basal layer [1, 20]. As observed in the present series, epithelial islands, satellite cysts, hyaline bodies, epithelial budding of basal layers and dystrophic calcifications have been described by others [4, 5, 8].

Surgical enucleation followed by bone curettage was the treatment of choice in the case of 61 tumours (95.3%), with this protocol being adopted by the Surgery Service where the patients were treated. According to Stoeltinga [2] and Maurette et al. [10], in addition to preserving important anatomical structures, conservative protocols such as marsupialization, enucleation and curettage reduce morbidity and the need for bone reconstruction, favouring faster social reintegration of the patient. Since most patients of this series were young adults, the choice of this therapeutic modality seems to have been adequate. However, the ideal treatment of KOT is still a matter of debate, because of the high recurrence rate of this tumour [18]. As a consequence, a wide variety of therapeutic modalities have been proposed, including curettage, enucleation, enucleation with Carnoy solution or liquid nitrogen, enucleation associated with peripheral osteotomy, marsupialization/decompression associated with secondary enucleation, and resection [7, 19, 24, 28, 29].

Six (13.05%) patients of this series presented recurrent KOTs. The wide variation in recurrence rates ranging from 0 to 62% [25] has been attributed to different periods of follow-up and to the diversity in the surgical techniques adopted [24]. It should be noted that the lesions of five syndromic patients included in this series were primary KOTs and therefore did not contribute to this rate. In this study, KOTs relapsed within a mean period of 25-36 months. These results agree with Stoeltinga [3] and Maurette et al. [10] who reported that most recurrences occur within a period of 5 years.

CONCLUSION

To the best of our knowledge, this is the second series of KOTs described in the Brazilian population, and it is consistent with previous reports. However, further retrospective data from other regions of our country should be accumulated through more extensive investigations to add new insights about keratocystic odontogenic tumours in the Brazilian population.

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Кератоцистични одонтогени тумор: искуство из североисточног Бразила

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КРАТАК САДРЖАЈ

Увод Кератоцистични одонтогени тумори изазивају посебно интересовање због њихове велике учесталости и удружености са синдромом карцинома невоидних базалних ћелија.

Циљ рада Циљ рада је била анализа клиничких и хистопатолошких одлика свих случајева са дијагностикованим кератоцистичним одонтогеним тумором у популацији Бразила.

Методе рада Код укупно 64 болесника анализирани су следећи параметри: удруженост кератоцистичних одонтогених тумора са синдромом карцинома невоидних базалних ћелија, пол и раса болесника, старост испитаника приликом постављања дијагнозе обољења, анатомска локација тумора, симптоми болести, радиографска обележја, историја рецидива, удруженост са зубима и лечење.

Резултати Кератоцистични одонтогени тумори су откривани чешће код жена него код мушкараца (1:0,84). Просечна старост болесника била је 31,5 година ($SD: \pm 16,6$). Десет тумора (16,4%) захватало је максилу, док је 51 тумор (83,6%)

утврђен на мандибули. Едем (12 болесника; 46,1%) праћен боловима и едемом (четири болесника; 15,3%) био је најчешћа клиничка манифестација обољења. Добро ограничена унилокуларна радиотранспарентност била је главни радиолошки налаз (29 болесника; 87,8%). Примећена је значајна удруженост мутилокуларног радиографског обрасца и рецидива ($p < 0,05$, Фишеров тест). Код 61 болесника (95,3%) тумор је одстрањен хируршком енуклеацијом уз киретажу кости, док је рецидив забележен код шест болесника (13%). Истраживање је показало да код кератоцистичних одонтогених тумора долази до појаве рецидива просечно у периоду од 25 до 36 месеци.

Закључак Упркос томе што су резултати овог истраживања слични налазима раније објављених студија, оно пружа значајан увид у кератоцистичне одонтогене туморе код становника Бразила.

Кључне речи: епидемиологија; одонтогени тумори; популација Бразила