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Odontogenic Keratocysts: A 10 year Retrospective Review of 209 Cases for Recurrence and Related Factors in an Iranian Population

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Abstract: The Odontogenic Keratocysts (OKC) are epithelial developmental cysts of the jaws with a higher frequency of recurrences due to the incomplete removal of the cyst, difficulty in access to the lesion locations or eruption of the new cyst in the place. The objective of the present study was to determine the frequency of OKC post-operative recurrences and the possible affective factors in patients referred to Dr. Shariati Hospital and Tehran Dental School during 1996-2006. In this retrospective descriptive study, 209 patients (61.2% males, 38.8% females) were selected by census sampling and assessed. Different characteristics of the OKC lesions were obtained from the patient's records or calling them. The effect of possible variables on the incidence of recurrence was statistically analyzed by Cox regression and the survival rate of the patients was determined by Kaplan-Meier test. The mean age of OKC involvement was 34.5 years and the most frequencies were observed in the third (62, 29.7%), fifth (40, 19.1%) and second (32, 15.3%) decades of the life. The most frequent OKC locations were mandibular (136, 65%), mandibular posterior (98, 46.9%), maxillary posterior (28, 13.4%) and maxillary anterios (12, 5.7%). Enucleation (202, 96.7%), curettage (76, 36.4%) and peripheral ostectomy (75, 35.9%) were the mostly used surgery techniques. Of the total patients, 37 individuals (17.7%) showed OKC recurrences after initial surgery, of which 14 cases (37.8%) occurred in the mandibular posterior and 6 cases (16.2%) in the maxillary posterior. Most cases had recurrences 12 months after the initial surgery (13, 35.1%). Aggressive curettage was statistically associated with the decreased recurrences while the gender, age, lesion location and other surgeries were not

statistically associated with the recurrence incidence. The recurrence ratio of 17.7% among OKC patients referred to Dr. Shariati Hospital during 1996-2006 was similar to the existing repost in the literature.

INTRODUCTION

Odontogenic Keratocyst (OKC) is a developmental odontogenic cyst known for its exclusive histopathologic characteristics and high rate of recurrence. OKCs are seen in a wide age range from the childhood to old ages; however, about 60% of the incidence rates were reported in 10-40 years old age group. The peak incidence is the second and third decades of life (60-80%) and significantlocation dominance has been noted for the posterior body of the mandible and ascending ramus[1].

In radiographic view, OKCs are seen as a unilocular well-circumscribed radiolucent area. In larger lesions, multilocular radiolucent areas can be seen, especially in the posterior mandible in the ascending ramus. Small OKCs are frequently asymptomatic being identified during routine radiographic examinations; however, larger OKC lesions are possibly associated with pain or drainage. OKCs grow anterio-posteriorly in the bone central socket without any distinct bony expansion. Multiple OKCs may possibly grow in a patient[1]. Keratocysticodontogenic lesions are diagnosed according to the histopathologic findings for which radiographic or clinical examinations are helpful hints only. As the cysts mimic radiologic views of different lesions, the assessment of radiographic and clinical findings and their correlations can be useful to develop a correct diagnosis.

Multiple OKCs are related with nevoid basal cell carcinoma syndrome[2] and the malignant transformation of OKCs has also been shown[3, 4]. The high recurrence rate and aggressive pattern of the OKC have suggested it as a benign neoplasm rather than a cyst[4].

Histologically, odontogenickeratocysts contain a layer of 6-10 cells with a basal layer of palisaded cells and corrugated parakeratin surface layer. Internal layer of the cyst socket contains corrugated parakeratinzed epithelial cells with some diffuse orthokeratinized areas[4].

The radiographic view of the OKCs is a unilocular or multilocular well-circumscribed radiolucent lesion with scalloped and corticated margins[6]. Involvement of an unerupted tooth is shown in 25%-40% of the cases. Radiographically, movement of impacted or erupted teeth, root resorption, root displacement or extrusion of erupted teeth may be present[5].

In contrast to other cysts, OKCs are prone to more recurrence rate after the treatment[1]. The recurrence rate has been reported to be 3.5% in the case of complete lesion removal and 39% in the cases the lesions being removed in different pieces. The highest recurrence rate was 50% for the mandibular posterior area and the overall OKCs recurrence rate is 30.5% too. The most recurrence rate has been reported in the fifth decade of life[7]. In one twentieth of OKCs, the lesions are orthokeratinized in type with less recurrence rate[8]. A reason for the OKC recurrences is thinner wall and possible remained parts during surgery as well as formation of new cysts from small daughter cysts (Marx and Stern). This hypothesis is accepted due to the higher rate of recurrence in the parakeratinizedkeratocysts compared to the orthokeratinized lesions. In the latter group, lower recurrences have been reported for the thicker cyst wall and simple removal of the cysts[9]. The cyst exceedingly high recurrence rate has resulted in many attempts to improve surgical techniques or develop novel treatment options.

The exact reason for the cyst recurrence remainsunknown; however, the surgical treatment option is mentioned to be as a related factor[9]. The most OKCs recur 5 years following the primary surgery but some recurrences have been reported after 10 years or more[1]. Therefore; long-term clinical and radiographic assessments are necessary to detect recurrence possibility.

The present study determined the frequency of OKC post-operative recurrences and the related factors in patients referred to Dr. Shariati Hospital and Tehran Dental School during 1996-2006.

MATERIALS AND METHODS

The present retrospective descriptive study was done on 209 records of the OKC patients referred to Dr. Shariati Hospital in Tehran and Tehran Dental School during 1996-2006. The study protocol was approved by the ethics committee of Tehran University of Medical Sciences, Tehran, Iran. The selection of Dr. Shariati Hospital and Tehran Dental School for this study was based on the higher number of patients referred to these centers for the treatment of oral and maxillofacial disorders. At first, the records of the patients were over viewed in the Department of Oral and Maxillofacial Surgery and studied.

All the studied lesions were diagnosed according to the histopathologic findings and the treatments were performed according the standard options. The data

including the patients' age, gender, lesion's recurrence, surgery option and lesion's involvement location were collected using a questionnaire. The site of involvement was classified by dividing the maxilla and mandible into 2 regions, the anterior and the posterior. In the cases of inadequate demographic data or invalid follow-up findings, the patients were excluded from the study.

To obtain the most valid data, we triedto call the patients and receive the information regarding different aspects of the OKCs. The patient's records were used as the data source in the cases with no telephone call. The assessments were done by a final year dental student who received adequate instructions of the field and calibrated before the study.

Due to the incomplete records and inability of the researchers to call all the patients in some cases; there were a few cases without any information regarding the patients' age or the lesions' location. The data were collected using frequency and percentage indices. Cos regression analysis was used to predict the effects of different parameters on the lesions recurrence while the patients'survival following surgical treatments was analyzed by Kaplan Meier analysis.

RESULTS

The study included 81 females (38.8%) and 128 males (61.2%). Two hundred and two patients (96.7%) were treated by enucleation, 5 (2.4%) by cutter, 76 (36.4%) by curettage, 75 (35.9%) by peripheral ostectomy, 21 (10.0%) by fresage and 15 (7.2%) by aggressive curettage. All cutter, curettage, peripheral ostectomy, fresage and aggressive curettage treatment options were performed in association with enucleation. Most OKC lesions had occurred in the mandible (136, 65%) while the mandibular posterior (98, 46.9%), maxillary posterior (28, 13.4%) and maxillary anterior (12, 5.7%) ranked in the next orders. In 11 (5.3%) cases; no data existed regarding the lesions location (Table 1).

The patients' age ranged from 10-78 years at the time of diagnosis (mean: 34.5 years). The most frequency of OKCs were observed in the third (62, 29.7%), fifth (40, 19.1%), second (32, 15.3%), fourth (31, 14.9%), sixth (20, 9.6%), eighth (8, 3.8%) and seventh (7, 3.3%) decade of life, respectively.

OKCs were located in the oral cavity midline in 11 (5.3%) patients; the syndrome was associated with a cyst in 4 (1.9%) cases; the tooth extraction was performed during surgery procedure in 16 (7.7%) cases; marsupialization surgical operation was done in 2 (1.0%) cases, Lefort 1 surgery was done in 1 (0.5%) case; complete resection of the jaw was performed in 5 (2.4%) cases and Caldwel surgical operation was performed for 1 (0.5%) patient.

Thirty seven (17.7%) of the studied patients showed the lesions recurrences after the treatment while there were no recurrences in 172 (82.3%) patients. Most lesions recurred 12 months after the primary surgery (13, 6.2%). The 3-year recurrence rate of OKCs was reported to be 24.8% (26 of 105 surgical cases) while the 5-year recurrence rate of the surgical removal of the OKCs was 31.0% (31 of 100) (Table 2).

Regarding Kaplan-Meier analysis, the mean and standard error of the patient's survival following the surgical removal of OKCs without any recurrences was 131.73 and 7.0 month (95% confidence interval: 118.01-145.45 months).

Cox regression showed the recurrence rate of the lesions to be decreased when using aggressive curettage. In the final regression model, it was found that aggressive curettage when accompanied with the peripheral ostectomy ofthe recurrence rate would be decreased. No other parameters of the lesions location, age, gender and different methods of surgery influenced the recurrence rate.

Table 1: Site of involvement in OKC patients referred to dr. shariati hospital in tehran and tehran dental school during 1996-2006

Site	Number	Percent
Maxilla	10	4.8
Mandible	21	10.0
Maxilla posterior region	28	13.4
Maxilla anterior region	12	5.7
Mandible posterior region	90	43.1
Mandible anterior region	8	3.8
Extensive maxillary anterior region	3	1.4
Extensive maxillary anterior-posterior area	7	3.3
Extensive maxillary posterior region	1	0.5
Extensive mandibular posterior area	8	3.8
Extensive mandibular anterior-posterior area	3	1.4
Extensive mandibular anterior area	1	0.5
Mandibular premolar area	5	2.4
Maxilla/mandible	1	0.5
No indentified	11	5.3

Table 2: Time of recurrence following surgery in OKC patients referred to Dr. Shariati hospital in tehranand tehran dental school during 1996-2006

Site	Number	Percent
No recurrence	172	82.3
7 (Months)	1	0.5
12	13	6.2
24	7	3.3
36	5	2.4
48	3	1.4
60	2	1.0
84	1	0.5
96	1	0.5
120	1	0.5
180	3	0.5

DISCUSSION

The recurrence rate of OKC lesions in the patients referred to the Dr. Shariati Hospital in Tehran and Tehran Dental School during 1996-2006 was 17.7% (37out of 209 patients). The recurrence rate of OKCs reported by different studies is given on Table 3.

Most lesions recurred 12 months after the initial surgery (13/37; 6.2% of total OKCs). The 3 year OKC recurrence rate was 24.8% (26/105) and 5 year recurrence ratio was reported to be 31.0% (31/100) too. Some studies showed higher incidence of recurrence 5 years following the initial surgery resembling our findings as 31 of 37 total recurrences were observed after 5 year post-surgery[10]. Therefore, routine radiographic examinations are recommended for the patients after the primary surgery to detect possible recurrence cases[11, 12].

According to Table 3, lower recurrence rates are noted in the recent investigations compared to the older studies. Less recurrence rates in the recent studies are possibly related to the development of more effective treatment modalities which limit epithelial proliferation following the surgery. These modalities include using carnoy's liquid (13) or cryoagent [43, 44] in the cyst linings prior to its removal. Therefore; in the case of remaining a piece or parts of lesions after the surgery they will disappear using these methods. Furthermore, removing superficial tissues as a part of the surgical procedure during cyst removal in the posterior mandibular areas as the cyst of most prevalent recurrence site, eliminates plenty epithelial remnants in the area[45]. These methods have been used as means of lowering recurrence by removing the remaining epithelium.

Table 3: The recurrence rate reported in the literature

Study	Total number	Recurrence
Pindborg and Hansen[13]	16	62.0
Toller[14]	55	51.0
Rud and Pindborg[15]	21	33.0
Panders and Hadders[13]	22	14.0
Borwne[16]	85	25.0
McIvor[17]	43	5.0
Payne[18]	20	45.0
Rittersman and Van Gool[19]	48	32.0
Dodoff *et al*.[20]	13	15.0
Forssell *et al*.[21]	38	29.0
Eversole *et al*.[22]	35	20.0
Brannon[5, 6]	283	12.0
Hodgkinson *et al*.[2]	74	39.0
Vedtofte and Praetorius[23]	57	51.0
Forssell[24]	121	40.0
Voorsmit *et al*.[25]	52	13.5
Ahlfors *et al*.[4]	255	27.0
Zachariades *et al*.[26]	16	25.0
Partridge and Towers[10]	45	27.0
Forssell *et al*.[27]	75	43.0
Brondum and Jensen[28]	44	18.0
Marker *et al*.[29]	23	8.7
El-Hajj and Anneroth[30]	87	30.5
Dammer *et al*.[31]	52	6.0
Bataineh and Al Qudah[11]	31	0.0
Stoelinga[32]	82	10.9
Myoung *et al*.[7]	132	58.3
August *et al*.[33]	11	18.0
Pogrel and Jordan[34]	10	0.0
Zhou *et al*.[35]	10	0.0
Morgan *et al*.[36]	40	22.5
Maurette *et al*.[37]	28	14.3
Varol etc	2	0.0
Chirapathomsakul[38]	51	22.6
Papagiannopoulos etc	42	2.4
Habibi *et al*.[39]	83	8.4
Madras and Lapointe[40]	27	29.0
Gonzalez-Alva *et al*.[41]	183	13.1
Pitak-Arnnop *et al*.[42]	120	26.0
Khodayari Namin etc	37	13.5
Present study	209	17.7

More difficulties exist to standardize the data of recurrences in the different studies. In some cases, there is multiple odontogenic keratocysts in a patient[46] and then a lesion recurrence status cannot be exactly validated as a new cyst possibly develops in the adjacent area. In addition, most studies like our investigation included syndrome patients too leading to the increased recurrence rate. In the case of excluding syndrome-associated patients from the study population, the recurrence rate will be decreased.

Some parameters may influence the recurrence rate of OKC lesions. Factors of the length of the follow-up period, the treatment modalities presented, the skill of the surgeon, size of the lesions and the number of the cases investigated are all important in this regard[47]. Furthermore, various clinical and pathologic parameters such as the patient's age, gender, the lesion involvement area and histopathologic findings are possibly effective in this regard. The relationship between OKC recurrence rate and sexof the patient is the issue of some debates. In the present study; sex, lesion site, the patient's age and different surgical modalities did not significantly influence the recurrence rate except to the aggressive curettage surgery which decreased the recurrence possibility. However, Ahlfors *et al*.[4] reported different recurrence rates regarding the patient's gender[4]. Similar to our findings, Myoung *et al*.[7] reported no relationship between the patient gender and OKC recurrence rate[7].

From the total of 37 OKC recurrences, 14 cases were located in the mandible's posterior area and the other 6 cases were reported in the maxillary posterior areas. Some studies have reported that the site of involvement could be related to the recurrence incidence[26, 16]. However, in the present investigation, the lesions involvement site did not significantly predict the recurrence incidence. El-Hajj and Anneroth[30] showed more recurrences in the lesions located in the mandible[30]. Similar findings have been reported in the other studies[17, 25]. One hypothesis given to this difference rate is the area's surgical accessibility in different areas. Lesions in the mandibular molar areas

could be larger in size before being symptomatic while complete removal of OKCs from the mandibular ramus would be difficult[7].

Although, with different surgical modalities used as OKC treatment option, enuclearion remains the most common method to remove these lesions which possibly explain the high recurrence rate of the lesions in turn[7, 48]. In the present study, 202 (96.7%) of the total 209 patients in the studied centers were treated with the surgical enucleation (alone or together with other techniques). According to Myoung *et al*.[7] findings, 99% of the treatments were done using this technique too[7].

The main objective of the treatment is to completely remove OKC lesions. However, some attempts must be made to reduce the recurrence rate and surgery complications too[49-51]. Resection treatment modality led to more improvements in the patients; although with multiple complications such as jaw deformities; suggesting this method must be limited to the cases of aggressive or recurrent lesions or to the patients their routine and exact follow-up examinations cannot be performed[9, 52, 53]. In addition, some argued that enucleation approach was inappropriate treatment modality due to the higher recurrence rate for which 62.5% has been reported as the peak recurrence rate[9, 52, 53].

Some mechanisms have been suggested regarding the OKC higher recurrence rate such as inadequate removal of the cyst wall, the presence of epithelial islands and micro-cysts, new cyst formation in the involvement area, presence of parakeratocysts and difficulty of access to the surgical area[4, 9, 51, 53].

The exact locations of the epithelial islands and microcystshad not been identified yet. They are possibly located in the connective tissue cyst wall, superficial soft tissue or cyst bony bed. The objective of using liquid nitrogen, carnoy solution or peripheral ostectomy is to remove epithelial islands and micro-cysts in the cyst surrounding bone. It has been shown that the recurrence rate will be significantly decreased using adjunctive treatment modalities together with the enucleation procedure[49,53]. According to the present study, recurrence rate decreased when aggressive curettage and enucleation were simultaneously used.

As epithelial islands and microcysts may be located in the superficial tissues of the cyst contact area especially in the mandibular retromolar and maxillary tubersit[49], freezing or removal of the adjacent osseous tissues did not affect the recurrence incidence. Furthermore, peripheral ostectomy may scatter microcysts embedded into the bone and increase the recurrence risk subsequently[53]. The present study showed that using peripheral ostectomy and aggressive curettage was effective to decrease OKC recurrence rate which maybe related to the efficacy of aggressive curettage treatment option.

The patient's age varied widely in the present study being different from 10-78 years. The peak incidence of OKCs was noted in the third (29.7%) and fifth (19.1%) decades of life for the studied population. El-Hajj and Anneroth[30] reported the most frequency of OKCs in the second decade of life[30]. Some showed the peak incidence in the second and fifth decades[7, 16] while the other suggested fifth[54] and sixth decades as the peak incidence ages. Myoung *et al*.[7] reported the mean age of OKC patients to be 30.8 years being less than our findings (34.5 years)[7]. Mean age of OKC patients have been reported 41.7 years by Morgan *et al*.[36], 41 years by Ahlfors *et al*.[4] and 37 years by Brannon (1976) (Brannon, 1976). Khodayari Namin etc suggested third (29.7%) and second (18.5%) decades of life as the peak age range of patient wassimilar to our findings. Bande[55] showed OKCs incidence to be higher in the third and fourth decades in the central India with a mean age of 28 years for males and 31 years for the females[55]. Differences in age distribution of OKC lesions can be related to the racial status of the studied individuals.

The incidence of the odontogenic cysts in the present study was highly reported in the males than females (61.2 Vs. 38.8%). Khodayari etc have reported a male predilection for the lesions (2.375:1). Ali and Baughman[56] reported the ratio of 1.3:1 with a male predilection being similar to the other studies[5-7, 56]. However, in some investigations; higher incidence of OKCs were reported in females than males[37, 57].

Maxillary (13.4%) and mandibular posterior areas (10%) were the most involved regions for the OKC lesions in the present study. Ali and Baughman[56] reported higher incidence of OKCs in the mandible (66.8%)[56]. According to Maurette *et al*.[37], mandible (angle and ramus areas) was the mostly involved area (5.3%) being similar to our findings to some degrees[37]. Khodayari Namin showed more involvement in the third molar area, jaw angle and ramus in an Iranian population. In a study done in the central India; more OKC lesions were observed in the mandibular angle and ramus area[55].

Retrospective studies cannot detect the cause and effect relationships between the different parameters due to the inability to control the role of interfering variables, not assessing the total population and some incomplete data. The records of patients in the health centers and hospitals are archived for the clinical objectives and not for the research aim being prone to some missing data. All these factors cause varied and scattered findings to be obtained regarding distribution of OKCs in terms of age, gender, location or their recurrence in the different studies.

CONCLUSION

Of total 209 patients, the recurrence ratio of 17.7% (37 patients) among OKC patients referred to Dr. Shariati Hospital during 1996-2006 was similar to the existing repost in the literature.

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