ORIGINAL ARTICLE

HISTOPATHOLOGICAL EVALUATION OF ODONTOGENIC KERATOCYSTS AND RADICULAR CYSTS IN PESHAWAR

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ABSTRACT

Odontogenic cysts are jaw lesions that may be misdiagnosed due to lack of complete data. Clinical, radiographic and histopathological correlation is required for the diagnosis of these cysts. The study was thus designed to determine frequency and compare the histopathological features of radicular cysts and odontogenic keratocysts in population of Northern Pakistan.

The study was conducted at Sardar Begum Dental College and Khyber College of Dentistry, Peshawar. Non-probability, consecutive sampling technique was used to select 70 cases of odontogenic cysts from 190 cystic jaw lesions. Formalin-fixed paraffin-embedded tissue samples of Odontogenic keratocysts (n=22) and radicular cysts (n=48) were retrieved from the archives of Khyber College of Dentistry and Sardar Begum Dental College, Peshawar. Frequencies of the cysts were calculated. These were then evaluated for histopathological variables which included thickness of epithelial lining, keratinization, foamy macrophages, mucous cells, Rushton bodies, cholesterol crystals and haemosiderin. Chi-square test / Fishers exact test was applied to compare cysts. The data was analyzed using SPSS version 21.

Frequency of the radicular cyst and odontogenic keratocyst was 68.5% (48N) and 31.5% (22N) respectively. The histopathological features showed presence of mucous cells, vacuolated cells, spongiosis, micro-abscesses, cholesterol crystals, hemosiderin and inflammatory infiltrate. The radicular cyst was the most prevalent in our study 48(68.5%), followed by the odontogenic keratocysts 22(31.5%). The histopathological features observed in these cysts are comparable with other populations of Pakistan and abroad.

Key Words: *Histopathological evaluation, Odontogenic keratocysts, Radicular cysts*

INTRODUCTION

One of the most common pathological lesions of the maxillofacial region is the odontogenic cyst. These cysts are seen most frequently in the jaws as odontogenic epithelial rests and have a very close association with the jaw bones.[1] In jaws, post- odontogenesis proliferation of the epithelial cells of Malassez, the reduced enamel epithelium and cell rests of Serres can give rise to odontogenic cysts. These lesions are mostly slow-growing, benign and non-invasive. Despite their benign nature, they may be the cause of some serious problems, like fracture of the maxilla or mandible or mobility of the teeth. These complications may occur due to the late diagnosis or no diagnosis of odontogenic cysts.[2]

Odontogenic cysts of the head and neck region can be classified as developmental or of inflammatory origin.[3] Odontogenic keratocysts (OKCs) are developmental in origin arising from dental lamina. They are locally aggressive with a high rate of recurrence, which necessitates correct diagnosis and ultimately correct surgical treatment. The World Health Organization (WHO) has included odontogenic keratocysts in the classification of tumours in 2005, and it is renamed as Keratocystic Odontogenic Tumour (KCOT).[4]

Radicular cysts are inflammatory odontogenic cysts as they form due to infection of the tooth pulp canal. The infection reaches the connective tissue of the periodontal ligament through the apical foramen. The inflammatory response stimulates the proliferation of epithelial rests of Malassez eventually forming

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radicular cyst.[5]

Due to similarity in clinical and radiological features of cystic lesions, a detailed clinical, radiographic and histological analysis is required for the correct diagnosis.[6]

MATERIALS AND METHODS

A descriptive study was carried out in patients who presented with cystic lesions of the jaws to two hospitals namely Sardar Begum Dental College and Khyber College of Dentistry Peshawar. The data was retrieved from the archives of the two mentioned hospitals from the time period of previous six years (2008-2014). The study was approved by the Ethical Committee of Gandhara University, Peshawar.

After careful radiological and histopathological examination of 190 cystic jaw lesions, 90 cases of odontogenic cysts were reviewed of which 70 cases were selected. Two odontogenic cysts namely radicular cyst and OKCs were included in the study. Non-odontogenic cysts, cases with incomplete data and all other odontogenic cysts were excluded. Deeper sections of some blocks revealed some cysts to be odontogenic tumour 'Ameloblastoma' on their histopathological evaluation, so these samples were also excluded from the study. Demographic data including age, gender, ethnicity and site were obtained from the archives of Khyber College of Dentistry Peshawar, whereas the formalin-fixed paraffin-embedded tissue blocks of samples were obtained from the archives of the City Medical laboratory Peshawar. New slides were prepared for evaluation and re-diagnosed by two consultant histopathologists. Frequencies of OKC and radicular cysts were calculated. The cystic lesions were then evaluated for histopathological variables which included presence or absence of keratinization, cytological atypia and tumour arising within cyst lining, foamy macrophages, mucous cells, vacuolated cells, Rushton bodies, spongiosis , ciliated cells , necrosis, micro-abscesses and Russel bodies, cholesterol crystals, hemosiderin and inflammatory infiltrate. Statistical analysis of the data were done using SPSS version 21. Mean and SD were calculated for age. Categorical variables were presented by frequency and percentage. Chi-square /Fishers Exact test was applied to compare both the cysts. Level of significance was kept at □=0.05 with 95% confidence interval. If *p* value is less than or equal to alpha (□=0.05) then the results are significant.

RESULTS

After careful histopathological evaluation, a total of 70 histologically proven cases of radicular cysts (n=48) and OKCs (n=22) were included in the study from two hospitals namely Sardar Begum Dental College and Khyber College of Dentistry Peshawar. All the patients were Pathans of the Peshawar District.

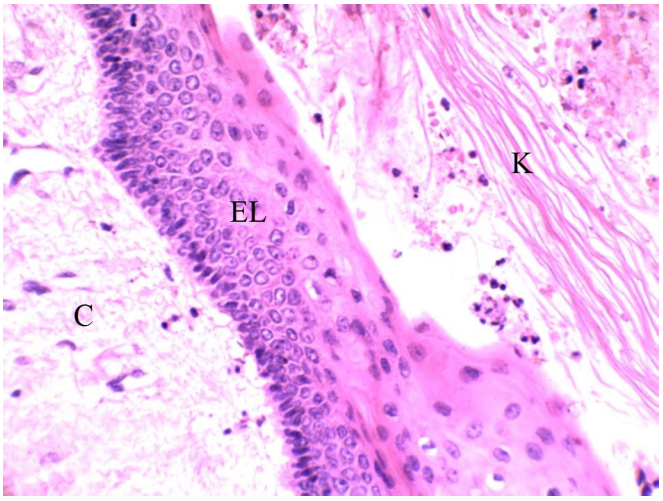

Fig 1: Odontogenic Keratocyst. High power view of epithelial lining (EL) showing palisaded basal layer and corrugated luminal surface. Lumen shows keratin (K). Lining is covered with fibrous capsule (C).

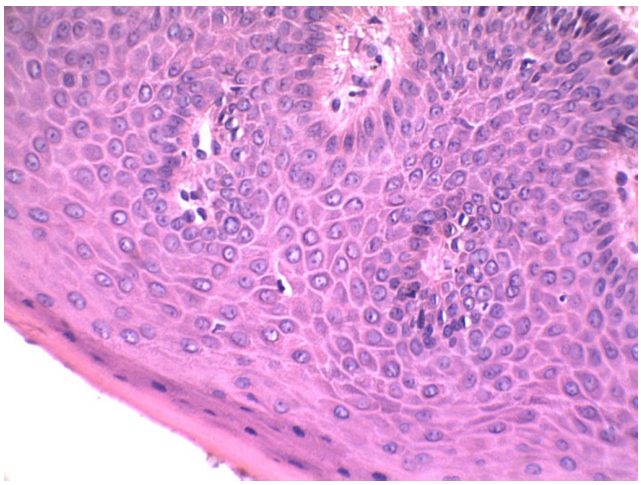

Fig 2: Radicular cyst. High power view showing cholesterol clefts (C) in the fibrous capsule.

TABLE 1: SITES OF OKCS AND RADICULAR CYSTS

	Odontogenic keratocyst	Radicular Cyst	p value
Anterior maxilla	6(27.27%)	32(66.7%)	<0.001*
Posterior maxilla	4(18.2%)	0	
Anterior mandible	2(9%)	10(20.8%)	
Posterior mandible	10(45.5%)	6(12.5%)	
	22	48	

p<0.05 is significant p value.* shows the value is significant.

TABLE 2: HISTOPATHOLOGICAL FINDINGS IN EPITHELIAL CELL LININGS OF OKCS AND RADICULAR CYSTS

Findings in epithelium		Odontogenic keratocyst	Radicular cyst	p value
Mucous cells	Present	1(4.5%)	11(22.9%)	0.09
	Absent	21(95.5%)	37(77.1%)	
Exocytosis	Present	----	10(20.8%)	0.03*
	Absent	22(100%)	38(79.2%)	
Spongiosis	Present	2(9.1%)	4(8.33%)	>0.05
	Absent	20(90.9%)	44(91.6%)	
Micro abscesses	Present	4(8.2%)	16(33.3%)	0.19
	Absent	18(81.8%)	32(66.7%)	
Epithelium-connective tissue interface rete ridges		8(36.36%)	42(81.5%)	<0.001*
Epithelium- connective tissue interface flat		14(63.63%)	6(12.5%)	

p<0.05 is significant p value.* shows the value is significant.

TABLE 3: FINDINGS IN THE CONNECTIVE TISSUE CAPSULE OF BOTH CYSTS

Findings in connective tissue capsule	Odontogenic keratocyst	Radicular cyst	p value
Loose stroma	18(81.8%)	40(83.3%)	>0.05
Dense stroma	4(18.2%)	8(16.67%)	
Hemorrhage	4(18.2%)	22(45.83%)	<0.001*
Cholesterol crystals	-	11(22.92%)	
Foreign body giant cells	-	4(8.33%)	
No Findings	18(81.8%)	11(22.92%)	
Chronic inflammation	10(45.45%)	39(81.25%)	<0.001*
Acute and chronic inflammation	4(18.2%)	9(18.75%)	
No Findings	8(36.36%)	0	

p<0.05 is significant p value.* shows the value is significant.

Mean age of the patients with radicular cyst (n= 48) was 24.81 ±14.08 years while mean age of patients with OKC (n=22) was 27 ±13.91 years. Male predominance was seen in radicular cysts 28(58.3%), while OKCs were more common in females 13 (59%). The anterior maxilla was the most predominant site for the occurrence of radicular cysts 32(66.6%) while the keratocysts 10(45.45%) were predominantly found in the posterior mandible. The radicular cyst was the most prevalent in our study 48(68.5%), followed by the odontogenic keratocysts 22(31.5%). The sites of OKCs and radicular cysts are given in Table 1.

The results of histopathological features assessed in the epithelial lining of OKCs and radicular cysts are as under:

Among diagnosed selected cases (n=70), 46(65.7%) of them were non-keratinized cysts and 24 (34.3%) showed keratinization of the epithelial cell lining. All of the OKCs (n=22) were keratinized whereas only few radicular cysts (n=2) demonstrated keratinization.

The epithelial lining is very important during histopathological examination of odontogenic cysts, as a large number of them have an entire and conserved epithelial lining. The data of this study indicates that most of the patients presented with thick epithelial lining. About 31(64.5%) of the radicular cysts and 1(4.5%) of the OKCs had a lining between 10-50 cells thick. A lining of 6-10 cells thick was found mostly in the odontogenic keratocysts 20(91%) and only 15(31.25%) of the radicular cysts. In the 1-5 cell thickness category, radicular cysts had 2(41%) whereas OKCs had only 1(4.5%) with thin lining. Histopathological findings in the epithelial lining of both the cysts are shown in Table 2.

Other features like cytological atypia, tumour arising within cyst lining, foamy macrophages, Rushton bodies, Russel bodies, ciliated cells and necrosis and were not found in any of the selected samples.

The fibrous connective tissue capsule showed a loose stroma in 40 (83.3%) of radicular and 18(81.8%)

of OKCs. Histopathological findings in the capsule of both the cysts are shown in Table 3.

Epithelial lining of odontogenic keratocysts and cholesterol clefts in the fibrous capsule of radicular cyst are shown in figures 1 and 2 respectively.

DISCUSSION

During tooth formation, there is a very complicated interaction of the connective tissues in the tooth bearing areas with the enamel organ. If the enamel organ is not completely resolved after completion of tooth formation, a number of lesions can arise which include odontogenic cysts and tumours. Due to similarities between these lesions and the different behaviors of the odontogenic cysts, we need to diagnose these cysts very accurately with the necessity for proper treatment planning.[7]

In the present study, the most common odontogenic cysts were the inflammatory radicular cysts 48(68.5%), followed by developmental OKCs 22(31.5%). These findings are in consistent with previous studies conducted by Bataineh et al [8] and Selvamani et al [9] in which the most common odontogenic cysts were radicular cysts. The larger number of inflammatory cysts i.e. the radicular cyst can probably be explained by the fact that there are probably more people with carious, non-vital teeth rather than with impacted teeth and keratocysts.

Mean age of the patients with radicular cysts was 24.81±14.08 years, while mean age for OKCs was 27±13.91 years. Similar results were shown in Nigerian and Iranian studies[1,10] with slight variation from our study.

In the present study, a slightly higher male predominance was seen in radicular cysts 28(58.3%) and female predominance was noted in OKCs 13(59%). This is in accordance with other studies.[3,11] This may be because of the fact that males are not good at maintaining oral hygiene, and negligence lead to carious lesions eventually ending in cyst formation.[5,10,12] Shuja Riaz</author></authors></contributors><titles><title>Frequency and Demography of Commonly Occurring Odontogenic cysts in Khyber Pakhtunkhwa (Pakistan Contrast results were reported in a Nigerian study.[1]

Majority of the radicular cysts (66.6%) were found in the anterior maxilla and the OKCs (45.5%) in posterior mandible. This is in accordance with studies conducted in our country.[11,13] The presence of maximum number of radicular cysts in the anterior maxilla is probably because the maxillary anterior teeth are more prone to caries and trauma making them non vital and leading to cyst formation. Also the presence of maximum number of odontogenic keratocysts in the posterior mandible supports the fact that they are associated with impacted third molars.[11]

In the present study, 46(65.7%) of the cases were non-keratinized cysts and 24 (34.3%) showed keratinization of the epithelial cell lining. All of the OKCs showed keratinization. The factors responsible for keratin formation are poorly understood. Mahasweran et al noticed that keratin production was a metaplastic process, influenced by inflammation and was due to an adaptation to the environment of the cyst contents. It was interesting to note that cysts with mild and moderate inflammation exhibited keratinization while the severely inflamed were non-keratinized. This may be due to the fact that mild and moderate inflammation causes mild epithelial hyperplasia which encourages keratinization, whereas severe inflammation is lethal to the epithelial cells which inhibits keratinization.[14]

Mucous cells were found in the lining of 11(23%) of radicular cysts and only 1(4.5%) of OKCs. Tsesis et al reported mucous cells in 47(6.6%) of radicular cysts which is lower than the present study. The presence of mucous cells and ciliated cells in epithelial lining of odontogenic cysts is a metaplastic change, in which squamous epithelial cells are replaced by mucous cells. This change occurs due to reprogramming activity in precursor cells of epithelial rests of Malassez and is mediated by cytokines.[15] Ciliated cells were not found in the present study.

Vacuolated cells were present in 10(20.8%) of radicular cysts and were not seen in any of the OKC. According to a case report by Priya et al, the vacuolated cells represent basically a stage in histogenesis of mucous metaplasia. Initially before metaplasia occurs, the cells become vacuolated and ultimately accumulate mucin granules forming mucous cells.[5] In a study by Hedge et al, a few of the vacuolated cells stained positive with PAS reagent thus supporting the fact that it is a stage in histogenesis of mucous cells.[16] PAS stain was not applied in the present study. Spongiosis was seen in 40(54%) of radicular cysts in a Brazilian study compared to 4(18.8%) in our study which might be due to their increased sample size.[17]

Cholesterol clefts were observed in the capsules of 11(23%) of the radicular cysts while none were observed in the OKCs. Various theories have been put forward for the origin of these crystals including degenerating erythrocytes, disintegrating lymphocytes, macrophages and plasma cells, and circulating plasma lipids.[18] In another study carried out in Chennai, the highest incidence of cholesterol clefts were present in the connective tissue capsule of 43.5% of radicular cysts while the lowest incidence was found in odontogenic keratocysts (17.1%). This high ratio present in radicular cysts supports the fact that inflammation has a role in cholesterol cleft formation.[19] Alcantara et al found out that major portion of the cholesterol came from dying inflammatory cells, irritation releasing lipids from their membranes. These crystals were an important factor in lesion persistence, since they acted as local irritants and were a source of continuous irritation.[20]

Hemorrhage was also found in 22(45.8%) radicular and 4(18.18%) of OKC's. Similar results were reported by Santos et al.[17] This high proportion of RBC's in the capsule also supports the theory that their disintegration products could be one of the sources of cholesterol crystals.[19] Macrophages engulf degenerated cells and become foamy due to lipids in their cytoplasm. These foamy macrophages have been reported by santos et

al[17] (n=10), but were not found in any of the cysts in our study.

Foreign body giant cells were present only in 4(8.3%) of radicular cysts and were not seen in OKCs. Since the crystals behave as foreign bodies and raise an inflammatory response, the foreign body giant cells whenever found are present in the vicinity of the cholesterol clefts.[19]A higher frequency (17%) of giant cells was observed in a Brazilian study, which can be attributed to the large number of cases selected.[17]

Most of the studies conducted worldwide focused on frequency of odontogenic cysts and their demographic details which include age, gender, site of the cysts without any morphological details.[2,3,4,6] Clinical, radiographic and histopathological evaluation is essential to successfully diagnose odontogenic cysts. Histopathological features were not evaluated in regional studies[11,13] as well as studies conducted in various parts of the world[9,12] which were highlighted in our study.

CONCLUSION

Oral pathologists should be aware of the histopathological features which differentiate cysts from one another, though they may appear similar on radiographs. Since each cyst has different histopathological features and different biological behavior, there is a dire need to study their morphology in detail for accurate diagnosis and effective management.

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2 Nighat Ara:	Conception and design of article, acquisition of data, analysis and interpretation of data, drafting of the manuscript.
3 Mir Rizwan Ahmed:	Proof Reading.
4 Nizam-Ud-Din Khan:	Provision of blocks from Lab and rediagnosis of slides.
5 Qiam-Ud-Din:	Provision of samples for the study.
6 Tariq Sarfaraz	Critical review of the manuscript.