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Research Article

Inflammation Severity in Radicular Cysts and Its Relationship with Age and Gender

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Abstract

Aim: In this study, in radicular cyst cases in our department; It was aimed to evaluate the severity of inflammation (active and chronic inflammation) and to investigate its relationship with age and gender.
Material and Method: Radicular cyst cases between 01.01.2013 and 31.01.2022 in Ordu University, Faculty of Medicine, Department of Pathology were included in the study. Ethical approval was taken from Ordu University Medical School, Clinical Trials Ethical Committee (2022/82). Preparations of the cases were found from the archive and examined microscopically to score the severity of inflammation. To examine any relationships that existed between categorical variables, Chi-square test was used. To determine any relationships between the score variables, correlation analysis was done.
Results: A statistically significant moderate negative correlation was observed between age and chronicity in women (r=-0.410, p=0.013). A statistically significant moderate positive correlation was observed between activity and chronicity scores in men (r=0.592, p<0.001). When all patients were considered, weakly significant negative correlation was found between activity and chronicity (r=0.312, p<0.001). While one was increasing, the other was increasing.
Conclusion: In radicular cyst cases, the severity of inflammation may differ from case to case. In our study, the severity of chronic inflammation was observed as high-grade (grade 3) in most of the cases, acute inflammation was found to be mild (grade 1) in most of the cases. It is thought that determining the severity and type of inflammation in the histopathological evaluation may be beneficial for diagnosis and treatment.

Keywords: Radicular cyst, odontogenic cyst, inflammation

INTRODUCTION

Odontogenic cysts are generally divided into inflammatory and developmental types according to their etiology. Developmental cysts; includes dentigerous cyst, primordial cyst, eruption and gingival cysts. Inflammatory odontogenic cysts include lateral periodontal cysts and radicular cysts (RC) (1). Inflammatory periapical lesions constitute 63.24% of the material examined in the oral pathology department (2). Apical inflammatory lesions are generally thought to occur with the progression of dental caries causing pulp necrosis (3). Ramachandran Nair et al. detected 39 (15%) of 256 periapical lesions as apical cysts (4).

RC is a subtype of apical lesions, and its prevalence varies between various studies. In a study by Johnson et al., it was reported that RC were observed with a rate of 54.6% among odontogenic cysts (5). Cystic lesions are partially or completely (true cyst) covered by epithelial lining and these lesions are defined as pathological cavity associated with damaged tooth apex (6,7). Microscopically, the capsule consists of cystic epithelium supported by connective tissue; stratified squamous epithelial tissue consists of several layers of cells (8,9).

RC are common lesions in daily dental practice. Histologically, the lumen of the cyst is lined by stratified squamous epithelium, which originates in the epithelial remnants of Malassez. The cyst wall consists of fibrous connective tissue containing a chronic infiltrate of

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inflammatory cells. Intense bone resorption by active osteoclasts contributes to the intraosseous expansion of the RC growing within the periapical bone tissue. However, the mechanisms related to cavity enlargement and epithelial lining formation are not fully known (10).

MATERIAL AND METHOD

Radicular cyst cases between 01.01.2013 and 31.01.2022 in ODU Faculty of Medicine, Department of Pathology were included in the study. Preparations of the cases were found from the archive. Hematoxylin&eosin (HE) stained preparations were examined microscopically to score the severity of inflammation. RC cases were divided into 3 grades according to the severity of inflammation. Each preparation is graded at 200X magnification. All samples were graded for inflammatory status in three consecutive microscopic fields. For inflammation, examination was performed starting from the epithelial-connective tissue border and extending to the lamina propria.

Grade I: Inflammatory cells, less than 1/3 per area,

Grade II: Inflammatory cells, 1/3 to 2/3 per area

Grade III: inflammatory cells scored more than 2/3 per area (10).

Data Analysis

Chi-square test was used to examine any relationships that existed between categorical variables. In the test, Likelihood ratio test statistic was used instead of Pearson's test statistic when the expected counts were <5 in the crosstabs. To determine relationships between the activity, Chronicity, and age, Spearman's rank correlation coefficient was calculated. The type I error rate was taken into account as 5%. IBM SPSS v28 (IBM, Armonk, NY, USA) was used as a statistical program.

RESULTS

Frequency analysis of the data was performed and a total of 70 patients, 51.4% female and 48.6% male, between 2013-2021 were included in the study. 36 patients were female, 34 patients were male. The mean age was found to be 36.64±15.52.

According to Table 1, RC was observed more frequently in the mandible (57.1%) as localization.

Table 1. Distribution of samples according to localizations and activity and chronicity scores

		n	%
Localization	**Maxilla anterior**	9	12.9
	Maxilla right	9	12.9
	Maxilla left	12	17.1
	Mandible anterior	5	7.1
	Mandible right	18	25.7
	Mandible left	17	24.3
Activity score	**0**	28	40.0
	1	33	47.1
	2	7	10.0
	3	2	2.9
Chronicity score	**1**	12	17.1
	2	23	32.9
	3	35	50.0

The relationships between age, activity and chronicity are shown in Table 2. The activity score did not change with increasing age in women and there was no significant relationship between them (r=-0.156, p=0.363). The chronicity score showed an inverse relationship with age, and a moderately significant negative correlation was determined between age and chronicity (r=-0.410, p=0.013). There was no significant relationship between activity and chronicity scores (r=0.312, p=0.064).

The relationship between age and activity in men was not statistically significant (r=-0.154, p=0.386). Similarly, there was no significant relationship between age and chronicity (r=-0.243, p=0.167). A moderately significant positive correlation was observed between activity and chronicity scores (r=0.592, p<0.001).

Considering all the patients, there was no statistically significant relationship between age and chronicity (r=-0.183, p=0.128), but there was a moderately significant negative correlation between age and chronicity (r=-0.354, p=0.003). A weakly significant positive correlation was also observed between activity and chronicity (r=0.312, p<0.001), while one was increasing, the other was increasing too.

Table 2. Relationship between age, activity and chronicity

			Age		Activity	
		n	r	p	r	p
Female	**Activity**	36	-0.156	0.363	0.312	0.064
	Chronicity	36	-0.410	0.013		
Male	**Activity**	34	-0.154	0.386	0.592	**<0.001**
	Chronicity	34	-0.243	0.167		
Total	**Activity**	70	-0.183	0.128	0.481	**<0.001**
	Chronicity	70	-0.354	0.003		

r: Spearman's rho correlation coefficient

According to Chi-square test, there was no significant relationship between localization and activity score (p=0.380). The activity score did not differ according to localizations (Table 3).

According to Chi-square test, there was no significant correlation between localization and chronicity score (p=0.599). The chronicity score did not differ according to localizations (Table 4).

According to the Chi-square test, the activity score did not differ significantly according to localization (p=0.207). The chronicity score also did not change according to localization (p=0.380) (Table 5).

Table 3. Relationship between localization and activity score

	Activity								Total	
	0		1		2		3			
Localization	n	%	n	%	n	%	n	%	n	%
Maxilla anterior	4	44.4	2	22.2	2	22.2	1	11.1	9	100.0
Maxilla right	2	22.2	7	77.8	0	0.0	0	0.0	9	100.0
Maxilla left	4	33.3	5	41.7	2	16.7	1	8.3	12	100.0
Mandible anterior	2	40.0	3	60.0	0	0.0	0	0.0	5	100.0
Mandible right	6	33.3	10	55.6	2	11.1	0	0.0	18	100.0
Mandible left	10	58.8	6	35.3	1	5.9	0	0.0	17	100.0
Total	28	40.0	33	47.1	7	10.0	2	2.9	70	100.0
p	0.380 (χ^2=16.037)									

χ^2: Chi-square test

Table 4: Relationship between localization and chronicity score

	Chronicity								Total	
	0		1		2		3			
Localization	n	%	n	%	n	%	n	%	n	%
Maxilla anterior	3	33.3	2	22.2	4	44.4	9	100.0	9	100.0
Maxilla right	0	0.0	4	44.4	5	55.6	9	100.0	9	100.0
Maxilla left	3	25.0	3	25.0	6	50.0	12	100.0	12	100.0
Mandible anterior	1	20.0	3	60.0	1	20.0	5	100.0	5	100.0
Mandible right	3	16.7	5	27.8	10	55.6	18	100.0	18	100.0
Mandible left	2	11.8	6	35.3	9	52.9	17	100.0	17	100.0
Total	12	17.1	23	32.9	35	50.0	70	100.0	70	100.0
p	0.599 (χ^2=8.307)									

χ^2: Chi-square test

Table 5. Relationship between localization and activity, chronicity score

		Location				Total		p
		Maxilla		Mandible				
		n	%	n	%	n	%	
Activity	0	10	33.3	18	45.0	28	40.0	0.207
	1	14	46.7	19	47.5	33	47.1	(χ^2=4.561)
	2	4	13.3	3	7.5	7	10.0	
	3	2	6.7	0	0.0	2	2.9	
	Total	30	100.0	40	100.0	70	100.0	
Chronicity	1	6	20.0	6	15.0	12	17.1	0.827
	2	9	30.0	14	35.0	23	32.9	(χ^2=0.380)
	3	15	50.0	20	50.0	35	50.0	
	Total	30	100.0	40	100.0	70	100.0	

χ^2: Chi-square test

According to Chi-square test, there was a significant correlation between activity and chronicity score (p<0.001). Activity score varied according to chronicity score (Table 6). The distributions of those with a chronicity score of 1, 2, and 3 in those with an activity score of 0 were 35.7%, 42.9%, and 21.4%, respectively. This ranking is 3.0%, 30.3% and 66.7% for those with an Activity score1, and 0.0%, 14.3% and 85.7% for those with an Activity score2, and 50.0%, 0.0%, and 50.0% in those with an Activity score3. Among those with an activity score of 0, those with chronicity 2 had the highest frequency (42.9%), those with activity scores 1 and 2 had a higher frequency of those with chronicity 3 (66.7% and 85.7%, respectively).In those with an activity score of 3, the patient with a chronicity score of 2 was never seen and half of the patients had a chronicity score of 1 (50.0%) and the other half had a chronicity score of 3 (50.0%). Chronic inflammatory cell infiltration is observed in figures 1 and 2.

Table 6. Relationship between activity and chronicity score

	Chronicity						Total	
	1		2		3			
Activity	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
0	10	35.7	12	42.9	6	21.4	28	100.0
1	1	3.0	10	30.3	22	66.7	33	100.0
2	0	0.0	1	14.3	6	85.7	7	100.0
3	1	50.0	0	0.0	1	50.0	2	100.0
Total	12	17.1	23	32.9	35	50.0	70	100.0
p	**<0.001** (χ^2=25.405)							

χ^2: Chi-square test

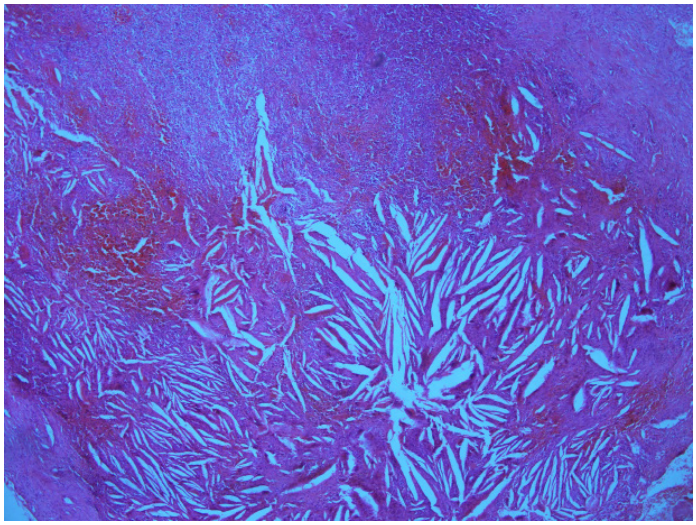

Figure 1. HEx200, Grade II score and cholesterol clefts

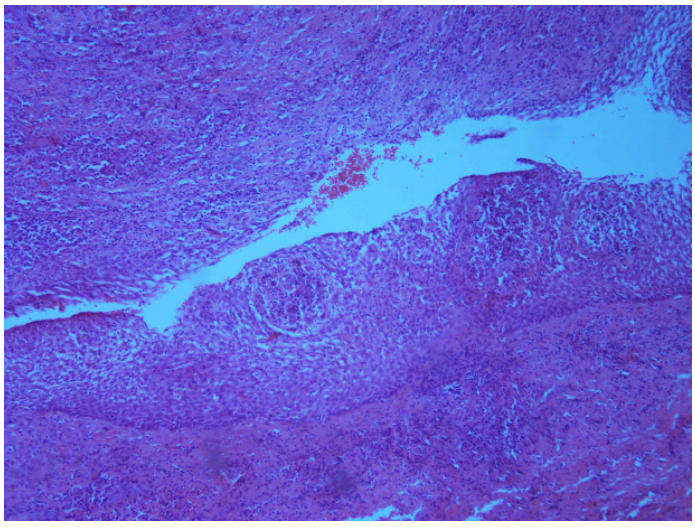

Figure 2. HEx200, Grade III score

DISCUSSION

RC's are common lesions in daily dental practice. RC's are defined as inflammatory odontogenic cysts of endodontic origin The cyst wall consists of fibrous connective tissue containing a chronic infiltrate of inflammatory cells (11).

Gutmann et al. observed a lack of standardization in naming apical lesions of endodontic origin (12). Johnson et al. found that RC are the most common odontogenic cyst, followed by dentigerous cyst and keratocystic odontogenic tumor (when classified as a cyst). They observed the rate of RC as 54.6% among odontogenic cysts (5). According to studies in the literature, RCs account for 6% to 57.69% of all periapical lesions. This variation can be attributed to differences in the definition of this cyst type (13,14).

In this study, it was aimed to evaluate the severity of inflammation in RC (active and chronic inflammation) and its relationship with age and gender. Histopathological evaluation is required to score the severity of inflammation.

According to Tsai et al., most of the inflammation in a radicular cyst is predominantly lymphocytic cell infiltration, they found in their study 16.7% grade I (mild inflammation), 30.0% grade II (moderate inflammation), and 53.3% grade III (severe inflammation) (10). According to Santos et al., chronic inflammatory infiltrate is predominantly observed in radicular cyst cases. In their study, 49.3% intense inflammation, 30.1% discrete inflammation, 20.5% moderate infiltrate are observed. Acute inflammation characterized by the presence of polymorphonuclear leukocytes (7 out of 73 cases) and mixed inflammation (2 cases) were observed at a very low rate (15). In a study in the literature, the intensity of the inflammatory infiltrate in periapical lesions was observed to be variable.

All periapical lesions examined by light microscopy displayed a large number of infiltrating inflammatory cells characteristic of the chronic granulomatous inflammatory process. Inflammatory infiltrate consisting of plasma cells, lymphocytes, macrophages and rarely polymorphonuclear (PMN) leukocyte accumulation was observed (16).

In Cohen's study, the epithelium of RC is predominantly infiltrated by neutrophilic polymorphonuclear leukocytes, also the connective tissue capsule is predominantly infiltrated by chronic inflammatory cells (17). Consistent with other studies, one study found plasma cells and lymphocytes associated with the fibrous capsule (13). Although intense inflammation was observed in the studies, the intensity of the inflammatory infiltrate showed differences. Proliferative activity in epithelial cells is thought to affect the degree of inflammation in RCs (18). According to Domingues et al., there is chronic infiltration of inflammatory cells, lymphocytes and plasma cells in RCs (8).

In our study, chronic inflammation was severe in 50.0% of the cases, moderate in 32.9%, and mild in 17.1%. Active inflammation was mild in 47.1%, moderate in 10.0%, intense in 2.0%, and active inflammation grade 0 was detected in 40.0% of the cases. These findings were evaluated in accordance with the literature. In the literature, there are generally studies on detecting the intensity of chronicity. Chen et al. found radicular cyst cases to be 57.3% in women and 42.7% in men in their study.

In our study, 51.4% of the cases were female and 48.6% were male. This finding was consistent with the literature. The incidence of RS is high among third-decade patients and male gender (19). According to Lin et al., RS is most commonly found in the third to sixth decades and, it has a slight male disposition (20). In one study, the mean age of RC was 40.5 years (cases ranged from 13 to 78 years).

Lesions were mostly detected in the 3rd and 5th decades of life (50.0% of the total cases) and were observed as 18.5% in the 4th and 14.2% in the 6th decade (21). In our study, the mean age was found to be 36.64. In the study of Lin et al., approximately 60% of RCs were found in the maxilla, which tends to the anterior maxillary teeth (20). According to Suarez et al., 60.0-80.0% of RCs are in the upper jaw and preferably include anterior teeth (22). In the study of Chen et al., 86.6% of the cases were found in the maxilla and 13.4% in the mandible (21).

Anatomically, apical cysts are seen in all tooth-bearing sites of the jaw, but they are more common in maxillary teeth than mandibular teeth (19). In our study, the majority of the cases were located in the mandible, 30 of them were located in the maxilla and 40 of them were located in the mandible. This finding was not consistent with the literature.

CONCLUSION

In conclusion, radicular cysts are usually detected incidentally on routine radiographs. They may not cause symptoms and clinical signs unless they are infected. Therefore, they are an entity that should be considered in the clinic. RCs may show different histopathological findings in the same lesion, suggesting morphological variations of RCs.

Variations in cyst diagnosis can be attributed to differences in the definition of this cyst type. In RC cases, the severity of inflammation may differ from case to case.

In our study, the severity of chronic inflammation was observed as high-grade (grade 3) in most of the cases, acute inflammation was found to be mild (grade 1) in most of the cases. It is thought that determining the severity and type of inflammation in the histopathological evaluation may be beneficial for diagnosis and treatment.

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