Journal of Dental Sciences (2020) 15, 132–135

Available online at www.sciencedirect.com

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journal homepage: www.e-jds.com

Original Article

Evaluation of concordance between clinical and histopathological diagnoses in periapical lesions of endodontic origin

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Received 26 November 2019; Final revision received 23 January 2020
Available online 18 April 2020

KEYWORDS
Diagnosis;
Histology;
Periapical lesion;
Periapical granuloma;
Radicular cyst

Abstract Background/purpose: Periapical lesions of endodontic origin are often diagnosed based on the clinical and radiological presentations that may be different from the histological diagnoses. The purpose of this study was to assess the concordance between the clinical diagnosis of these lesions and the histopathological diagnoses and to analyze their clinical and pathological features.

Materials and methods: Biopsies of periapical lesions of endodontic origin diagnosed in the histopathology laboratory between 2006 and 2017 were retrieved from the database and used to conduct this retrospective review. Clinical data were obtained, and tissue samples were re-evaluated. The overall agreement between the clinical and histological diagnoses was tested utilizing the Cohen kappa (k).

Results: A total of 317 periapical biopsy specimens were included in this study which consisted of 137 periapical granulomas, 174 periapical cysts, and six periapical scars. Generally there was weak overall agreement between the clinical and histological diagnoses of periapical granuloma and periapical cysts (Cohen kappa, $k = 0.059$).

Conclusion: The findings of this study indicate that clinical/radiographic examinations are not able to preoperatively determine whether a periapical lesion is a cyst or a granuloma and highlights the importance of developing a reliable nonsurgical diagnostic method to differentiate periapical lesions.

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https://doi.org/10.1016/j.jds.2020.01.007

Introduction

Periapical radiolucent lesions are one of the most common radiographic findings in dental practice. Most of these lesions are the sequelae of pulpal inflammation and necrosis.[1,2] The classification of these inflammatory lesions is based on histopathological features, which include periapical granulomas, cysts, abscesses and scars.[3] Nair et al. reported that there are two distinct types of radicular cysts: the true cysts, cavities completely enclosed in epithelial lining and pocket cysts, those containing epithelium lined cavities which opens into the root canals. Precise differentiation between these types of cysts requires serial sectioning of whole lesions including the root apex, which is not always possible in the clinical sitting.[4] The initial management for most of these inflammatory periapical lesions is usually nonsurgical endodontic treatment.[5] There have been controversies regarding the probability of a cyst healing after nonsurgical root canal treatment, as it is almost impossible to confirm the diagnosis of a cyst without a surgical intervention.[6] Consequently, there has been a great desire to have reliable nonsurgical means to preoperatively determine whether a periapical lesion is a cyst or a granuloma. This has led to many studies attempting to develop nonsurgical diagnostic methods.

Howell and his coworkers performed a cytologic evaluation of aspirated fluids from the root canal and inspected these samples for the presence of epithelial cells to correlate the findings with the diagnosis of radicular cysts.[7] That study was not reliable for several reasons: the possible contamination of the aspirate by mucosal epithelial cells, the presence of odontogenic rest cells in granulomas, and the small sample size. Cunningham and Penick used a contrast medium to determine the presence of a cyst or a granuloma.[8] The investigators did not find a correlation between the postinjection radiographic image and the histological diagnosis. Another attempt used polyacrylamide gel electrophoresis, which showed some promise; however, the results were not reproduced.[9] More recently, cone-beam computed tomography (CBCT) scans have been proposed as a preoperative, noninvasive method for the differential diagnosis of radicular cysts and granulomas. Simon et al. reported that CBCT can distinguish periapical granulomas from cysts.[10] Meanwhile, Rosenberg et al. (2010) reported that CBCT was an unreliable diagnostic tool.[11]

Nevertheless, all the aforementioned techniques are either not conclusive or unreliable. Until a consistent preoperative diagnostic method is established, dental practitioners will continue to diagnose periapical pathologies based on clinical and radiographic presentations. The standard means of differentiating radicular cysts from granulomas is surgical biopsy and subsequent histopathological evaluation.[12] The evaluation of the ability of the clinical assessment to correctly diagnose periapical lesions may be useful in preoperatively determining whether a periapical lesion is a cyst or a granuloma and may help to conduct future studies that properly assess the response of radicular cysts to nonsurgical root canal therapy. Therefore, the aim of this study was to assess the concordance between the clinical diagnosis of periapical lesions of endodontic origin and the histopathological diagnoses and to analyze the clinical and pathological features of these lesions.

Materials and methods

The archives of the histopathology laboratory of the College of Dentistry [location masked for blind review], were retrospectively reviewed for all of the periapical lesions of endodontic origin that were documented between 2006 and 2017. The inclusion criteria of the cases were as follows: 1- periapical lesions associated with a permanent tooth (except the third molar); and 2- intact periapical lesions that were obtained during endodontic surgery or from extracted and endodontically treated teeth. Hematoxylin and eosin (H&E) slides were retrieved. The diagnosis of the retrieved cases was confirmed or modified by two independent pathologists, and a consensus diagnosis was reached in all cases. The diagnosis of the cases was made according to the following criteria. Periapical granuloma was diagnosed based on the histological findings of soft connective tissue that was morphologically consistent with granulation tissue in addition to the presence of inflammatory cell infiltrate. There was no microscopic evidence of squamous-lined epithelium. The diagnosis of a cyst was made when there was microscopic evidence of fibrous connective tissue with cystic organization, definitive foci of stratified squamous-lined epithelium and the presence or absence of inflammatory cells within the lining or the wall of the cyst. Odontogenic rests that were present within the fibrous connective tissue were not considered indications of a cystic epithelial lining. A scar was defined as dense fibrous connective tissue, and an abscess was defined as a collection of pus. Clinical data, including endodontic status, age, gender, location, tooth type and clinical diagnosis, were obtained from the pathology request forms. In cases submitted with more than one clinical diagnosis (7.3% of cases), the first diagnosis was considered to represent the clinically preferred diagnosis. All patient information was confidential, and the research protocol was reviewed and approved by the Institutional Review Board of [location masked for blind review] (Research project no. [Masked for blind review]). All the data obtained from this study were tabulated and analyzed using frequency distributions by SPSS (Chicago, IL, USA). To determine the interrater reliability between the two pathologists, we calculated the Cohen kappa (k). Moreover, the overall agreement between the clinical and histological diagnoses of periapical granuloma and periapical cysts was also tested using the Cohen kappa.

Results

A total of 317 periapical biopsy specimens from 307 patients were included in this study, corresponding to around 16% of the biopsy volume for the 12-year period. The mean patient age was 35.8 years (SD = 13.03), with a slight female predilection (53.3%) (Table 1). The periapical lesions occurred more frequently in the maxilla and accounted for 59.9% of the patients. The most frequent region for periapical lesions was the anterior region (39.4%) followed by the molar region (36%), and the most commonly involved tooth was the first molar (30.3%) (Table 2).

Table 1 Distribution of 317 periapical biopsy specimens according to age and gender.

		Periapical granuloma n (%)	Periapical cyst n (%)	Periapical scar n (%)
Age groups*	10–19	5 (3.7)	17 (10.1)	0 (0)
	20–29	40 (29.6)	52 (30.8)	1 (16.7)
	30–39	36 (26.7)	46 (27.2)	1 (16.7)
	40–49	32 (23.7)	20 (11.8)	4 (66.7)
	50–59	16 (11.9)	24 (14.2)	0 (0)
	60–69	6 (4.4)	8 (4.7)	0 (0)
	70–79	0 (0)	1 (0.6)	0 (0)
	80–89	0 (0)	1 (0.6)	0 (0)
Gender				
	Male	59 (42.8)	87 (50.3)	2 (33.3)
	Female	79 (57.2)	86 (49.7)	4 (66.7)

*7 missing data.

Histologically, the 317 periapical lesions consisted of 138 periapical granuloma, 173 periapical cysts, and six periapical scars. Interrater reliability test indicated that agreement between the two pathologists was strong (k = 0.895). The comparison between clinical and histologically confirmed diagnoses are shown in Table 3. From 138 cases histopathologically diagnosed as periapical granuloma, 55.8% had the correct clinical diagnosis, while the agreement between periapical cyst diagnoses was 51.4% and no agreement for periapical scars. Generally there was weak overall agreement between the clinical and histological diagnoses of periapical granuloma and periapical cysts (k = 0.059).

Table 2 Distribution of 317 periapical biopsy specimens according to jaw, region and tooth type.

		Periapical granuloma n (%)	Periapical cyst n (%)	Periapical scar n (%)
Jaw*	Maxilla	90 (66.2)	96 (56.5)	4 (66.7)
	Mandible	46 (33.8)	74 (43.5)	2 (33.3)
Region*	Anterior region	52 (38.2)	69 (40.6)	4 (66.7)
	Premolar region	38 (27.9)	20 (11.8)	1 (16.7)
	Molar region	44 (32.4)	69 (40.6)	1 (16.7)
	More than one region +	2 (1.5)	12 (7.1)	0 (0)
Tooth**	Central incisor	16 (11.9)	21 (12.4)	1 (16.7)
	Lateral incisor	17 (12.6)	28 (16.5)	0 (0)
	Canine	5 (3.7)	6 (3.5)	1 (16.7)
	First premolar	22 (16.3)	5 (2.9)	0 (0)
	Second premolar	16 (11.9)	14 (8.20	1 (16.7)
	First molar	35 (25.9)	60 (35.3)	1 (16.7)
	Second molar	7 (5.2)	8 (4.7)	0 (0)
	More than one tooth+	17 (12.6)	28 (16.5)	2 (33.3)

*5 missing data, ** 6 missing data, + when two or more adjacent teeth are endodontically involved and the lesion cannot be assigned to a single tooth.

Table 3 Comparison of clinical and histopathological diagnoses.

Clinical Diagnosis	Histopathological diagnosis		
	Periapical granuloma n = 138	Periapical cyst n = 173	Periapical scar n = 6
Periapical Granuloma	77	58	3
Periapical cyst	41	89	1
Periapical abscess	3	2	0
Periapical scar	2	0	0
Others*	8	15	0
Not stated	7	9	2

*other clinical diagnoses and non-specific terms such as periapical lesion, odontogenic cyst, glublomaxillary cyst, and keratocyst.

Discussion

Periapical lesions of endodontic origin are the most common pathological processes in the periapical region. These lesions are eventually diagnosed as periapical granulomas, cysts, abscesses, or scars. The literature shows significant discrepancies regarding the prevalence of each type of lesion. The prevalence of periapical granulomas ranged from 45% to 94%, and the prevalence of cysts ranged from 6% to 44%.[3,13–17] In the present study, of the 317 cases, 54.6% were apical cysts, 43.5% were granulomas and 1.9% were scars. The variations of these results and those found by previous reports may be due to the different histological criteria used in the diagnosis or may be due to the inherent bias of the samples analyzed. As some clinical practices recommend obtaining a periapical biopsy only in cases of failed endodontic treatment or when there are large radiolucent lesions, these clinical factors may affect the profile of the sample. A review of the literature shows a general correlation between the prevalence of periapical lesions and the maxillary jaw,[3,18,19] which is in agreement with the present study, as it showed that almost 60% of the cases occurred in the maxilla. This could be attributed to the fact that maxillary teeth are more prone to trauma or are more often treated for esthetic reasons.

Distinguishing radicular cysts from granulomas does not directly affect prognosis in clinical settings.[20] However, from a scientific research perspective, there is a great need to have this information to be able to evaluate the response of nonsurgical endodontic interventions. Few studies have attempted to compare the clinical diagnoses of inflammatory periapical lesions with the histological findings. Diegues et al. evaluated the correlation between the clinical diagnosis of periapical inflammatory lesions and the histopathological results.[21] Out of 191 cases, only 113 had matched clinical and histopathological diagnoses. Another similar study found that the overall agreement between the clinical and histopathological diagnoses was 59%.[22] Another study compared the clinical and radiographic features with a histological diagnosis of 19 periapical lesions.[23] The diagnosis was accurate in 54.3% of the cases. Kuc et al. found that there was exact clinical and histologic

agreement in the diagnosis of periapical cysts, granulomas, or abscesses in 59.3% of histologically confirmed cases.[15]

The current study found that 55.8% of periapical granulomas had the correct clinical diagnosis, while the agreement between periapical cyst diagnoses was 51.4%, and there was no agreement for periapical scars. These percentages are similar to those found by the aforementioned reports; however, in this study, a larger number of cases was studied when compared to that in other studies.[21–23] Furthermore, the overall agreement between the clinical and histological diagnoses of periapical granulomas and periapical cysts was tested using both the percent agreement and Cohen kappa, which was in contrast to previous reports that tested the agreement with only the percent agreement. It is recommended to calculate both the percent agreement and Cohen kappa when measuring agreement among data to overcome the limitations of each method.[24] In the current study, there was weak overall agreement between the clinical and histological diagnoses of periapical granulomas and periapical cysts ($k = 0.059$). The reason for the discrepancies between the clinical and pathological diagnoses and the weak agreement could be attributed to the similar radiographic appearances of the lesions and the fact that it is almost impossible to radiographically differentiate cystic and solid lesions. Although there are some clinical indicators such as size/chronicity of the lesions that could be utilized to distinguish the periapical lesions,[25] however they are not accurate.

In conclusion, the findings of this study indicate that clinical/radiographic examinations are not able to preoperatively determine whether a periapical lesion is a cyst or a granuloma and highlights the importance of developing a reliable nonsurgical diagnostic method to differentiate periapical lesions.

Declaration of Competing Interest

The authors have no conflicts of interest relevant to this research.

Acknowledgement

This is a non-funded research and there has been no financial support for this work that could have influenced its outcome.

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