Original Article

Clinicopathological comparison of periapical cyst and periapical granuloma in a cohort of Tamil population

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Abstract

Aim: The aim of this study was to present and analyze detailed clinicopathological data of periapical cysts (PCs) and periapical granuloma (PG) in a cohort of 135 cases from the South Indian Population.

Methodology: The present study included 135 cases of PC and PG out of 2696 biopsies submitted over 3 years. The clinicodemographic data which included age, gender, location, radiographic appearance, and treatment were collected along with the histopathological examination of the biopsied specimen. Data were entered in a Microsoft Excel spreadsheet, 2021, and analyzed using SPSS software ver. 26.

Results: There were 71 cases of PG and 64 cases of PC. The mean age of occurrence in PG was slightly lower than cases in PC. Irrespective of the group, there was a clear male preponderance, and maxillary permanent central incisors were most commonly affected. However, no significant difference was noted. Radiographically, PC significantly showed more well-defined corticated radiolucent lesions compared to PG where most cases were ill-defined (69.01%). Histologically, all cases showed classic features for diagnosis with additional histological characteristics which may aid in diagnosis.

Conclusion: PG was more common than PC. There was a predilection for the male gender in both lesions. The actual incidence of these lesions would be actually high, as some cases are lost to private practitioners, and not all the lesions are submitted for histopathological examination.

Keywords: Cyst; granuloma; periapical; radiolucent

INTRODUCTION

Periapical radiolucencies are commonly encountered by a clinician, with a wide range of differential diagnoses ranging from commonly inflammatory cystic lesions to comparatively uncommon odontogenic pathologies.[1] It has been widely accepted that histopathological examination of the tissue provides the definitive diagnosis and is regarded as the "gold-standard test," and thus predicts and may at times change the course of the treatment plan. Among these periapical radiolucencies, periapical cysts (PCs) and granulomas, always associated with nonvital teeth, are the most common inflammatory lesions formed secondary to insult to the pulp, most commonly due to dental caries.[2-4] History of trauma may be elucidated in many other cases, particularly in children and young adults.[5,6] However, in some cases, with large carious lesions in children with good host immune response, instead of necrosis, the pulp shows hyperplasia which is regarded as pulp polyp/chronic hyperplastic pulpitis.[7]

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Despite being common gnathic cystic lesions, there are only a few published studies pertaining exclusively to PC and granulomas from the Indian population, many comprising the class of all odontogenic cysts collectively.[8-10] The aim of the present study was thus to present detailed clinicopathological data of PC and periapical granuloma (PG) in a cohort of 135 cases from the South Indian population. Furthermore, a comparison was made with a relatively uncommon variant of PC, the residual cyst.

METHODOLOGY

Study design and sample selection

The present retrospective cross-sectional study was conducted in the Department of Oral Pathology and Microbiology, after seeking approval from the Institutional Human Ethical Clearance Board (IHEC/SDC/FACULTY/22/OPATH/011). Records of all the patients were screened and reviewed during 3 years (January 2021 to December 2023), who demonstrated periapical radiolucencies associated with nonvital tooth. Inclusion criteria were: (a) availability of complete clinical and demographic profile, (b) presence of an associated nonvital tooth as tested by physical or electric pulp testing, (c) availability of radiographs and radiographic evidence of a periapical radiolucency, and (d) histopathological confirmation of PG/PC.

All the cases where the histopathological diagnosis was nonspecific (including chronic inflammatory lesions), or diagnosis other than PC/PG (such as any named odontogenic development cyst or a tumor) was rendered, or the formalin-fixed paraffin-embedded tissue blocks or slides were not available for re-evaluation were excluded from the study. The clinicodemographic data which included age, gender, location, radiographic appearance, and treatment were collected along with the histopathological examination of the biopsied specimen. For ease of categorization, the cases were divided into anterior (teeth #1-3) and posterior segments (teeth #4-8) for both jaws. Furthermore, reported cases of residual cysts were also included for comparison.

Statistical analysis

The results were tabulated, and entered in a Microsoft Excel spreadsheet 2013 (Microsoft Corporation, Redmond, Washington, United States). Descriptive analyses were done for the demographic and clinical data. Finally, we generated a database using the IBM SPSS Statistics for Windows, Version 26.0 (Released 2019; IBM Corp., Armonk, New York, United States) software. Statistical analysis was done using the Chi-square test, and $P \leq 0.05$ was considered significant statistically.

RESULTS

Sample characteristics

Two thousand and two hundred twenty-six oral and maxillofacial biopsies were received in the department during 3 years, out of which 135 cases of PG and PC were included in the study (5.14% of all the pathology specimens submitted). Eight cases of paradental cysts, the closest histological mimicker of PC, were excluded after clinical and radiographic correlation. For comparison, 11 cases of residual cysts were also included during the course of the study. There were 64 cases (47.41%, 64/135) of PC and 71 cases (52.59%, 71/135) of PG. The mean age for PG was 29.80 ± 10.68 years (median 29 years, range 7–59 years), which was lower than the cases of PC 32.69 ± 12.24 (median 31.5 years, range 7–62 years). The cases of residual cysts were seen at even higher age (mean 34.45 ± 15.81; median-33 years). No statistically significant difference was noted between the study groups. There was overall marked preponderance for the male gender (90M:45F; ratio 2:1). A similar trend was noted when both pathologies were analyzed individually (PG-1.63M:1F; PC-2.56M:1F). However, no statistically significant difference was seen between the two groups with regard to gender (*P* value 0.150). With regard to residual cysts, cases were almost equally distributed among males and females (6M:5F). There was an associated carious lesion or history of trauma in 63/71 cases of PG and 49/64 cases of PC, and no relevant history could be retrieved for the remaining cases. Although not significant, the lesions in the anterior segment were more frequently associated with a positive history of trauma.

With regard to the site, most cases were seen in the maxilla (93/135, 68.9%) compared to 31.1% of cases in the lower jaw (42/135). Irrespective of the lesion, the maxillary anterior segment was the most frequently affected segment; 48/71, 67.61% of PG and 64.06% (41/64 cases) of PC. For PG, the mandibular anterior segment was the second most commonly affected site (16/71, 22.53%), but the mandibular posterior segment was the second most commonly affected site for PC (11/64, 17.2%). However, there was no statistically significant difference noted between the two study groups with regard to location (*P* value 0.280). All the cases were seen in permanent dentition except four cases (1 PG and 3 PC). Maxillary central incisors showed maximum incidence of PG and PC among anterior teeth.

Radiographic data were available for all 135 cases and included mainly intraoral periapical radiographs; orthopantomograms were available for occasional cases. Radiographically, all cases were single unilocular radiolucencies. The borders of the radiolucent lesions were segregated into ill-defined borders without cortication and well-defined lesions with cortication. PC showed a significantly higher number of well-corticated

lesions (53/64, 82.8%) in comparison to 22/71 cases PG (*P* value 0.000). Detailed features and comparative values are shown in Table 1.

Histopathological features

All seventy-one cases of PGs showed three features: (1) the presence of dense mixed/chronic inflammatory reaction in fibrous connective tissue, (2) the presence of foamy macrophages in sheets or focal clusters, and (3) areas of hemorrhage [Figure 1]. Additional histopathological features were noted in a few cases. Six cases (8.46%) showed evidence of lumenization/cystification, 4 (5.63%) cases demonstrated fragments of spongiotic nonkeratinized epithelium, and 14 (19.72%) cases showed clusters of cholesterol clefts with foreign body-type multinucleated giant cells.

The presence of an epithelium-lined lumen with an inflamed cyst wall was a consistent feature of all 64 cases; the epithelial lining was nonkeratinized stratified squamous epithelium [Figure 2a]. A stratification of cyst was noted in 52 (81.25%) cases. Starting at the lumen, the cysts were nonkeratinized odontogenic epithelium, with an inflamed subepithelial wall moderately or densely by lymphoplasmacytic infiltrate and a more peripheral densely collagenous wall devoid of inflammation. 29 cases showed arcading of the epithelium (45.31%), Rushton bodies were noted in 3 (4.69%) cases, 18 showed ciliated epithelium (all maxillary), 39 cases had evidence of cholesterol clefts with foreign body-type multinucleated giant cells (60.93%), and 17 cases showed Russell bodies in the wall [Figure 2b-d]. All residual cysts showed nonkeratinized odontogenic epithelium with minimal inflammatory infiltrate in the adjacent wall.

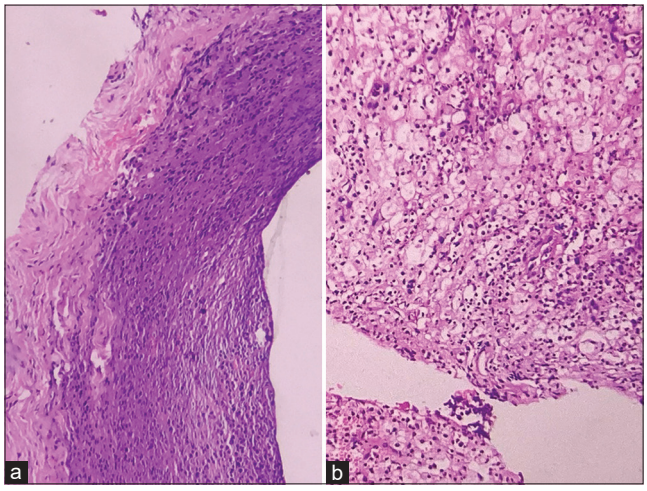

Figure 1: Photomicrographs of H and E-stained sections of periapical granuloma showing dense chronic inflammatory reaction (a, ×100) and sheets of foamy macrophages (b, ×400)

Treatment and follow-up

All cases were managed by root canal therapy with enucleation/excision of lesions with or without apicectomy and retrograde restoration. None of the cases recurred.

DISCUSSION

Inflammatory cysts of jaws are a heterogeneous group of cystic lesions that arise resultant to epithelial proliferation within loci of inflammatory cells and could be the result of a number of variegated causes. Inflammatory cysts

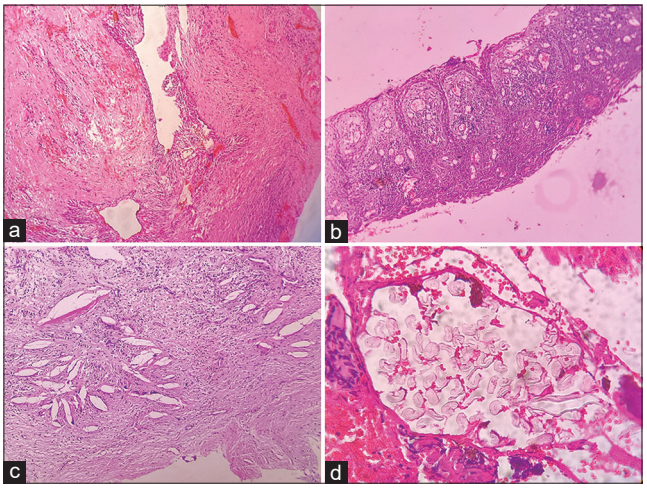

Figure 2: Photomicrographs of H and E-stained sections of periapical cyst showing (a) nonkeratinized odontogenic epithelium lining the cyst cavity (×40), (b) arcading of epithelium, (c) cholesterol clefts, and (d) Rushton bodies (×400)

Table 1: Details of comparative clinicodemographic features of periapical cysts and periapical granuloma

Parameter	Periapical granuloma (*n*=71)	PC (*n*=64)	*P*
Age (years)	29.80±10.68	32.69±12.24	0.149#
Gender	Males: 44 Females: 27 Ratio: 1.63 male: 1 female	Males: 46 Females: 18 Ratio: 2.56 male: 1 female	0.150#
Location, *n* (%)	Maxillary anterior: 48 (67.61) Mandibular anterior: 16 (22.53) Maxillary posterior: 2 (2.82) Mandibular posterior: 5 (7.04)	Maxillary anterior: 41 (64.06) Mandibular anterior: 10 (15.62) Maxillary posterior: 2 (3.12) Mandibular posterior: 11 (17.2)	0.280#
Radiographic feature, *n* (%)	Ill-defined: 49 (69.01) Well-defined: 22 (30.99)	Ill-defined: 11 (17.2) Well-defined: 53 (82.8)	0.000*

*Statistically significant, #Nonsignificant. PC: Periapical cyst, PG: Periapical granuloma

other than PC were not included in the study, which differ in localization and etiology from the commoner PC. PC, synonymously known as radicular cysts, comprise 35%–87% of all odontogenic cysts and arise from the epithelial remnants of periodontal ligament following necrosis of the pulp.[11-13] Little information is available regarding PC and granuloma from the Indian cohort;[8-10] thus, the present study was conducted to demonstrate clinicodemographic and histopathological features of these common inflammatory periapical lesions.

A definite preponderance was noted for both for the male gender. This is in concordance with the previous Indian studies.[8-10] The higher prevalence in males in the present study could be justified by the fact that in most cases, particularly in the anterior, there was a previous history of trauma which could be directly correlated with more indulgence of boys in outdoor sports, a common source of dentoalveolar injuries. It is worth noting that a reverse trend was noted in the data available from other countries where females were more commonly affected.[11,14,15] Other studies showed almost an equal ratio.[16,17] In line with previous studies, we found that the anterior region of the maxilla was the most frequently affected site for both PG and PC.[11] Maxillary central incisors were the most commonly affected tooth in our study; however, in a study from Brazil, Tavares *et al*. showed that the upper lateral incisor was the most affected tooth.[11] Alotaibi *et al*. and Chen *et al*. also showed a slightly higher incidence in the lateral incisors.[18,19] The authors were of the opinion that the higher prevalence of periapical lesions in the maxillary lateral incisors could be due to the higher frequency of caries, trauma, and wide anatomical variation in the tooth morphology. Overall, the maxillary anterior segment was affected more than the mandibular for both PG and PC, while, akin to the data presented by Tavares *et al*., the mandibular posterior segment showed a second higher frequency for a PC.[11] Other authors also demonstrated similar results.[15-17] Results in our study were not significant, possibly due to a comparatively lower number of cases than in the aforementioned study.

It is believed that the PG is a precursor of the PC. A balance between cell death and proliferation is involved in the pathogenesis of these two lesions. PG arises from chronic inflammatory stimuli resulting from pulpal necrosis, microbial interaction, or a periapical abscess. The inflammatory cells in the PG activate the cell rests, causing their proliferation and eventually leading to the formation of PC.[20] The pathogenesis of PC is best explained in three phases. Under the influence of bacterial antigens, endotoxins, and inflammation, the dormant epithelial cell rests of Malassez begins to proliferate (phase of initiation).[21] This is followed by the phase of cyst formation, where the central cells undergo liquefactive degeneration/necrosis (nutritional deficiency theory) or the proliferating epithelium surrounds the abscess cavity (abscess theory).[22] The cyst then enlarges by osmosis, increasing the intracystic pressure (phase of enlargement).[21] Numerous cytokines, cells, and enzymes are involved in this step. Inflammatory cells like polymorphonuclear neutrophils are known to play an important role in cyst enlargement. These cells form channels along the entire length of the epithelium, to reach the central cystic cavity and cause enlargement.[23] Cytokines, namely, interleukin (IL)-1, IL-6, and tumor necrosis factor-α, are identified in the keratinocytes of the cyst lining and result in bone resorption.[24] Furthermore, Leonardi *et al*. reported that the extracellular matrix also takes part in the pathogenesis of these two lesions.[25] Upregulation of MMP-13 plays an important role in the formation of radicular cysts from the PG.[25] Disequilibrium between TIMP-1 and MMP-1 further assists the expansion of this cystic space.[26]

Histological examination of the excised tissue is the gold standard for diagnosis, although radiographic appearance could serve a clue. We found a significant difference between the radiographic appearance of PG and PC, the latter being more well corticated than PG supporting the prevailing concept of an indolent course of the development of PC through PG. Leite *et al*. could demonstrate more inflammatory cells in the cases of PG compared to cysts and opined that there is a higher antigenic stimulation in PG.[27] Apart from the main diagnostic histopathological features for the diagnosis of PG and PC, we could demonstrate some unusual features that may not be of clinical significance but are important for understanding the pathogenesis of these lesions, such as epithelized PG, early cystification of PG or the presence of Rushton/Russell bodies in PC, collectively serve clue in etiopathogenesis, chronic nature, and role of inflammatory chemokine or cytokines in the generation of these lesions. The incidence of Rushton bodies was much lower in our study than previously explained.[19,28] Irrespective, root canal therapy with or without apicectomy is the treatment of choice.[29,30]

CONCLUSION

The results of the present study showed that PG was more common than PC. There is a male predilection for both lesions. The actual incidence of these lesions would be actually high, as some cases are lost to private practitioners, and not all the lesions are submitted for histopathological examination.

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Conflicts of interest
There are no conflicts of interest.

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