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ORIGINAL ARTICLE

Retrospective analysis of nonendodontic periapical lesions misdiagnosed as endodontic apical periodontitis lesions in a population of Taiwanese patients

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Abstract

Objective We aimed to evaluate nonendodontic periapical lesions clinically misdiagnosed as endodontic periapical pathoses in a population of Taiwanese patients.

Materials and methods Cases (2000–2014) of histopathological diagnoses of nonendodontic periapical lesions were retrieved from all cases with a clinical diagnosis of radicular cyst, apical granuloma, or apical periodontitis in the institution. These cases were regarded as misdiagnosed nonendodontic periapical lesions, of which the types and frequencies, in addition to the demographic data, were determined.

Results Four thousand and four specimens were clinically diagnosed as endodontically associated pathoses, of which 118 cases (2.95%) received a histopathological diagnosis of a nonendodontic pathologic entity, the most frequent lesion being keratocystic odontogenic tumor (KCOT, $n = 38$, 32.20%), followed by fibro-osseous lesion ($n = 18$, 15.25%), and dentigerous cyst ($n = 13$, 11.02%). Nine malignant lesions in the periapical area [squamous cell carcinoma ($n = 7$, 5.93%), adenoid cystic carcinoma ($n = 1$, 0.85%), and Langerhans cell histiocytosis ($n = 1$, 0.85%)] were also noted.

Conclusions A wide variety of histopathological diagnoses, including benign odontogenic and non-odontogenic cystic and tumorous lesions and infectious diseases, as well as malignant lesions, was noted in these 118 cases of nonendodontic periapical lesions. Squamous cell carcinoma was the most predominant malignancy of nonendodontic periapical lesions misdiagnosed as apical periodontitis lesions from imaging examination overlooking the clinical findings.

Clinical relevance The current data form a useful basis for clinicopathological investigation and educational teaching regarding nonendodontic periapical lesions misdiagnosed as endodontic apical periodontitis lesions.

Keywords Endodontic periapical lesions · Nonendodontic periapical lesions · Oral squamous cell carcinoma · Ameloblastoma · Adenoid cystic carcinoma

Hsun-Yu Huang and Yuk-Kwan Chen made equal contributions.

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Introduction

Periapical lesions resulting from infected root canal systems are the most common pathologic conditions within the alveolar bone. Radicular cysts, periapical granulomas, and apical periodontitis represent approximately 90% of all periapical lesions in a study of 1966 [1] whereas the occurrences were about 88, and 73% respectively in two more recent studies of 2010 [2] and 2012 [3]. However, nonendodontic lesions can also occur in the alveolar bone and may lead to misdiagnosis of periapical lesions of endodontic origin, especially when these lesions are located around the periapical area related to teeth with pulp necrosis that have received endodontic treatment. Despite some dental

clinicians arguing the cost and benefit of histopathological examination of periapical lesions [4–6], a review of the English language literature revealed that the reported frequencies of nonendodontic periapical lesions misdiagnosed as endodontic apical periodontitis lesions in different countries ranged from 0.65 to 6% [1, 7–13]. The misdiagnosed endodontic periapical lesions consisted of a wide variety of diseases, including benign and malignant lesions [14]. To our knowledge, a survey of the frequencies and types of misdiagnosed nonendodontic periapical lesions in Taiwanese patients has not yet been performed. So, the current study aimed to provide updated information about nonendodontic periapical lesions misdiagnosed clinically as endodontic periapical pathoses in a population of Taiwanese patients, which was also compared with previous studies performed in other countries [1, 7–13].

Materials and methods

Cases of histopathological diagnoses of nonendodontic periapical lesions were retrieved from a total of 4004 cases with a clinical diagnosis of radicular cyst, apical granuloma, or apical periodontitis from the Department of Oral Pathology of our institution between 2000 and 2014. These cases were regarded as misdiagnosed cases, of which the types of histopathological diagnoses, frequencies, ages, and locations were recorded. Surgical procedures used to acquire the specimens included curettage, excision, incision, and enucleation. The clinical diagnoses were made by endodontists and oral and maxillofacial surgeons, while the histopathological diagnoses were rendered by board-certified oral and maxillofacial pathologists. Cases with histopathological diagnoses of bone chip, sequestrum, condensing osteitis, and scar tissue were excluded, because the former three disease entities are cases of nonspecific inflammation, and scar tissue is regarded as a non-inflammatory lesion.

Statistical analyses (Chi-square test, Fisher's exact test, and binominal proportion test) of the frequency, gender, and location of nonendodontic periapical lesions were performed using the SAS Statistical Package (Version 9.1.3, SAS Institute Inc., Cary, NC, USA). In order to have a strict statistical manipulation on the P values, multiple testing-adjusted P values were determined using the Bonferroni correction method (threshold of $P = P_0/N$; $P_0 = 0.05$, N = number of categories to be tested) [15]. As the number of categories to be tested (i.e., histopathological diagnosis) in Table 1 was 18, the Bonferroni correction method (threshold of $P = 0.00278$ (P_0/N); $P_0 = 0.05$, $N = 18$) was applied to execute multiple testing-adjusted corrections. Therefore, the results were considered significant when the P value was <0.003 (i.e., 0.05/18). On the other hand, as four different studies of cases with inconsistent diagnoses in clinical and histologically were included, as shown in Table 2 [1, 12, 13, present study] and Table 3 [11–13, present study], the results presented in those tables were considered significant when the P value was <0.013 (0.05/4). Similarly, the data shown in Table 4 were regarded as significant when the P value was <0.006 (0.05/8), because eight different studies were included [1, 7–13, present study].

Results

Within the 15-year period, a total of 4004 cases was clinically diagnosed as endodontically associated periapical pathoses, of which 118 cases (2.95%) were rendered a histopathological diagnosis of nonendodontic pathologic entities.

The frequencies and demographic data of the various cases of nonendodontic periapical lesions are summarized in Table 1. Briefly, a wide variety of histopathological diagnoses, including benign odontogenic and non-odontogenic cystic and tumorous lesion and infectious diseases, in addition to malignant lesions, was noted in these 118 cases of nonendodontic periapical lesions. Overall, more male patients (male to female ratio = 1.15:1) were noted in the population of nonendodontic periapical lesions in the current study, but this was not statistically significant ($P > 0.05$). Additionally, about 61% ($n = 72$) of the nonendodontic periapical cases occurred in the mandible in the present study, which was statistically significantly higher than the occurrence in the maxilla ($P = 0.0167$). The first most frequent nonendodontic periapical lesion was keratocystic odontogenic tumor (KCOT) ($n = 38$, 32.20%), followed by fibro-osseous lesions ($n = 18$, 15.25%), and dentigerous cyst ($n = 13$, 11.02%). Considering the comparison of the frequency of occurrence of these first three most common nonendodontic periapical lesions, KCOT was found to be of borderline statistical significance as compared with fibro-osseous lesions ($P = 0.0075$) and was statistically significant as compared with dentigerous cyst ($P = 0.0005$). No significance was noted in a comparison of fibro-osseous lesions and dentigerous cyst ($P > 0.05$).

Worthy of note, in the current study, nine malignant nonendodontic lesions were located in the periapical area (7.63%), comprising squamous cell carcinoma ($n = 7$, 5.93%), adenoid cystic carcinoma ($n = 1$, 0.85%), and Langerhans cell histiocytosis ($n = 1$, 0.85%). The frequency of squamous cell carcinoma was higher than the frequencies of the other two malignant lesions, but this was not statistically significant ($P = 0.0339$). Furthermore, all the cases of squamous cell carcinoma were located in the mandible with all of them to be due to bony invasion from the mucosal lesions. Additionally, it is also important to note the relative high frequency of ameloblastoma in the periapical area ($n = 11$, 9.32%).

Table 1 Types, frequencies, and demographic data of the nonendodontic periapical lesions in the current study

Histopathological diagnosis	Number (percentage, %)	Gender		Age range (years)	Location	
		Male	Female		Maxilla	Mandible
Keratocystic odontogenic tumor	38 (32.20)	25	13	16–83	15	23
Fibro-osseous lesion	18 (15.25)	5	13	12–70	0	18
Dentigerous cyst	13 (11.02)	6	7	8–59	7	6
Ameloblastoma	11 (9.32)	4	7	16–61	1	10
Squamous cell carcinoma*	7 (5.93)	6	1	36–71	2	5
Calcifying odontogenic cyst	7 (5.93)	4	3	17–49	6	1
Fissural cyst (nasolabial, nasopalatine cyst)	5 (4.21)	3	2	28–69	5	0
Foreign body granuloma	3 (2.54)	1	2	48–52	3	0
Actinomycosis	3 (2.54)	2	1	48–59	0	3
Squamous odontogenic tumor	2 (1.70)	0	2	25, 41	0	2
Odontogenic fibroma	2 (1.70)	1	1	24, 28	1	1
Odontogenic myxoma	2 (1.70)	1	1	13, 22	1	1
Lateral periodontal cyst	2 (1.70)	2	0	52, 63	2	0
Glandular odontogenic cyst	1 (0.85)	1	0	35	1	0
Myxofibroma	1 (0.85)	0	1	36	1	0
Adenoid cystic carcinoma*	1 (0.85)	1	0	56	0	1
Langerhans cell histiocytosis*	1 (0.85)	1	0	37	1	0
Neurofibroma	1 (0.85)	0	1	30	0	1
Total	118 (100.00)	63	55	8–83	46	72

*Malignant lesion

Discussion

With careful analysis of medical and dental history, as well as detailed physical and radiographic examination, an endodontic lesion can be distinguished from a nonendodontic periapical lesion; however, a review of the English language literature revealed that a wide variety of nonendodontic periapical lesions are still being misdiagnosed as endodontic

Table 2 Comparisons of the patient gender and locations of nonendodontic periapical lesions in the current study with those reported in three previous studies [1, 12, 13]

	Present study (Taiwan, 2015)	Kontogiannis et al. (Greece, 2015) [13]*	Ortega et al. (Chile, 2007) [12]*	Bhaskar (USA, 1966) [1]*
Gender				
Male	63 (53.39%)	30 (57.69%)	11 (42.31%)	19 (37.25%)
Female	55 (46.61%)	22 (43.31%)	15 (57.69%)	32 (62.75%)
Male:female	1.15:1	1.36:1	0.73:1	0.59:1
Total number of nonendodontic periapical lesions	118	52	26	51**
Location				
Mandible	72 (61.02%)	22 (44.00%)	10 (38.46%)	26 (52.00%)
Maxilla	46 (38.98%)	28 (56.00%)	16 (61.54%)	24 (48.00%)
Total number of nonendodontic periapical lesions	118	50**	26	50***
Total number of cases	4004	1521	4006	2308

*Reference number

**Data was unavailable in two cases

***Data was unavailable in three cases

Table 3 Comparisons of the types and frequencies of histopathological diagnoses of nonendodontic periapical lesions in the current study with those reported in three previous studies [11–13]

Histopathological diagnosis	Present study (Taiwan, 2015)	Kontogiannis et al. (Greece, 2015) [13]*	Ortega et al. (Chile, 2007) [12]*	Kuc et al. (Canada, 2000) [10]*
Keratocystic odontogenic tumor	38	18	11	0
Fibro-osseous lesion	18	4	1	1
Dentigerous cyst	13	2	0	0
Ameloblastoma	11	1	0	0
Squamous cell carcinoma**	7	0	0	0
Calcifying odontogenic cyst	7	3	1	0
Fissural cyst (nasolabial, nasopalatine cyst)	5	0	1	1
Foreign body granuloma	3	2	1	0
Actinomycosis	3	1	0	0
Squamous odontogenic tumor	2	0	1	0
Odontogenic fibroma	2	0	0	0
Odontogenic myxoma	2	0	0	1
Lateral periodontal cyst	2	6	1	1
Glandular odontogenic cyst	1	10	0	0
Myxofibroma	1	0	0	0
Adenoid cystic carcinoma**	1	0	0	0
Langerhans cell histiocytosis**	1	1	0	0
Neurofibroma	1	0	0	0
Focal osteoporotic marrow defect	0	1	0	0
Metastatic carcinoma**	0	1	0	0
Dental follicle	0	1	0	0
Chronic sinusitis	0	0	3	0
Central giant granuloma	0	0	3	2
Hemangioma	0	0	1	0
Amalgam tattoo	0	0	1	0
Multiple myeloma**	0	0	0	1
Ameloblastic odontoma	0	1	0	0
Ameloblastic fibroma	0	0	1	0
Calcifying epithelial odontogenic tumor	0	0	0	1
Total number of nonendodontic periapical lesions	118	52	26	8
Total number of cases	4004	1521	4006	805

*Reference number

**Malignant lesion

periapical lesions, the frequency being as high as 6% [9]. Compatible with previous studies performed in different countries [1, 7–13], 2.95% of clinically diagnosed endodontic periapical pathoses cases were rendered a histopathological diagnosis of nonendodontic pathologic entities in the current study, which is, to the best of our knowledge, the first study of this type in Taiwan.

Comparisons of the patient gender and location of the nonendodontic periapical lesions in the present study with those of three other studies performed in Greece [13], Chile [12], and the USA [11] are presented in Table 2. The male to female ratio in the present study was 1.15:1, which was consistent with the data of Kontogiannis et al. (1.36:1) [13], but in contrast to the reports of Ortega et al. (0.73:1) [12] and Bhaskar (0.59:1) [1], in which more female patients were noted [1, 12]. On the other hand, about 61% of the nonendodontic periapical lesions in the present study occurred in the mandible, which was higher than the percentage reported by Bhaskar (52.00%) [1] ($P > 0.05$), without statistical significance, and was higher than the findings of the studies of

Table 4 Comparisons of the frequencies, the most frequent lesions, and the number of malignant nonendodontic periapical lesions in the current study with those reported in previous studies [1, 7–13]

Authors (year of publication) [reference number]	Total number of cases	Nonendodontic periapical lesions (%)	The most frequent nonendodontic periapical lesion	Number (percentage) of malignancies
Bhaskar (1966) [1]	2308	2.30	Cementoma (52.83%)	0 (0.00%)
Seltzer et al. (1967) [7]	87	1.15	Fibrous dysplasia (10.00%)	0 (0.00%)
Stockdale & Chandler (1988) [8]	1108	0.80	Not available	0 (0.00%)
Spatafore et al. (1990) [9]	1659	6.00	Not available	Not available
Nobuhara & del Rio (1993) [10]	150	4.60	Lateral periodontal cyst (42.86%)	0 (0.00%)
Kuc et al. (2000) [11]	805	0.99	Central giant cell granuloma (40.00%)	1 (12.50%)
Ortega et al. (2007) [12]	4006	0.65	Keratocytic odontogenic tumor (42.31%)	0 (0.00%)
Kontogiannis et al. (2015) [13]	1521	3.42	Keratocytic odontogenic tumor (34.62%)	2 (7.69%)
Present study	4004	2.95	Keratocytic odontogenic tumor (32.20%)	9 (7.63%)

*Reference number

Kontogiannis et al. (44.00%) [11] (P = 0.0422) and Ortiga et al. (38.46%) [12] (P = 0.0355), in which more maxilla cases were found [12, 13].

Comparisons of the types and frequencies of histopathological diagnoses of nonendodontic periapical lesions in the current study with the data reported in the three previous studies [11–13] are presented in Table 3. In concurrence with the three previous studies [11–13], there was a wide spectrum of histopathological diagnoses of nonendodontic periapical lesions in the current study, comprising cysts and neoplasms of odontogenic and non-odontogenic origin, malignancies of epithelial, salivary gland, hematologic and metastatic origin, and infectious diseases. On the other hand, in cases of malignancy, oral squamous cell carcinoma, which was not identified in the other three studies [9–11], was the most predominant disease entity (n = 7) in this study; this may be associated with the high frequencies of the oral habits of alcohol drinking, betel-quid chewing and cigarette smoking in Taiwan, which are related to a risk of oral epithelial malignancy [16]. Moreover, all cases of squamous cell carcinoma in the current study were located in the mandible, suggesting that particular clinical attention in cases of unhealed lesions in the mandible in patients at high risk of oral epithelial malignancy is required [16]. However, it should be aware that for those cases of squamous cell carcinoma being regarded as misdiagnosed nonendodontic periapical lesions in the present study were based on imaging examination neglecting the clinical findings.

No cases of KCOT were noted in the report of Kue et al. [9]; however, KCOT was the most common nonendodontic periapical lesion in the current study, as well as in the studies of both Kontogiannis et al. [13] and Ortega et al. [12]. Additionally, in the present study, the frequency of KCOT in the mandible (60.5%) was higher than that in the maxilla (39.5%), and there was a slight male predilection (1.92:1); these findings were consistent with previous studies [3, 17]. On the other hand, the percentages of occurrence of the five most frequently found lesions (73.73%) in the present study were statistically significantly higher than those of the corresponding disease entities in the studies of Kontogiannis et al. [13] (P = 0.0012), Ortega et al. [12] (P = 0.0060), and Kuc et al. [11] (P = 0.0009).

The frequency, the most frequent lesion, and the number of malignancies of nonendodontic periapical lesions in the current study and eight previous studies [1, 7–13] are shown in Table 4. In two [12, 13] of the eight previous reports, as well as in the present study, KCOT was the most frequent nonendodontic periapical lesion; the percentage in the current study (32.20%) being compatible with the findings of Ortega et al. (42.31%) [12] and Kontogiannis et al. (34.62%) [13]. There were no malignant cases of nonendodontic periapical lesions in five of the eight previous studies [1, 7, 8, 10, 12]; however, it is worthy of note that the present study comprised the greatest number of cases of malignancy (n = 9), the percentage (7.63%) being similar to that reported in the study of Kontogiannis et al. (n = 2, 0.13%) [13] but lower than that reported by Kuc et al. (n = 1, 0.12%) [11] ($p > 0.05$).

In conclusion, we have described in detail the frequencies, types, and demographic data of nonendodontic periapical lesions misdiagnosed as apical periodontitis lesions in a population of Taiwanese patients. Similar trends were observed to those presented in previous reports from other countries; however, some detailed information was different, perhaps due to different geographic distributions and different inclusion criteria. Moreover, oral squamous cell carcinoma, which was not reported in the other studies [1, 7–13], was the most predominant malignant disease entity of nonendodontic periapical lesions misdiagnosed as endodontic apical periodontitis lesions relied on radiographic examination overlooking the clinical findings in the present study. Hence, the current data provide a basis for both clinicopathological investigation and educational teaching related to

nonendodontic periapical lesions misdiagnosed as apical periodontitis lesions. In addition to careful examination of medical and dental history, as well as physical and radiographic examination, a biopsy is strongly recommended for those cases particularly with relatively large periapical bony destruction to acquire a definite histopathological diagnosis before any surgical intervention. On the other hand, the tissues removed from routine enucleation or curettage of periapical lesions are also recommended to submit for histopathological examination.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Due to the retrospective nature of the present study, informed consent was waived in accord with the institutional review board (Institutional Review Board of Kaohsiung Medical University Chung-Ho Memorial Hospital) standards of our institution.

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