Clinical Practice

Histopathologic Examination to Confirm Diagnosis of Periapical Lesions: A Review

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Abstract

Most periapical lesions are represented by inflammatory cysts, granulomas, abscesses or fibrous scars. These inflammatory conditions are often termed “endodontic lesions” because pulpal necrosis is the initiating event in their pathogenesis. Although rare, other clinically confusing periapical lesions have been extensively documented in numerous case reports and short case series. These lesions represent a wide range of pathosis, including various developmental cysts, infections, benign but locally aggressive lesions, and malignancies. The literature describing these lesions and the value of a histopathologic examination in diagnosis is reviewed.

MeSH Key Words: jaw neoplasms/pathology; odontogenic cysts/pathology; periapical diseases/pathology

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Periapical lesions resulting from necrotic dental pulp are among the most common pathologic conditions within alveolar bone. Although there are numerous reports of nonendodontic benign or malignant lesions presenting in the periapical area, the large majority are periapical granulomas, cysts or abscesses. As a result, periapical tissue is often submitted for histopathologic review only if there are concerns about the clinical diagnosis, rather than for a routine audit to confirm the clinical diagnosis. The frequency of clinical screening to decide whether biopsy submission is warranted and the extent to which this has an impact on accurate diagnosis are not known. Several studies1–4 have suggested that between 0.7% to 5.0% of periapical biopsies result in contributory histopathologic findings. However, these studies are almost certainly biased by the previously described clinical selection process. Other histologic studies5,6 of periapical lesions describing only inflammatory periapical lesions of endodontic origin represent an unresolved inconsistency. This paper reviews and discusses the literature related to histopathologic diagnosis of periapical lesions, with an emphasis on cases showing unusual findings.

Guidelines for Histopathologic Examination

The requirement for histologic examination of periapical tissues in nonhospital settings has received surprisingly little discussion. Several authors7–10 have recommended that those periapical lesions not responding to conservative endodontic therapy should undergo histopathologic evaluation. The guidelines11 of the American Association of Endodontists indicate microscopic examination of a periradicular lesion is appropriate any time there is recoverable tissue. However, at least one author,12 indicating a high level of confidence in the clinical diagnostic process, has argued that careful systematic clinical diagnosis will differentiate endodontic from nonendodontic pathosis and that routine submission of endodontic surgical specimens is of no advantage to the patient. Biopsy submission would, therefore, depend on clinical suspicion. Presumably, from this perspective, the failure to submit periapical tissue in cases that subsequently prove to be of nonendodontic origin would be regarded as an avoidable clinical misdiagnosis.

Retrospective Studies of Periapical Biopsies

Histopathologic diagnoses that identify a pathosis other than periapical granuloma, cyst, abscess or fibrous scar are defined as significant in this discussion. Although these diagnoses are estimated to be between 0.7% and 5.0% of all periapical biopsies,11–6 no published data describe the frequency with which periapical lesions are submitted for histopathologic examination. Submission of only those selected cases that have caused clinical concern would artificially increase the percentage of periapical biopsies...
showing significant findings. Preliminary data suggest that selective submission is a common practice.16

On a cautionary note, an unknown number of nonendodontic periapical lesions, initially diagnosed and treated as endodontic cases, would also be excluded from these survey studies, thus decreasing the percentage of significant periapical biopsies. Exclusion could occur in 2 ways. The first could occur when a periapical lesion in an endodontically treated case is belatedly submitted for examination after the lesion shows unexpected aggressive behaviour. These lesions would not be classified as endodontic cases and would be excluded from retrospective studies of periapical lesions. The second category of cases are those in which benign but expansile periradicular lesions, such as lateral periodontal or nasopalatine duct cysts, were misdiagnosed and the tooth treated endodontically. Subsequent surgery of the nonresolving periapical lesion would result in clinical success. However, the misdiagnosis and inappropriate treatment would not be identified.

### Review of the Literature Describing Unusual Periapical Pathosis

There have been many reports documenting clinically confusing periapical lesions, although their incidence is unknown. Various developmental cysts, fibro-osseous lesions, infections, granulomatous inflammatory conditions and a wide range of benign or malignant neoplasms have been described. Additionally, radiographically confusing anatomic superimpositions have been discussed. Table 1 shows the numbers and types of lesions that have been described. These are reviewed in the following sections.

### Cysts

Cysts that mimic endodontically mediated periapical lesions include odontogenic keratocysts,9,17–20 nasopalatine duct cysts,21,22 contiguous residual cysts and lateral periodontal cysts.6 Within this group, the odontogenic keratocyst (OKC) is the most important because of its propensity for recurrence and aggressive behaviour. About 0.7% of putative radicular (periapical) cysts represent OKCs.19 In one large OKC study,17 11.2% of the OKCs were identified de novo in the site of previously extracted teeth. Although it is possible that the teeth in these cases were removed for reasons unrelated to the contiguous radiolucency, this finding suggests the possibility that a periapical OKC prompted the tooth removal.

Other cyst types are not as aggressive. However, if root canal treatment is done in these cases, the cysts would continue to enlarge, independent of the success of the endodontic treatment. Further periapical surgery of the nonendodontic lesion would result in resolution.

### Infections

Although actinomycosis is the most commonly documented infection,24–34 histoplasmosis35 and aspergillosis6,36

<table>
<thead>
<tr>
<th>Category</th>
<th>Type</th>
<th>No. of cases</th>
<th>References</th>
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<td></td>
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<td></td>
<td>Lateral periodontal cyst</td>
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<td>Residual cyst</td>
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<td>23</td>
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<td></td>
<td>Othera</td>
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<td>3</td>
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<tr>
<td>Infections</td>
<td>Actinomycosis</td>
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<tr>
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<td>Histoplasmosis</td>
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<td>Aspergillosis</td>
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<tr>
<td>Benign aggressive lesions</td>
<td>Central giant-cell granuloma</td>
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<td>1, 4, 6, 9, 13, 37–40</td>
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<td>Otherb</td>
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<td>Lymphoma</td>
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<td>Otherc</td>
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<td>6, 60, 61</td>
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*aGlobulomaxillary cyst: No longer a valid diagnosis.
*bCentral ossifying fibroma, 2 myxomas, central odontogenic fibroma, Pindborg tumour, 2 osteoblastomas, 3 cases of Langerhans cell disease.
*cCementomas were interpreted from description to represent early periapical cemental dysplasia (see reference 1). Other = 1 fibro-osseous lesion, not otherwise specified, 1 monostotic fibrous dysplasia.
*dIncludes adenocarcinoma and metastatic lesions.
*eLeukemia, 2 cases of multiple myeloma.
have also been described. These case reports typically describe the infections as a complication of endodontic treatment and not as a primary pathosis in the periapical area. However, identification of this complication is necessary to initiate appropriate follow-up antibiotic therapy.

**Benign Aggressive Lesions**

The most documented locally destructive lesion that has been mistaken for periapical disease is the central giant-cell granuloma. This benign lesion of unknown origin was once thought to represent a reparative process. These lesions demonstrate a range of aggressive behaviour that is difficult to predict. In at least one case, the associated tooth did not respond to electric pulp testing, but the pulp subsequently appeared vital after an opening was made to access the pulp. This suggests that vitality testing can be unreliable when lesions encroach on the root apex.

Other reported lesions have been central ossifying fibroma, Pindborg tumour, Langerhans cell disease, osteoblastoma and the central odontogenic fibroma. Generally, delayed identification of these lesions would result in more extensive bone destruction and greater morbidity, but would not normally be expected to be life-threatening.

**Benign Fibro-osseous Lesions**

A specific type of fibro-osseous lesion called “periapical cemental dysplasia,” which develops around root apices, represents a well-recognized diagnostic challenge. Diagnosis is particularly difficult for early lesions that do not show mineralization on radiographs. A multifocal presentation is helpful for discerning their nonendodontic nature, although focal presentations occur. Careful clinical assessment, including taking a history of the affected area, radiographs and vitality testing, should usually establish the diagnosis. Radiographic features are more definitive in the later mineralizing stages. Typically treatment is not indicated in these cases.

**Granulomatous Inflammation**

Granulomatous inflammation has been specifically described and distinguished from the granulation tissue found in periapical granulomas. Granulomatous inflammation can be elicited by a variety of agents, such as foreign materials, cholesterol derived from cell necrosis, or fungal and mycobacterial infections. However, this type of inflammation is relatively common in periapical biopsy material and might not result in a separate classification of the lesions showing this feature. The role of granulomatous inflammation in endodontic failure does not seem to be well understood but, in theory, could be important. At least one report indicated that foreign body–induced granulomatous inflammation in periapical tissues resulted in a lesion that was refractory to endodontic therapy.

**Malignant Lesions**

Misdiagnosed malignant neoplasms cause the greatest concern and represent about 12% of documented cases. Presumably these cases are relatively rare and the documentation is disproportionate because of the significance of the missed diagnosis. A wide range of primary or metastatic malignant lesions have been reported, including osteosarcoma, lymphoma, plasma-cell tumours and leukemia; however, the most commonly reported malignancies are various forms of carcinoma. Atypical features, summarized by Hutchison and others, that suggest the possibility of neoplastic involvement include minimal caries, root resorption, irregular radiolucency, localized tooth mobility, anesthesia and failure of the periapical lesion to resolve after root canal treatment. Tooth vitality is also an important finding, but this determination may be difficult if the lesion encroaches on the apex.

**Anatomic Superimpositions**

Anatomic superimpositions are an obvious concern, but should not present a diagnostic problem. The most common presentation is the superimposition of the mental foramen. An unusual case involving a median mandibular salivary gland inclusion has been described as a confounding radiographic presentation that suggests periapical disease.

**Conclusions**

A wide range of nonendodontic pathoses presenting in the periradicular region has been documented. The clinical implications vary depending on the lesion. The frequency with which this occurs is not known, but clinical sensitivity to these possibilities is important to minimize the possibility of misdiagnosis. It is useful to remember that vitality tests are not always reliable, necrotic and vital tissues can co-exist in the same tooth, and a nonvital tooth is not necessarily the reason for a periapical lesion. Finally, the extent to which a nonendodontic lesion encroaching on the apex of a tooth can influence vitality testing has not been clarified.

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**References**


