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Periapical actinomycosis: A clinicopathologic study

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Objective. We sought to evaluate the incidence and clinical outcome of an accidental finding of actinomycotic colonies in periapical lesions submitted for histologic examination.
Study design. The study included all periapical biopsy specimens submitted for histologic examination between 1997 and 2000. Sections of paraffin-embedded tissues, 5 μm, were cut and stained by using hematoxylin and eosin, periodic acid–Schiff, and the Gram stain. The presence of typical branching colonies of filamentous bacteria staining positive for periodic acid–Schiff and Gram stain was indicative of *Actinomyces*.
Results. Typical actinomycotic colonies were identified in 17 of 963 (1.8%) periapical biopsy specimens. The mean patient age was 42, and males were predominant (65%). The maxilla was the most frequently involved site (65%), with equal distribution in the anterior and posterior areas. Radiographically, most cases presented as well-demarcated radiolucent lesions. Malignancy was suspected in 3 cases. Of the periapical lesions, 15 were epithelialized, and in 4 cases, a true epithelial-lined lumen was found, which was diagnosed as a radicular cyst. A residual cyst was diagnosed in 1 case, and in 1 case, an epithelial lining was not identified. Treatment included surgical curettage and a short course of antibiotic therapy. Healing was uneventful in all cases.
Conclusion. Periapical actinomycosis is not common. Its outcome is favorable after surgical curettage supplemented by short-term antibiotic treatment. The relationship of periapical actinomycosis with the more serious cervicofacial actinomycosis should be evaluated.
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Actinomycosis is an indolent, slowly progressive infection caused by anaerobic or microaerophilic bacteria that normally colonize the mouth, colon, and vagina. It is most commonly caused by the Gram-positive bacterium *Actinomyces israelii*. Less common causes of the disease are *Actinomyces naeslundii*, *Actinomyces odontolyticus*, *Actinomyces viscosus*, *Actinomyces meyeri*, and *Propionibacterium propionicus*.[1] Recently, a new species, *Actinomyces radicidentis*, has been isolated from apical periodontitis.[2] Four clinical forms of actinomycosis account for most of these human infections: the cervicofacial, thoracic, abdominopelvic, and cerebral forms. Cervicofacial actinomycosis presents as a chronic, slowly evolving induration in the mandibular-preauricular region, often accompanied by fistular tracts to the skin that discharge typical sulfur granules.[3] Invasion of the microorganism is usually a result of the disruption of the mucosal barrier after trauma or dental manipulation. In rare instances, cervicofacial actinomycoses instigate serious complications, such as central nervous system involvement and disseminated disease.

Periapical actinomycosis is believed to be a nonresolving periapical lesion associated with actinomycotic infection and has been suggested as a contributing factor in the perpetuation of periapical radiolucencies after root canal treatment.[4,5] A diagnosis is usually made by identifying the typical actinomycotic colonies in a surgical specimen.[4] Periapical actinomycosis is thought to be rare; only 45 cases have been published in the literature, mostly as case reports and as small series

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Table I. Clinical data and pathologic diagnosis of cases with periapical actinomycosis

Case	*Jaw*	*Tooth*	*Fistula*	*Previous endodontics*	*Clinical diagnosis*	*Treatment*	*Pathologic diagnosis*	*No. of colonies per slide*
1	Upper	Lateral incisor		Yes	RC	Apicoectomy	EPL	2
2	Upper	Lateral incisor	Yes	Yes	RC	Apicoectomy	EPL	8
3	Upper	Central and lateral incisors		No	RC	Apicoectomy	RC	1
4	Upper	Lateral incisor and canine	Yes	No	CGCG, Tu	Apicoectomy	RC	10
5	Upper	Lateral deciduous tooth		No	RC	Extraction	Granuloma	1
6	Upper	First molar		Yes	RC	Extraction	EPL	2
7	Upper	First molar		Yes	RC, CO	Extraction	EPL	3
8	Upper	First molar		No	RC	Extraction	RC	3
9	Upper	First molar		NI	Granuloma	Root resection	EPL	3
10	Upper	Second molar		NI	RC	Extraction	RC	1
11	Upper	Second and third molars		No	Tu	Extraction	EPL	3
12	Lower	First premolar		No	Residual cyst	Enucleation	Residual cyst	1
13	Lower	Second premolar	Yes	NI	RC	Extraction	EPL	4
14	Lower	First molar		Yes	Abscess	Extraction	EPL	4
15	Lower	First molar	Yes	No	Tu	Extraction	EPL	1
16	Lower	First molar	Yes	No	Abscess	Root resection	EPL	10
17	Lower	Third molar	Yes	No	Perio-endo	Extraction	EPL	1

RC, Radicular cyst; *EPL,* epithelialized periapical lesion; *Tu,* malignant tumor; *CO,* condensing osteitis; *CGCG,* central giant cell granuloma; *NI,* no information.

of cases.[4,6,7] Nevertheless, it is assumed to be more frequent than is commonly believed.[4,8] There are only limited data on the frequency of periapical actinomycosis among periapical lesions[9] or on the correlation between periapical and cervicofacial actinomycosis.

The purpose of the present study was to evaluate the incidence of an accidental finding of actinomycotic colonies in periapical lesions submitted for histologic examination. Analysis of the clinical features, treatment, and outcome of these cases made it possible to compare these lesions with the classic cervicofacial actinomycosis.

MATERIAL AND METHODS

All periapical biopsy specimens submitted to the oral pathology laboratory at Tel Aviv University between 1997 and 2000 were retrospectively reviewed. The material submitted to the laboratory by oral surgeons was mostly curetted. The study included cases with detailed clinical information including age, sex, clinical diagnosis, and radiographs of the lesion or a description of the radiographic findings. Only cases with a clinical diagnosis of periapical pathosis (cyst, granuloma, or abscess) were selected for the study.

Tissue samples were fixed in 10% buffered formalin and embedded in paraffin. For each case, random 5-μm sections were cut and stained with hematoxylin and eosin, periodic acid–Schiff, and Gram stain. All slides were reviewed by 2 of the researchers (A.H., I.K.) to confirm the diagnosis. Cases in which the pathologic diagnosis was not an inflammatory periapical lesion were excluded.

A diagnosis of a radicular cyst was made on the basis of an identifiable lumen or part of a lumen, lined by epithelium. However, because the study made use of archival material, most lesions were curetted, and the submitted material was fragmented in some cases. Histologic differentiation between a true radicular cyst and a granuloma with epithelial strands could not be accurately performed. Cases in which epithelial strands were present but with no clear epithelial-lined lumen were designated as *epithelialized periapical lesions*. In addition, because the biopsy specimens did not contain root tips, structural reference to the root canals of the affected teeth was not possible.

The presence of characteristic branching colonies of filamentous bacteria that stained positive with periodic acid–Schiff and Gram stain was indicative of *Actinomyces*. The number of colonies per slide was recorded.

RESULTS

Typical actinomycotic colonies were identified in 17 of 963 (1.8%) periapical biopsy specimens. Table I summarizes the clinical data. Patient ages ranged from 16 to 75 years (mean, 42 years), and males were predominant (11 men and 6 women). The maxilla was the most frequently involved site (11 cases,

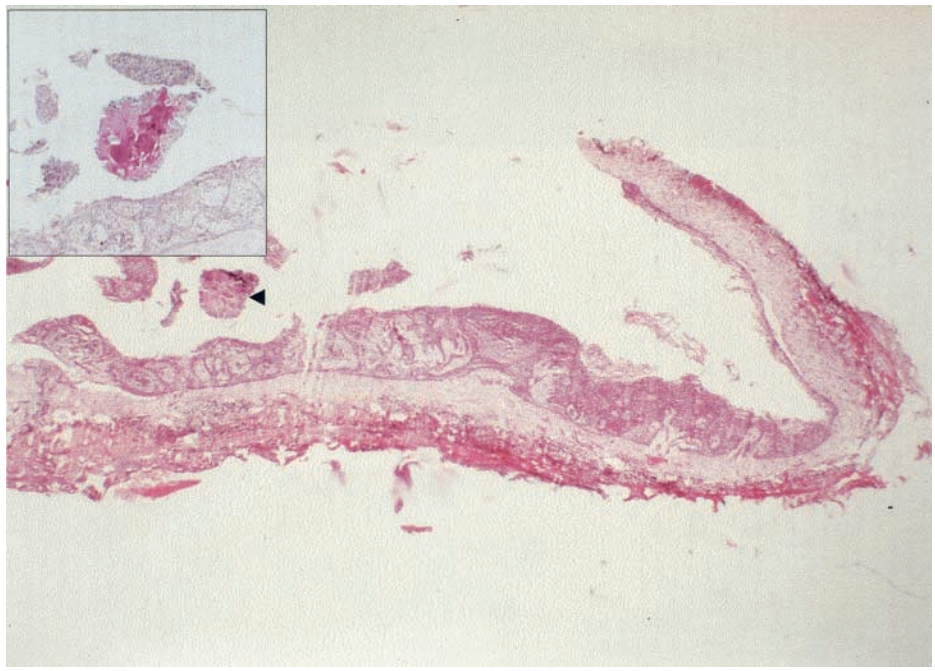

Fig 1. A radicular cyst. Note the epithelial lining of the cyst and the actinomycotic colony in the lumen (*arrowhead*) (hematoxylin-eosin, original magnification ×10). Inset: Periodic acid–Schiff stain of the actinomycotic colony (original magnification ×20).

65%), with equal distribution in the anterior and posterior areas. The lower jaw was affected in 6 cases (35%), all associated with molars and premolars. Radiographically, most cases presented as radiolucent lesions with well-defined borders; however, in cases 4, 11, and 15, the radiographic margins were blurred. In case 7, a radiopaque lesion that resembled condensing osteitis was observed near the radiolucent lesion in the maxillary right first molar. Periodontal involvement was noticed in 4 cases (24%), and sinus tract involvement was evident in 6 cases (35%). In 5 cases, the involved teeth were endodontically treated. A review of the patients' radiographs revealed reasonable endodontic treatment.

The submitted clinical diagnosis was radicular cyst in most cases (Table I); an abscessed tooth was diagnosed in 2 cases. Three cases were clinically suspected to be malignant because of blurred radiographic margins (cases 4, 11, and 15), and associated paresthesia was suggestive of malignancy in 1 case (case 4). The clinicians did not suspect actinomycosis in any of the cases.

The histologic diagnosis was true radicular cyst in 4 cases (24%; Fig 1); in 11 cases (65%), the lesion consisted of inflammatory granulomatous connective tissue with strands of epithelium but with no discernible lumen. These lesions were diagnosed as epithelialized periapical lesions (Fig 2). One case was diagnosed as a residual cyst, and in 1 case no epithelium was identified and the diagnosis was apical granuloma. It was impossible to accurately classify the 963 periapical lesions in the manner described by Nair[9] because of the limitation of the technique by which the biopsy specimens were obtained. However, 694 cases (72% of the lesions) were epithelialized, representing either radicular a cyst or a periapical granuloma with epithelial strands.

In 14 of 17 cases, fewer than 4 actinomycotic colonies per slide were found, and in 3 cases, more than 8 separate colonies were identified. The actinomycotic colonies presented as isolated masses of filamentous bacteria with a central area of necrosis and radiating filaments (Fig 3). Eosinophilic club-shaped extensions were seen at the periphery of the filaments in most of the colonies. Multiple coccoid bacteria were also found throughout the colonies. Most colonies were surrounded by an inflammatory infiltrate composed of mainly polymorphonuclear leukocytes, lymphocytes, and plasma cells (Fig 4).

Treatment included extraction of the affected tooth or root, along with curettage of the lesion in 13 cases. Apicoectomy was performed in 4 cases. The reason for the treatment decision was not mentioned in the referral chart. In all cases, surgery was followed by oral antibiotics, usually amoxicillin 1.5 g per day for 10 days. The patients' prognosis was excellent; healing was uneventful in all cases.

DISCUSSION

The reported incidence of an accidental finding of actinomycotic colonies in surgical material obtained

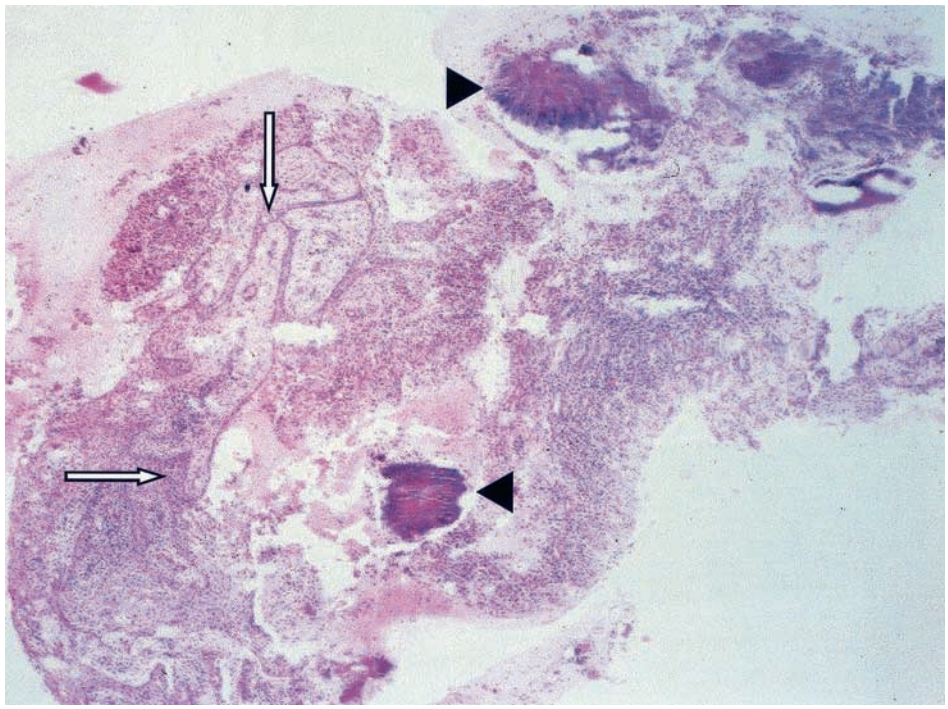

Fig 2. An epithelialized periapical lesion. No discernible lumen can be identified. Note the actinomycotic aggregate (*arrowhead*) and the epithelial strands (*arrow*s) (hematoxylin-eosin, original magnification ×20).

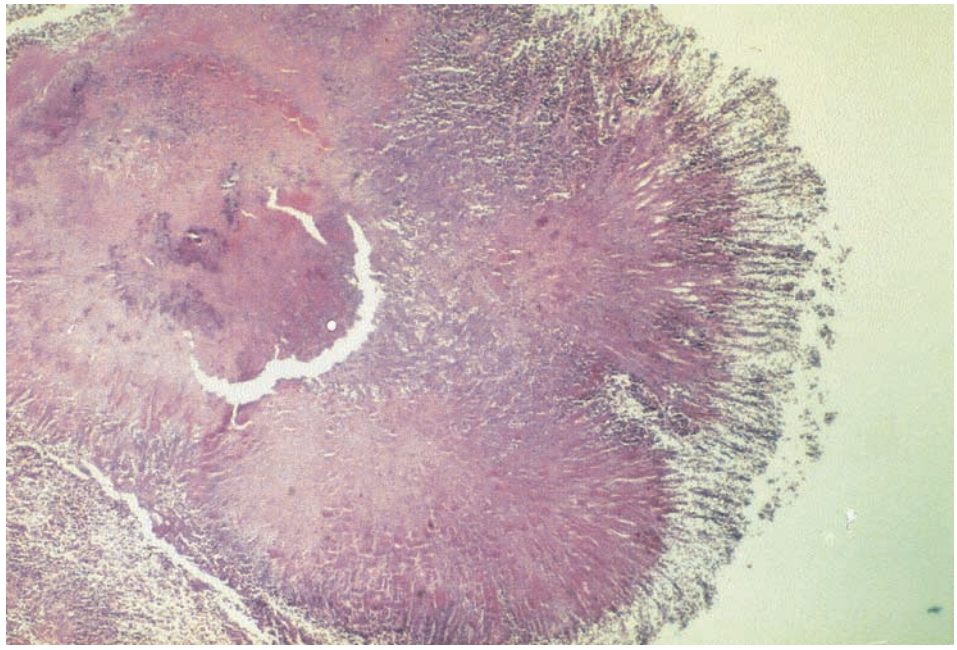

Fig 3. Actinomycotic aggregate with central necrosis and club-shaped extension of filaments (periodic acid–Schiff, original magnification ×100).

from periapical lesions is less than 5% of all periapical lesions.[4,10,11] In the present study, the incidence was only 1.8% of all periapical material submitted for histologic examination. It is important to stress that other bacterial infections, such as nocardiosis, have a similar histologic presentation; however, such instances are extremely rare in the jaws.[3,12] To make an absolute identification, anaerobic culture, biochemical tests, and

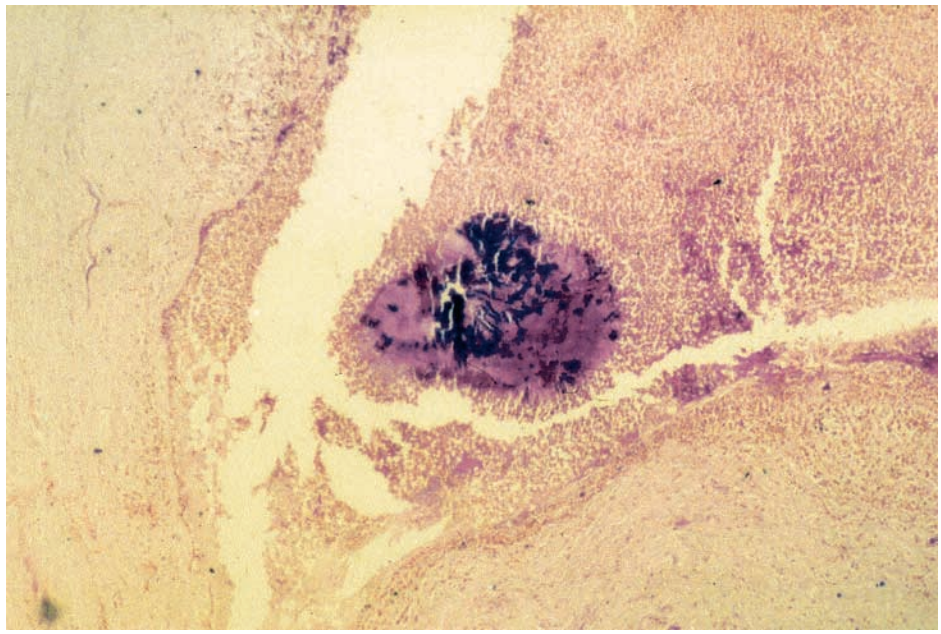

Fig 4. Actinomycotic aggregate surrounded by inflammatory cells within an epithelialized periapical lesion (Gram stain, original magnification ×200).

gas chromatography are required; however, these procedures are not relevant in most cases of periapical actinomycosis because the diagnosis is usually made after fixation and embedding of the surgical material. Monoclonal antibodies against *Actinomyces* were used by Happonen et al,[13] but they are not available commercially and therefore are not routinely used.

Actinomycotic infection in periapical lesions could be more prevalent than reported.[5] Samuels and Martin[8] reported an exceptionally large number of cases of cervicofacial actinomycosis. Over a 6-year period, 184 cases of microbiologically proven cervicofacial actinomycosis were found, including cases of periapical actinomycosis. The study was based on cultured, not biopsy-proven, *Actinomyces*; therefore, it is difficult to make any comparisons. In a recent literature review, Sakellariou[4] found only 45 reported cases of periapical actinomycosis, but he concluded that it is not as rare as commonly believed. The results of the present study are in agreement with those of a previous study[9] that showed that the prevalence of actinomycotic infection is indeed low and therefore should not be considered a common cause of endodontic failure.

Actinomyces has been found extraradicularly and in the infected root canals, which are the primary port of entry.[14] Nair and Schroeder[10] reported 2 cases of periapical actinomycosis; in one of these the organism was observed in the apical root canal. The correlation of the intraradicular presence of the organism with periapical actinomycosis was not established. In most published cases, however, the organism was identified in the body of the periapical lesion.

The association among root canal treatment and the development and propagation of the actinomycotic infection is not clear. Because *Actinomyces* is commonly present as an oral commensal, the microorganism can reach the periradicular tissue whenever the coronal seal is lost and root canal obturation does not impede saliva leakage.[15] The aggregation of the microorganism in colonies probably helps it to escape the host defense system and persist in the periapical area.[16] Although most reported cases in the literature are associated with a long and complicated endodontic history,[4,6] periapical actinomycosis can develop in the absence of root canal therapy. Nair and Schroeder[10] found actinomycotic infection in 2 of 45 periapical lesions, with no previous endodontic treatment. In the present study, root canal treatment was performed in only 5 of the 14 cases in which the endodontic status was recorded.

The prevalence of radicular cysts in periapical lesions is reported to be between 6% and 55%. However, when the histopathologic diagnosis is based on a random or limited number of serial sections, most epithelialized periapical lesions are wrongly classified as radicular cysts.[17] Recently, in a well-designed study, Nair et al[18] found that, overall, 52% of periapical lesions were epithelialized, but only 15% were cysts. They defined a *true apical cyst* as a cavity completely enclosed with epithelial lining

Table II. Comparison between cervicofacial and periapical actinomycosis

Patient data	*Cervicofacial*	*Periapical*
Mean age (y)	40	42
Sex	M > F	M > F
Predominant jaw	Mandible	Maxilla
Location	Soft tissues	Intrabony
Fistula	Multiple, on skin	Few, intraoral
Antibiotic course	Prolonged	Short
Healing	Slow	Uneventful
Complications	Occasional	Rare

and an apical pocket cyst when the cyst lumen opened to the root canal. In the present study, all cases but 1 were epithelialized, and in 5 cases an established epithelial-lined lumen was identified. Happonen[6] found that granulomas were associated with cases of periapical actinomycosis more often than cysts were (8 and 6 instances, respectively). However, the histologic criteria for the diagnosis were not reported. The high frequency of epithelialized periapical lesions in the present study could be attributable to the fact that maxillofacial surgeons send most of the biopsy specimens to our laboratory; therefore, most are large, long-standing, complicated lesions. It can also be hypothesized that the presence of long-standing actinomycotic colonies in periapical tissue, along with the inflammatory infiltrate, can induce epithelial proliferation. This hypothesis should be further investigated.

Table II summarizes the clinical features of periapical actinomycosis on the basis of the present study, along with previous ones,[6,7] and compares them with those of cervicofacial actinomycosis.[3] Periapical actinomycosis is directly associated with the teeth, most commonly the maxillary teeth, in contrast to the mandibular predilection in cases of cervicofacial actinomycosis. Furthermore, the symptoms are milder in periapical actinomycosis, and fistulation is most commonly intraoral. The clinical sign of multiple skin fistulae, which is considered typical in cervicofacial actinomycosis, is uncommon in periapical cases. The outcome of patients with periapical actinomycosis is excellent; in most cases, curettage of the lesion combined with a short course of antibiotics is sufficient to induce healing without complications.

Periapical actinomycosis has been regarded in the literature as a mild form of cervicofacial actinomycosis[9] for which prolonged antibiotic treatment is necessary. The results of the present study, along with the review of the literature, do not support this approach. Most cases of periapical actinomycosis do not differ clinically from other periapical lesions, and the outcome after surgical treatment is good. However, one should remember that, in some cases, microorganisms could invade the surrounding structures and propagate into cervicofacial actinomycosis. In these cases, a more vigorous treatment approach should be taken.

CONCLUSION

Periapical actinomycosis is uncommon. Cases of periapical actinomycosis have a favorable outcome after conservative surgical curettage along with short-term antibiotic treatment. The exact contribution of *Actinomyces* to the perpetuation of the periapical lesion should be further investigated. Histologic examination of all periapical lesions that are surgically curetted is mandatory.

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