Acute Primary Actinomycosis Involving the Hard Palate of a Diabetic Patient

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Actinomycosis is a relatively rare infection caused by saprophytic bacteria of the oral cavity and gastrointestinal tract that can become pathogenic. The chronic hyperglycemia of diabetes mellitus induces events that promote structural changes in various tissues and are associated with problems in wound healing. This infection remains largely unknown to most clinicians because of its different presentations, and palatal involvement is extremely rare. This report describes the case of a 46-year-old woman who was diagnosed with actinomycosis involving the hard palate. The main clinical, histopathologic, and therapeutic characteristics and differential diagnosis of actinomycosis are reviewed. To date, 3 cases of actinomycosis involving the hard palate have been reported.

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Actinomycosis is a slowly progressing infection caused by anaerobic or microaerophilic, gram-positive, non–spore-forming, non–acid-fast bacteria of the genus Actinomyces. The species most frequently isolated is Actinomyces israelii. Three distinct clinical forms of the disease have been described: cervicofacial, abdominopelvic, and thoracopulmonary, with the first being the most common.1,2

Oral and cervicofacial diseases are commonly associated with dental caries and extractions, gingivitis and gingival trauma, infection in erupting secondary teeth, chronic tonsillitis, otitis or mastoiditis, diabetes mellitus, immunosuppression, malnutrition, and local tissue damage caused by surgery, neoplastic disease, or irradiation.3 The chronic hyperglycemia of poorly controlled diabetes mellitus induces events that promote structural changes in various tissues and are associated with problems in wound healing and a greater susceptibility to infections.4–6

Actinomycosis mimics different diseases and exhibits different symptoms, a fact that makes its diagnosis difficult.7 Most commonly, it presents as a slowly progressive, indolent, indurated infiltration with multiple abscesses, fistulas, and sinuses. A less common form is acute and rapidly progressive, with fever and a fluctuating swelling that resembles a typical pyogenic infection.7,8 The differential diagnosis includes tuberculosis (scrofula), fungal infections, nocardiosis, suppurative infections by other organisms, and neoplasms.3

Microscopic analysis shows an outer zone of granulation tissue consisting of collagen fibers around central purulent loculations that contain abundant neutrophils that surround multiple “sulfur granules.”

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These granules appear as a basophilic mass with a radiating border of eosinophilic clubs after routine staining.3,9

This report describes the fourth case of primary actinomycosis involving the hard palate and discusses the main clinical, histopathologic, and therapeutic characteristics and differential diagnosis of this rare presentation of the disease.

Report of Case

A 46-year-old woman was seen at the Department of Oral and Maxillofacial Surgery, Federal University of Rio Grande do Norte (Natal, Brazil) with a 4-day history of a painful lesion on the hard palate that caused dysphagia. The patient had a 3-year medical history of poorly controlled type 2 diabetes mellitus and was being treated with metformin, although she reported discontinuing the treatment 2 months before the appearance of the lesion. The patient had been a smoker for 20 years, consuming 1 pack of cigarettes per day.

Intraoral examination showed an ulcerative lesion on the left side of the hard palate that measured approximately 1 cm in diameter and exhibited bone destruction and exposure with an overlying yellow-white slough (Fig 1). Several teeth were missing and the patient presented extensive carious lesions, supra- and subgingival dental calculi, extensive root exposure caused by gum recession, and a coated tongue. The patient denied episodes of bleeding, purulent discharge, headache, heaviness of the checks, cough with expectoration, respiratory distress, epistaxis, fatigue, anorexia, weight loss, fever, or more cardinal signs of inflammation. No lesion or symptom was identified in the oropharynx or hypopharynx or in any other region of the body, and there was no evidence of cervical lymphadenopathy.

Based on the clinical presentation, the diagnostic hypotheses were necrotizing sialometaplasia, salivary gland neoplasm, and oral squamous cell carcinoma. An incisional biopsy was performed and histopathologic analysis showed the presence of microscopic aggregates of tangled filaments characterized by a central eosinophilic mass from which numerous peripheral basophilic rays extended (Figs 2 through 4). The surrounding connective tissue was dense and fibrous and contained a discrete inflammatory infiltrate consisting of neutrophils, lymphocytes, and plasma cells. Some foreign body–type multinucleated giant cells and areas of necrosis also were identified.

Based on the microscopic findings, material was collected for culture and identification of the microbial agent. However, because the culture result was negative, a new sample was collected, seeded onto sheep blood agar, and incubated under anaerobic conditions.
The resulting colonies consisted of gram-positive bacilli that were negative by Ziehl-Neelsen staining. No β-hemolysis was observed. Next, the material was examined using the VITEK automated identification system (bioMérieux, Marcy l’Etoile, France), which identified *Actinomyces naeslundii* with 97% agreement. Some laboratory tests were performed (Table 1) to confirm the efficacy of the equipment. The diagnosis of actinomycosis was thus confirmed.

The patient was treated orally with amoxicillin (500 mg) 3 times per day for 4 weeks, which resulted in complete regression of the lesion.

**Discussion**

*Actinomyces* species are saprophytic bacteria of the oral cavity and gastrointestinal tract. The bacteria exhibit a low degree of virulence and are commonly found in the saliva and in dental plaque. However, under certain circumstances that compromise anatomic barriers and host susceptibility, their pathogenic form can cause actinomycosis.10,11

In addition to precarious oral hygiene, the present patient had diabetes mellitus. It is believed that the high concentration of glucose in the wound fluid of patients with diabetes is the main reason for the increased bacterial growth seen in these patients.5,12,13 According to Hirsch et al.,5 nondiabetic patients can resist bacterial invasion much more efficiently, whereas diabetic patients are more likely to succumb to the bacterial challenge. In addition, it is well known, although not completely understood, that diabetes mellitus impairs wound healing.

The typical actinomycosis infection is chronic in nature; however, it may be atypical with subacute or acute clinical manifestations.14 Samuels and Martin14 described 3 distinct presentations of the disease: acute painful swellings with duration shorter than 1 month; chronic long-standing infections with duration longer than 3 months; and unsuspected microbiologically proved actinomycotic lesions. Although the present patient did not show all signs and symptoms of acute inflammation, according to the classification of Samuels and Martin,14 the case can be categorized as the acute type of actinomycosis as a result of the presence of a painful lesion that occurred within a short period.

Actinomycosis involving the hard palate is extremely rare, and only 3 cases have been reported in the literature7 (Table 2). The first case was a cocaine user who had a circular and necrotic defect in the hard palate without nasal communication on probing.15 The second case presented a necrotic ulceration along the hard palate with overhanging yellow-green slough, in addition to perilesional erythema and boggy- ness with reactive swelling of the upper lip.11 The third case was characterized by a firm, infiltrative ulcerated plaque and significant tissue destruction and deformity, with an overlying yellow-white slough.7

The clinical diagnosis of actinomycosis is difficult because its onset is not specific and the differential diagnosis covers a wide range of diseases.16 Its variable clinical presentations are generally considered representative of malignancy rather than of an infectious process,3 as seen in the present case. From this perspective, the diagnosis of actinomycosis on admission is correct in fewer than 10% of cases.15

Different pathologic entities were considered in the differential diagnosis of the present case. Necrotizing sialometaplasia, a benign reactive necrotizing inflammatory process involving the minor salivary glands of the hard palate,17 was one of them. The most commonly proposed and generally accepted etiology for this condition relates to ischemia and, although not all cases will be correlated with an obvious etiologic event, clinical history is helpful in its diagnosis.18 The present case denied any surgical procedure or other traumatic injuries that could be considered potential predisposing factors. Moreover, the microscopic features of necrotizing sialometaplasia (pseudoepitheliomatous hyperplasia of the overlying epithelium, squamous metaplasia of the salivary ducts, and acinar necrosis) were not found.
Because the palate is one of the most common sites for the development of primary salivary gland neoplasms, a malignant salivary gland tumor was included in the differential diagnosis of the present case. The most likely candidates based on frequency of occurrence are mucoepidermoid carcinoma, adenoid cystic carcinoma, and polymorphous low-grade adenocarcinoma. However, although more aggressive tumors such as salivary duct carcinoma should be considered, the development of a tumor of the reported extent and bone destruction within such a short period would be highly unlikely.

The propensity of actinomycosis to mimic squamous cell carcinoma is well known. In agreement with this aspect, the authors also hypothesized that the present lesion was an epithelial malignant tumor based on the rapidly destructive evolution of the disease and the fact that the patient had been a smoker for 20 years. However, although more aggressive tumors such as salivary duct carcinoma should be considered, the development of a tumor of the reported extent and bone destruction within such a short period would be highly unlikely.

The propensity of actinomycosis to mimic squamous cell carcinoma is well known. In agreement with this aspect, the authors also hypothesized that the present lesion was an epithelial malignant tumor based on the rapidly destructive evolution of the disease and the fact that the patient had been a smoker for 20 years. However, carcinomas of the hard palate often present as a papillary or exophytic growth rather than a flat or ulcerated lesion, as observed in the present case.

Although not pathognomonic, histologic features of actinomycosis are the presence of sulfur granules whose centers exhibit basophilic staining with eosinophilic rays and that are surrounded by neutrophils. The present case differs from previously reported cases by exhibiting microscopic aggregates that did not show the established pattern when stained by routine techniques. In addition, neutrophilic inflammation was scarce. To the authors’ knowledge, this is the first case exhibiting this staining pattern, which could not be clarified satisfactorily. The mild intensity of the inflammatory infiltrate was probably due to the short duration of the lesion and the systemic condition of the patient. Leukocyte dysfunction is common in patients with diabetes mellitus, and the metabolic anomalies of the disease associated with decreased chemotaxis cause inadequate migration of neutrophils and macrophages to the site of aggression.

Culture results are negative in more than 50% of cases of actinomycosis and an incisional biopsy is frequently necessary for diagnosis of the disease. In view of the difficulty in identifying the microbial agent, 2 bacterial cultures were necessary in the present case, because the first culture result was negative. The second culture identified *A naeslundii* as the causative agent of the infection. In the oral cavity, this micro-organism plays an important role in dental biofilm formation and gingival inflammation. It is believed that this bacterium can induce the destruction of soft and hard tissues through root canals and the gingival sulcus, playing a key role in the onset of periodontal disease or in the transition from gingivitis to periodontitis.

Treatment of the present case consisted of the oral administration of penicillin as recommended in the literature, and the patient presented complete regression of the lesion.

In conclusion, the diagnosis of infection with *Actinomyces* species in oral tissues represents a challenge because of the variable clinical manifestations of the disease. However, health care professionals should be aware of the presence of ulcerative, destructive

### Table 2. CASES OF ACTINOMYCOSIS INVOLVING THE HARD PALATE REPORTED IN THE LITERATURE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Age (yr)/Gender</th>
<th>Duration</th>
<th>Condition</th>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubin and Krost</td>
<td>1995</td>
<td>58/M</td>
<td>—</td>
<td>cocaine snorting</td>
<td>nasal congestion, yellow sputum, and purulence</td>
<td>intravenous aqueous penicillin + oral clindamycin; intravenous penicillin</td>
</tr>
<tr>
<td>Herman et al</td>
<td>1998</td>
<td>65/F</td>
<td>2 wk</td>
<td>chronic lymphocytic leukemia</td>
<td>pain, malaise, generalized prostration, difficulty eating and swallowing</td>
<td>intravenous penicillin</td>
</tr>
<tr>
<td>De et al</td>
<td>2011</td>
<td>32/M</td>
<td>2 yr</td>
<td>normal</td>
<td>—</td>
<td>intravenous crystalline penicillin G</td>
</tr>
<tr>
<td>Present case</td>
<td>2013</td>
<td>46/F</td>
<td>4 days</td>
<td>diabetes mellitus</td>
<td>dysphagia and pain</td>
<td>penicillin</td>
</tr>
</tbody>
</table>

Abbreviations: F, female; M, male.

oral lesions because they can mimic malignant conditions. Among the previously reported cases of actinomycosis of the hard palate, this is the first report in which *A. naeslundii* was identified as the causative agent.

**References**