Case Report

Longstanding suppurative granulomatous inflammation of the infratemporal fossa

Brian E. Kinard, DMD, MD a,*, Kelly R. Magliocca, DMD, MPH b, Jeannette Guarner, MD c, Cecile A. Delille, MD, MSc d, Steven M. Roser, DMD, MD e

a Resident-in-Training, Department of Surgery, Division of Oral and Maxillofacial Surgery, Emory University School of Medicine, Atlanta, GA, USA
b Clinical Assistant Professor, Department of Pathology and Laboratory Medicine, Emory University, Atlanta, GA, USA
c Professor, Department of Pathology and Laboratory Medicine, Emory University, Atlanta, GA
d Assistant Professor, Department of Medicine, Division of Infectious Diseases, Emory University, Atlanta, GA, USA
e Professor and Chief, Department of Surgery, Division of Oral and Maxillofacial Surgery, Emory University School of Medicine, Atlanta, GA, USA

ARTICLE INFO

Article history:
Received 26 January 2015
Revised 7 December 2015
Accepted 15 February 2016
Available online 23 February 2016

Keywords:
cervicofacial actinomycosis
suppurative granuloma
non-necrotizing granulomatous inflammation

ABSTRACT

The purpose of this article is to present the clinical course, multidisciplinary management contributions, and outcome of a patient diagnosed with suppurative granulomatous inflammation in the posterior maxillary soft tissue region.

A 50-year-old white male presented with a 5-year history of a gradually enlarging posterolateral left maxillary soft tissue mass and concomitant decrease in maximal incisal opening (MIO) to 4 mm. A firm, painless, nonmobile submucosal mass was palpable lateral to the left maxilla without drainage or lymphadenopathy. Computed tomography (CT) with contrast defined a 3 × 5 cm mildly enhancing mass in the left infratemporal fossa. The microscopic analysis was significant for several clusters of filamentous amphophilic material (suggesting sulfur granules) surrounded by granulomatous inflammation, including neutrophils. The morphologic appearance of the filamentous material in combination with the clinical presentation generated suspicion for Actinomyces; however, further workup was non-diagnostic. In efforts for definitive diagnosis, the specimen was directed to the CDC for 16S ribosomal RNA testing, which showed evidence of Strepococcus sanguinis and Campylobacter gracilis, known Actinomyces companion organisms. Empiric treatment for Actinomyces yielded clinical improvement.

This case serves as a briefing for this form of uncommon inflammation and additionally serves to prime the reader on the distinction between actinomycosis, the clinical syndrome, and Actinomyces, the bacteria. We present this case, perhaps from more of a philosophical standpoint, to illustrate the manner in which a longstanding, clinically significant, destructive process in an unusual anatomic location was successfully resolved via collaborative interdisciplinary management and months of effort.

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1. Introduction

Suppurative granulomatous inflammation is defined by epithelioid histiocytes and multinucleate giant cells with a central collection of polymorphonuclear leukocytes (PMNs), and may occur in association with necrotizing or non-necrotizing granulomatous inflammation. Based on light microscopic observations alone, suppurative granulomatous inflammation (SGI) is an end process of many diverse, usually infectious disease processes (Table 1) [1]. The purpose of this article is to present the clinical course, multidisciplinary management and outcome of a patient diagnosed with SGI inflammation in the posterior maxillary soft tissue region.

2. Case presentation

A 50-year-old white male presented with a 5-year history of a gradually enlarging posterolateral left maxillary soft tissue mass and concomitant decrease in maximal incisal opening (MIO) to 4 mm. The patient originally underwent evaluation and biopsy at a hospital out of state, but due to socioeconomic considerations, relocated and presented to our institution 4 years after this initial evaluation. The formal biopsy results were unavailable, but per report, consistent with inflammatory changes. Past medical history was...
significant for hypothyroidism and an active 32 pack-year smoking history. The patient denied a history of trauma and denied undergoing any recent dental procedures. There were no systemic signs or symptoms of illness except for a chronically elevated white blood cell count ranging from 10-13.4 × 10³/mcL. A firm, painless, non-mobile submucosal mass was palpable lateral to the left maxilla without drainage or lymphadenopathy. Multiple carious teeth were present.

Computed tomography (CT) with contrast defined a 4 × 3 × 5 cm mildly enhancing mass in the left infratemporal fossa with erosion of the left posterior tuberosity and sinus wall without extension into the ipsilateral maxillary sinus (Figures 1 and 2). The leading clinicoradiographic differential diagnosis included infectious etiologies, mesenchymal neoplasms, and lymphoproliferative disease. An incisional biopsy was performed under local anesthesia revealing yellowish–pink material, and microscopically was interpreted as SGI. Grocott’s methenamine silver (GMS), Periodic acid Schiff (PAS) and Acid fast bacillus (AFB) stains performed on the biopsy sample were negative for fungal and acid fast organisms respectively. In an effort to obtain viable culture material, CT-guided fine needle biopsy (FNB) was performed within a deep portion of the lesion and demonstrated rare non-necrotizing granulomas (PMNs not identified) present in a background of fibrosis without evidence of malignancy. The material submitted for microbiological analysis was positive for growth of Streptococcal species. Formal consultation with the Infectious Diseases service was initiated. Autoimmune work-up and urine fungal antibody panels were negative. A chest radiograph was obtained and interpreted as normal. Removal of non-vital tooth #15 was accomplished, along with a final open biopsy under local anesthesia for purposes of obtaining additional culture material. Portions of the specimen were submitted for microbiology analysis with the remainder processed as routine tissue microscopy. The microscopic analysis was significant for several clusters of filamentous amphophilic material (suggesting sulfur granules) surrounded by granulomatous inflammation, and abundant neutrophils, diagnostic of SGI (Figures 3 and 4). Unfortunately, this material was not evident on deeper sections of the tissue block or on special stains, including the review of the AFB, PAS, GMS, Gram and Warthin–Starry stains performed to identify organisms. Final microbiology culture data were negative for Mycobacterium tuberculosis (MTB) via PCR and for other mycobacteria. Fungal cultures grew 1 + Candida albicans, which was not consistent with the clinical picture and interpreted as a contaminant.

The morphologic appearance of the filamentous material in combination with the clinical presentation generated suspicion for Actinomycosis; therefore, doxycycline treatment (100 mg twice daily) was initiated empirically, as the patient reported a remote history of penicillin allergy. In an attempt to objectively confirm the actinomycosis, the formalin-fixed paraffin-embedded specimen was directed to the United States Centers for Disease Control and Prevention (CDC) for 16S ribosomal RNA testing, which showed evidence of Streptococcus sanguinis and Campylobacter gracilis. Doxycycline photosensitivity was reported despite sunscreen use at a 2-month

<table>
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<td>Entities associated with necrotizing or non-necrotizing suppurrative granulomatous inflammation [1]</td>
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<tr>
<td>Chromomycosis</td>
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<td>Pheohyphomycosis</td>
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<td>Sporotrichosis</td>
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<td>Non-tuberculosis (atypical) mycobacterial infections</td>
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<td>Blastomycosis</td>
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<td>Paracoccidioidomycosis</td>
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<td>Blastomycosis-like pyoderma</td>
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<td>Actinomycosis</td>
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<td>Cat-scratch disease</td>
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<td>Lymphogranuloma venereum</td>
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<td>Superficial pyoderma gangrenosum</td>
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<td>Ruptured cysts and follicles</td>
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**Figure 1.** Preoperative axial computed tomographic view, bone window. Arrows designate expansile soft tissue mass of infratemporal fossa, eroding posterior wall of the left maxillary sinus.

**Figure 2.** Preoperative coronal computed tomographic view, soft tissue window. Arrows designate expansile soft tissue mass of infratemporal fossa, eroding posterior–inferior wall of the left maxillary sinus.
follow-up visit. The antibiotic regimen was then changed to amoxicillin/clavulanic acid when further inquiry into the details of the penicillin allergy revealed that the previously reported reaction had been a mild rash at 5 years of age without signs of anaphylaxis. A 4-week course of levofloxacin was added for coverage of possible superinfection or co-infection with methicillin-resistant Staphylococcus aureus (MRSA). After 6 weeks of amoxicillin/clavulanic acid, MIO had increased to 16 mm. At 6 months of amoxicillin/clavulanic acid therapy, MIO had increased to 38 mm, and the decision, in conjunction with the Infectious Diseases team, was made to discontinue antibiotic therapy. Repeat imaging was not pursued in light of the positive clinical progress.

3. Discussion

Chronic granulomatous inflammation may be classified as necrotizing and non-necrotizing. Necrotizing granulomatous inflammation may be further characterized as suppurative when neutrophils are identified and, in most cases, is suggestive of an infectious etiology. An interdisciplinary and/or multidisciplinary approach to patient management is often required. When presenting in the oral cavity, head and neck region, the patient is often referred to Oral and Maxillofacial Surgery (OMFS) for evaluation, surgical management of suspicious infectious foci where appropriate, as well as acquisition of diagnostic material for histology and microbiology; both Clinical and Anatomic Pathology are needed for interpretation of culture, molecular results and histology; and colleagues in Medicine, including subspecialty disciplines, such as Infectious Diseases are essential for management. The long-standing course of the disease and association with the oral cavity location raises the distinct possibility of actinomycosis, an uncommon disease caused by filamentous Gram-positive anaerobic bacteria from the Actinomycetaceae family [2], which are notoriously difficult to culture and/or positively identify [3]. Actinomyces are normal oral flora with low virulence but can become pathogenic when introduced submucosally through a dental infection or masticatory trauma and supported by anaerobic flora. In a classic case, macrophages are able to engulf but are unable to clear Actinomyces, and granulomas develop [4]. Actinomycosis, classically described as a minimally painless slow-growing lump or bump of the jaws, can resemble a broad range of pathological entities: granulomatous disease, mycotic infections, and malignant and non-malignant tumors [5]. From a microbiological perspective, actinomycoses are almost always polymicrobial infections, with over 95% of culture-confirmed cervicofacial cases having aerobic or anaerobic bacterial companions thought to strengthen or complement the invasive abilities of Actinomyces. Both alpha-hemolytic Streptococcal species and C. gracilis have been implicated as companion organisms in culture-proven cervicofacial actinomycosis cases, as was suspected in the present case [6].

Although cervicofacial disease accounts for 55% of actinomycosis syndromes, only four cases of infratemporal actinomycosis have previously been reported in the English language literature [7-10]. It is not uncommon to have actinomycosis without sulfur granules present on pathologic specimen. Anaerobic Actinomyces can be extraordinarily difficult to culture, with culture confirmation noted to be as low at 50% due to overgrowth of associated bacteria, lack of proper anaerobic conditions, or prior antibiotic treatment [3]. Should bacterial culture confirmation fail, a presumptive diagnosis of actinomycosis can still be made. Often, visualization of sulfur granules on hematoxylin and eosin is supportive, but in this case, the presumptive diagnosis of actinomycosis was associated with the patient’s historical components, including the long-standing history of disease, detection of ‘companion’ organisms, and clinical response to antibiotics known to be effective for Actinomyces. Imaging of the lesion in this unusual location was important as decreased MIO of 4 mm limited the benefit of an intraoral exam. Specifically in this case, CT imaging excluded a temporomandibular joint intracapsular origin and demonstrated spread without regard to fascial planes, similar to the pattern described in actinomycosis. The literature characterizes the CT and magnetic resonance imaging (MRI) findings of actinomycosis as an ill-defined soft tissue mass with inflammatory reaction, which disregards fascial planes [11,12]. Actinomycosis infection does not spread through lymphatic or vascular routes [4].

In summary, we present this report for multiple reasons. First, OMFS and pathologists routinely encounter diseases related to acute or chronic inflammation, but SGI is decidedly uncommon in practice. Therefore, the case serves as a briefing for this form of uncommon inflammation and additionally serves to prime the reader on the distinction between actinomycosis, the clinical syndrome, and Actinomyces, the bacteria. Next, this report captures the elegant H&E microscopic findings of SGI in this unusual set of clinical and radiographic circumstances. Finally, we present this case, perhaps from more of a philosophical standpoint, to illustrate the manner in which a long-standing, clinically significant, destructive process
in an unusual anatomic location, was successfully resolved via collaborative interdisciplinary management and months of effort. It is entirely possible that the true nature of the infectious agent may have been positively identified by PCR at the CDC as S. sanguinis and C. gracilis; therefore, our purpose is not to underscore what we can definitively prove, rather, how this team managed care in the setting of marked ambiguity.

Consent
Written informed consent was obtained from the patient for publication of this case report and case series and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflict of interest
The authors declare that there are no conflicts of interest.

References