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ID TEACHING CASES

Ocular Actinomycosis Mimicking Meningioma

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Orbital actinomycosis is an unusual clinical manifestation of orbital infection caused by *Actinomyces* species. Herein we report a case of orbital actinomycosis in a 67-year-old woman with recurrent swelling and erythema around her left eye with an orbital mass initially thought to be a meningioma.

Keywords. ocular actinomycosis; meningioma.

CASE

The case was a 67-year-old female with chronic obstructive pulmonary disease who presented with recurrent erythema and swelling around her left eye. One year before this presentation, she developed erythema and swelling around her left eye. She initially saw her primary care doctor and was suspected to have sinusitis. Over the next several months, she was treated with several courses of oral antibiotics for a presumptive diagnosis of recurrent sinusitis. Her symptoms improved each time she took antibiotics, which included courses of clindamycin, levofloxacin, and trimethoprim-sulfamethoxazole (TMP/SMX). However, she repeatedly relapsed within 1–3 months after discontinuation. She was evaluated by her local ophthalmologist and otolaryngologist to rule out a nasopharyngeal source of her ocular issues, but no pathology was identified.

Two months after completing her prior course of antibiotics, she again developed erythema, which was now associated with left ptosis and discharge from her left eye, leading to additional workup. She did not have any recent travel or risk factors for tuberculosis. She denied any preceding trauma. Vital signs were unremarkable, and she was afebrile. Physical examination revealed erythema and swelling around her left eye and left ptosis (Figure 1). Laboratory findings were significant for a white blood cell count of 12 600/mm^3. Magnetic resonance imaging (MRI) of the left eye demonstrated an enhancing mass in the superior aspect of her left orbit measuring ~1.7 cm × 0.7 cm (Figure 2A). Computed tomographic imaging (CT) demonstrated hyperostosis of the left superior orbital wall (Figure 2B). Based on the CT and MRI appearance of the lesion, specifically hyperostosis, meningioma was suspected by the radiologist. Neurosurgery and ophthalmology were consulted, and she underwent anterior orbitotomy with incisional biopsy of the mass along with debridement of her left orbital roof at the frontal bone with curettage. Intraoperatively, purulent material was expressed from the mass. Surgical pathology was not suggestive of malignancy but did reveal sulfur granules with abundant filamentous, branching bacteria (Figure 3). As the initial concern was for malignancy (especially meningioma), no culture was sent. Infectious diseases was consulted postoperatively.

Given the findings on pathology, there was concern for an infectious process, with *Actinomyces* and *Nocardia* being the most likely pathogens. Therefore, empiric treatment with ceftriaxone and TMP/SMX was initiated to empirically cover both of these pathogens. The remaining specimen was sent for broad-range 16S ribosomal DNA polymerase chain reaction amplification with next-generation sequencing (Molecular Diagnosis Microbiology Section, University of Washington, Seattle, WA, USA), which identified *Actinomyces israelii* among a variety of resident ocular flora, none of which shared the morphology of *Actinomyces*. TMP/SMX was discontinued 12 days later, and she completed a 2-week course of ceftriaxone with a good response. She was then transitioned to oral amoxicillin monotherapy. At 3-month follow-up, she was asymptomatic, and amoxicillin was continued for a total of 6 months. She was last seen by ophthalmology 3 months later, and she remained symptom free.

Actinomycosis is an indolent, slowly progressive infection caused by gram-positive facultatively anaerobic bacteria, primarily from the genus *Actinomyces*. It is most commonly caused by *Actinomyces israelli* [1] and can mimic a number of other conditions, including malignancy. Therefore, it requires a high degree of clinical suspicion to make the diagnosis. In our case, the patient was initially suspected to have meningioma due to her MRI and CT findings.

The frequency of oral cavity colonization with *Actinomyces* is nearly 100% by 2 years of age [2]. It can often be cultured from the gastrointestinal tract, bronchi, and female genital tract; however, in certain instances it can lead to chronic infections. Although actinomycosis commonly occurs in the oral–cervicofacial area, orbital actinomycosis is extremely rare [3]. A literature review of 10 ocular actinomycoses cases by Poyoong

Received 8 March 2020; editorial decision 11 May 2020; accepted 14 May 2020.

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DOI: 10.1093/ofid/ofaa170

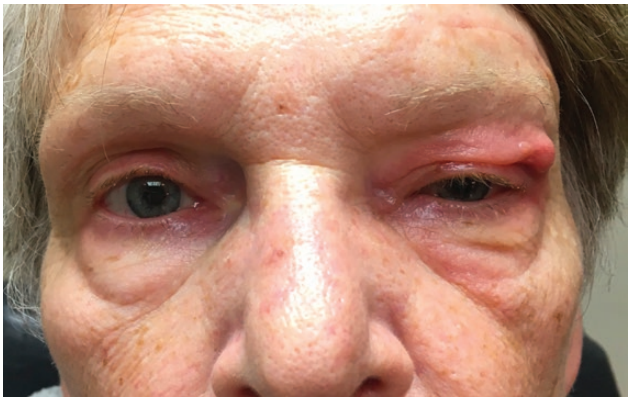

Figure 1. Erythema and swelling around left eye.

et al. revealed that most of the previously reported cases were either caused by infections in paraorbital organs or following injury [3]. Tooth extraction history and chronic steroid use were the most common predisposing factors. Ophthalmoparesis and ptosis were the most commonly reported symptoms. The entry point in our patient was not clear given that she did not have any infection or injury around her left orbit. However, our patient did not have a formal dental evaluation, and transient bacteremia resulting in orbital infection (hematogenous spread) could not be ruled out.

Actinomycosis is usually diagnosed by culturing the organism, requiring incubation under anaerobic conditions for a minimum of 14 days to optimize yield [4]. Sulfur granules seen on histopathology are highly suggestive of actinomycosis, but they can occasionally be seen in other infections such as nocardiosis, chromoblastomycosis, and botryomycosis. These granules contain a collection of bacteria surrounded by inflammatory debris and oval basophilic masses with eosinophilic clubs at the fringes. In the correct clinical setting, the finding of beaded gram-positive rods along with sulfur granules is strongly suggestive of actinomycosis, although they can be difficult to distinguish from Nocardia on morphology alone [2]. The diagnosis has improved significantly with identification by 16S ribosomal rDNA amplification and sequencing [5]. In this case, the additional application of next-generation sequencing allowed molecular identification of *A. israelii* among a mix of incidental normal flora. Though there is no specific image finding characteristic for actinomycosis, intracranial actinomycosis with hyperostosis has been reported where en-plaque meningioma was initially suspected [6].

Actinomyces spp. are susceptible to a wide range of antimicrobial agents. Recent studies in Europe demonstrated that most were susceptible to β lactams (including benzylpenicillin, amoxicillin, ceftriaxone, meropenem, and piperacillintazobactam), doxycycline, clindamycin, erythromycin, linezolid, and clarithromycin [7, 8], whereas fluoroquinolone susceptibility was mixed. The duration of antibiotic treatment depends on the initial burden of disease, performance of surgical resection/debridement, and the patient's response to treatment [9]. In some refractory cases, additional surgical drainage or excision is required. In fact, a case series by Payoong et al. demonstrated that 8 out of 10 ocular actinomycosis cases required surgical interventions [3]. Generally, a total of 6–12 months of treatment with antibiotics is recommended for actinomycosis. The mortality rate is reported to be between 0% and 28% depending on the site of infection and the time to diagnosis. The highest mortality has been reported in actinomycosis with central nervous system involvement [10].

Although actinomycosis most commonly occurs in the oral–cervicofacial area, orbital actinomycosis has rarely been reported. Orbital actinomycosis can mimic neoplastic processes and needs to be suspected when sulfur granules are seen in the pathology specimen. Though the radiographic finding of hyperostosis of bone is frequently seen in meningioma, a response to antimicrobials should raise the suspicion of actinomycosis. Although culturing this organism is the gold standard, 16S rRNA sequencing is reported to be helpful for identifying *Actinomyces* spp. in the absence of growth on culture.

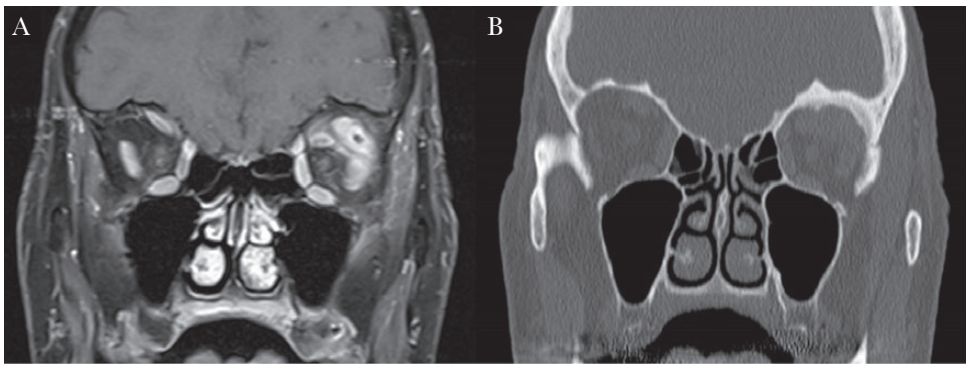

Figure 2. A, Coronal enhanced T1-weighed magnetic resonance image with fat suppression depicts enhancing mass in the superior aspect of the left orbit. B, Coronal computed tomographic image demonstrates hyperostosis of the left superior orbital wall associated with the mass lesion, consistent with meningioma.

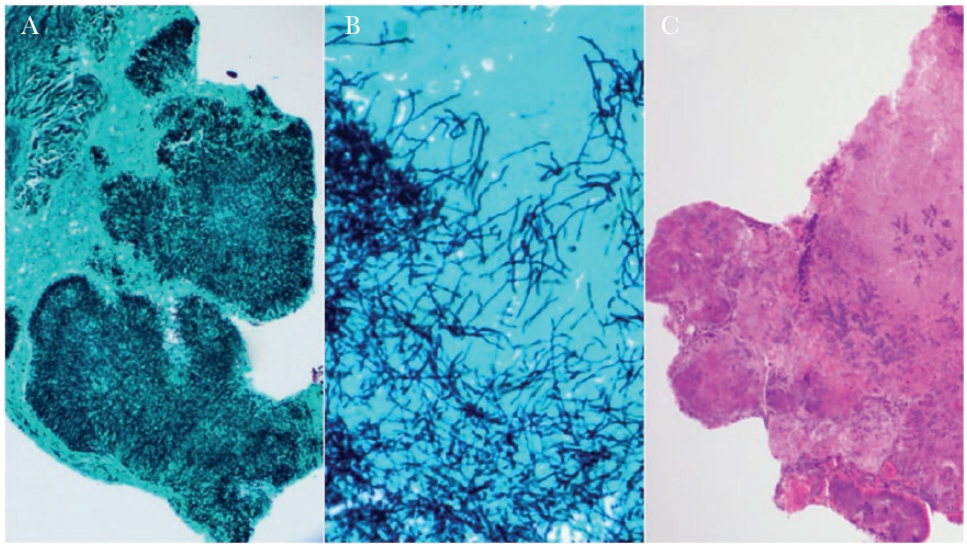

Figure 3. A, Gomori methenamine silver stain (GMS) staining of the resected orbital mass demonstrates sulfur granules (dense aggregates of gram-positive filamentous non-spore-forming rods, consistent with *Actinomyces* spp.; 4X objective). B, On high power (100X objective, GMS) the filamentous, branching structure of the bacteria is evident. C, On initial hematoxylin and eosin stain (4X objective), sulfur granules are evident but individual bacteria are indistinct.

Acknowledgments

Financial support. None.

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Pulverer G, Schutt-Gerowitt H, Schaal KP. Human cervicofacial actinomycoses: microbiological data for 1997 cases. Clin Infect Dis **2003**; 37:490–7.
2. Wong VK, Turmezei TD, Weston VC. Actinomycosis. BMJ **2011**; 343:d6099.
3. Payoong P, Saetiew N, Putcharoen O, Suankratay C. Orbital and pulmonary actinomycosis: the first case report and literature review. Case Rep Infect Dis **2018**; 2018:4759807.
4. Smego RA Jr, Foglia G. Actinomycosis. Clin Infect Dis **1998**; 26:1255–61; quiz 62–3.
5. Kuyama K, Fukui K, Ochiai E, et al. Identification of the actinomycete 16S ribosomal RNA gene by polymerase chain reaction in oral inflammatory lesions. Oral Surg Oral Med Oral Pathol Oral Radiol **2013**; 116:485–91.
6. Deora H, Beniwal M, Rao S, et al. Wolf in sheep's clothing: intracranial actinomycosis masquerading as en-plaque meningioma. Surg Neurol Int **2018**; 9:39.
7. Smith AJ, Hall V, Thakker B, Gemmell CG. Antimicrobial susceptibility testing of *Actinomyces* species with 12 antimicrobial agents. J Antimicrob Chemother **2005**; 56:407–9.
8. Hansen JM, Fjeldsøe-Nielsen H, Sulim S, et al. Actinomyces species: a Danish survey on human infections and microbiological characteristics. Open Microbiol J **2009**; 3:113–20.
9. Brook I. Actinomycosis: diagnosis and management. South Med J **2008**; 101:1019–23.
10. Acevedo F, Baudrand R, Letelier LM, Gaete P. Actinomycosis: a great pretender. Case reports of unusual presentations and a review of the literature. Int J Infect Dis **2008**; 12:358–62.