Case Report: Ozena in Immigrants of Differing Backgrounds

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Abstract. Ozena, or atrophic rhinitis, is a chronic nasal process seen in Africa, India, and the Middle East. It is marked by the triad of fetid nasal discharge, crusting, and atrophy, and is often associated with *Klebsiella* infection. We present cases of ozena with nasal *Klebsiella* in three unrelated patients, including two east African children and one Saudi adult. All three patients grew *Klebsiella* species in culture and required prolonged treatment with multiple methodologies, including antibiotics, saline rinses, and surgical debridement. They differed greatly in time from presentation to diagnosis, and demonstrated various stages of the disease process. Ozena is rarely seen in the United States, and when it is seen, it is often misdiagnosed. Lack of prompt, adequate treatment can lead to long-term sequelae such as obliteration of nasal architecture, anosmia, sinus and skull base destruction, and social disenfranchisement due to the extreme foul smell of the nasal discharge. Clinicians should maintain a high index of suspicion for primary atrophic rhinitis when presented with its classic symptoms. Culture-directed and prolonged therapy with appropriate follow-up is a necessary component of a successful treatment plan.

INTRODUCTION

Ozena is a type of primary atrophic rhinitis caused by the bacterial species *Klebsiella pneumoniae ozaenae*.¹ Although previously more common in the United States, it has decreased in prevalence drastically in the past century, most likely due to antibiotic use.² Ozena remains an important disease process throughout parts of Africa, the Middle East, and India, and physicians in other parts of the world may see this disease due to travel or migration.³

The classic triad of an ozena infection is crusting, interior nasal atrophy resulting in a roomy cavity, and a fetid discharge.⁴ Other related symptoms include epistaxis, anosmia, subjective congestion, and in advanced stages, deformities of the nose and perforation of the septum or skull base. This destruction can be progressive and is permanent—there is no regrowth once gone. Another common feature is squamous metaplasia: a histopathologic change from ciliated respiratory epithelium to nonciliated squamous epithelium.⁵ This leads to a loss of clearance of mucous, contributing to further infection and progression of disease. The bacteria itself lend to the destruction of the cilia.⁶ These changes are irreversible. However, the metaplasia does not seem to be associated with malignant transformation.⁷ The foul odor is often likened to the “foreign body smell” that may occur when an object is lodged in the nose, resulting in unilateral purulent discharge. The smell can be so pungent that these individuals are ostracized in social situations, such as at school or work, leading to significant hardship and anguish for the affected individual.

The underlying pathology is that of a necrotizing infection via an obliterating endarteritis.¹ There is destruction of the mucosa, glands, underlying bone, and nerves resulting from the damage of the underlying blood vessels. As the tissue necroses and ulcerates, crusts are formed. Removal of these crusts can lead to exposure of the eroded vessels, resulting in

epistaxis. The loss of nerves leads to anosmia, which leaves the patient unaware of the foulness of the nasal discharge. The nerve destruction is also the cause of the subjective congestion. Although the nasal cavity is actually larger after destruction of the turbinates, the nerves that sense airflow are destroyed and so the nasal valve is perceived by the patient as being blocked.

CASE REPORTS

We present cases of nasal *Klebsiella* infection in three unrelated patients, including two east African children and one Saudi adult. They were not previously diagnosed or treated for this infection in their home countries. None of the patients had a history of sinus surgery.

Patient 1: 11-year-old Somali male who spent time in a Kenyan refugee camp and recently immigrated. The primary otolaryngology visit was a year and a half after his initial presentation of “allergic rhinitis” with pale, edematous turbinates, and cervical lymphadenopathy. Interim symptoms had progressed to bilateral intermittent epistaxis and foul-smelling mucopurulent drainage. Treatment over this time course included amoxicillin, amoxicillin/clavulanic acid, intranasal steroids, and cetirizine, with little improvement. Sinus computed axial tomography (CT; Figure 1) and cultures were ordered. The patient was then taken to the operating room (OR) for functional endoscopic sinus surgery and debridement, with a working diagnosis of foreign body versus a necrotizing infection. In the OR, it was apparent that the inferior turbinates and ethmoid sinus tissues were destroyed. The middle turbinates were partially eroded with purulence and exudative discharge covering the distorted landmarks. Cultures demonstrated growth of *K. pneumoniae ozaenae*. The patient required bimonthly in-office debridement, prolonged treatment with amoxicillin/clavulanic acid, and saline rinses after surgery. Recurrence 5 months later was treated with ciprofloxacin and nebulized tobramycin. There were no signs of active infection 1 year after surgery, and treatment was discontinued.

Patient 2: 21-month-old Ethiopian female who came from a different Kenyan refugee camp than patient 1. The primary otolaryngology visit was 11 months after arrival in the

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FIGURE 1. Coronal cut of patient 1. Computed axial tomography scan showing decreased middle turbinates, absent inferior turbinates and ethmoid air cells, and atrophic mucosa.

United States and 4 months after the onset of a thick, copious, foul-smelling nasal discharge. This had progressed from intermittent cervical lymphadenopathy, clear to colored mucous, fevers, and halitosis, which had been unresponsive to treatment with azithromycin, amoxicillin, and amoxicillin/clavulanic acid. On examination, there was crusting throughout the atrophic-appearing nasal mucosa. The turbinates appeared decreased in size and cervical lymphadenopathy was present. A CT (Figure 2) was performed. Cultures were obtained, with growth of *K. pneumoniae ozaenae* and *Streptococcus pneumoniae*. Treatment included amoxicillin/clavulanic acid, cefdinir, and sulfamethoxazole/trimethoprim with nebulized tobramycin over a 6-month period. The treatment course was complicated by the patient's inability to comply and follow up with care. The *Klebsiella* species also developed new resistance to amoxicillin/clavulanic acid on

FIGURE 2. Coronal cut of patient 2. Computed axial tomography scan showing complete absence of turbinates, destruction of maxillary antrum, and atrophic mucosa.

follow-up culture during this treatment period. She is currently asymptomatic and treatment was halted, though follow-up surveillance continues.

Patient 3: 67-year-old Saudi Arabian male, distant history of work in road construction, long-time U.S. resident. This patient presented to the otolaryngology clinic primarily for anosmia of a 40-year duration with intermittent bloody nasal discharge. Examination showed absent turbinates with scarring and crusting. Cultures grew *K. pneumoniae* (not further speciated). CT showed atrophy of soft tissue and bone. His treatment included saline irrigations, which were transitioned to gentamicin rinses. He completed a 2-month treatment cycle of gentamicin with 3 weeks on/1 week off with excellent results—resolution of all symptoms except for persistent anosmia. It is unclear if this treatment was curative or simply gave him symptomatic relief, given the intermittent nature of his disease. The plan is to repeat this treatment cycle if crusting or epistaxis returns.

DISCUSSION

Physicians unfamiliar with the entity can easily misdiagnose ozena, as early symptoms are nonspecific and the classic ozena triad does not usually become apparent until after significant destruction has occurred. Clear rhinorrhea may be the first noticeable symptom along with an irritated nasal mucosa, mimicking allergic rhinitis. However, nonresponse to nasal steroids such as fluticasone and lack of seasonal or triggering factors may help differentiate atrophic rhinitis from allergic rhinitis. The rhinorrhea associated with early ozena may be intermittent, also clouding the clinical picture. As the disease progresses, it may appear to the untrained eye as an atypical sinusitis. The main differences between sinusitis and primary atrophic rhinitis include pain sensation, unilateral drainage, clinical course, and response to antibiotics, all of which are typically absent in ozena. A single 10–14 day course of amoxicillin should be sufficient to treat uncomplicated rhinosinusitis.⁸ In contrast, ozena may transiently respond to amoxicillin, but typically returns to baseline symptoms once the initial short course of antibiotics have been completed.

In tropical regions, there is clinical overlap between ozena and other infections. For instance, noma (cancrum oris), a disease of extreme poverty, often begins with gingival ulceration that can progress to gangrenous and deforming skin lesions. It usually occurs in young children and is preceded by a severe illness such as measles or malaria.⁹ Mucocutaneous leishmaniasis can cause destructive mucosal lesions in the nose and mouth, and mimics many diseases. This should be considered when a patient presents from an endemic region. Diagnosis can be made by skin biopsy with histopathology, culture, or polymerase chain reaction.¹⁰

Another *Klebsiella* infection can present similarly to ozena in its earliest stage. Rhinoscleroma is caused by *Klebsiella pneumoniae rhinoscleromatis* and initially its symptoms are nasal congestion and persistent purulent discharge.¹¹ In contrast to the destruction of tissue in ozena, the next stage of rhinoscleroma involves the development of a painless mass. The mass can continue to grow and distort and destroy facial architecture. This disease is endemic in Egypt and other tropical parts of Africa, Central and South America, and parts of eastern Europe.¹²

There are many avenues for treatment, but no standard of care.¹ A 2012 review by Mishra and others tried to assess the effectiveness of different treatments by comparing their outcomes and long-term benefits, but could not find randomized controlled studies that met their inclusion criteria.¹³ Many authors argue that ozena is not curable and the aim of treatment is simply abatement of symptoms. No one treatment modality, however, can address all symptom causes. Antibiotics tend to be a mainstay of treatment and, similar to other bacterial infections, should be guided by culture results and susceptibility testing. This is important given that the infection is chronic and the gram-negative rods, particularly *Klebsiella*, are increasingly resistant to antibiotics. Many physicians may prescribe saline nasal rinses or sprays for daily use in keeping the area clean and preventing crust formation. In some cases, debridement of the overlying crusts and necrotic portions may be required to facilitate healing. There are limited options for addressing the enlarged nasal cavity or deformities of advanced disease, with variable results from surgical intervention. In our series, the treatment approaches centered on culture-based sensitivities with frequent reevaluation. Crusting was addressed with saline or antibiotic rinses, and in one extreme case, surgical intervention. We believe that a tailored approach led to the positive outcomes.

Ozena is an uncommon disease in the United States. As the immigrant populations from areas of east Africa and other endemic regions continue to increase, however, it may become more common in both the primary-care provider's and the otolaryngologist's office. Because of the chronic and destructive nature of this disease, it is important to be aware of its classic symptoms and the repercussions of failed or noninitiated treatment.

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REFERENCES

1. deShazo RD, Stringer SP, 2011. Atrophic rhinosinusitis: progress toward explanation of an unsolved medical mystery. *Curr Opin Allergy Clin Immunol* 11: 1–7.
2. Moore EJ, Kern EB, 2001. Atrophic rhinitis: a review of 242 cases. *Am J Rhinol* 15: 355–361.
3. Lee YJ, Moore LS, Almeyda J, 2011. A report of a rare case of *Klebsiella ozaenae* causing atrophic rhinitis in the UK. *BMJ Case Rep pii*: bcr0920114812.
4. Flint PW, Haughey BH, Lund VJ, Niparko JK, Richardson MA, Robbins KT, Thomas JR, 2010. Nonallergic rhinitis. *Cummings Otolaryngology*, 5th edition. Elsevier, 696–697.
5. Singh I, Raizada RM, Chauturvedi VN, Jain SK, Ingole SN, 1999. Study of histopathological changes in atrophic rhinitis. *Indian J Otolaryngol Head Neck Surg* 51: 21–24.
6. Ferguson JL, McCaffrey TV, Kern EB, Martin WJ 2nd, 1990. Effect of *Klebsiella ozaenae* on ciliary activity in vitro: implications in the pathogenesis of atrophic rhinitis. *Otolaryngol Head Neck Surg* 102: 207–211.
7. Bist SS, Bisht M, Purohit JP, Saxena R, 2011. Study of histopathological changes in primary atrophic rhinitis. *ISRN Otolaryngol* 2011: 269479.
8. Rosenfeld RM, Andes D, Bhattacharyya N, Cheung D, Eisenberg S, Ganiats TG, Gelzer A, Hamilos D, Haydon RC 3rd, Hudgins PA, Jones S, Krouse HJ, Lee LH, Mahoney MC, Marple BF, Mitchell CJ, Nathan R, Shiffman RN, Smith TL, Witsell DL, 2007. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg* 137: S1–S31.
9. Enwonwu CO, Falkler WA, Phillips RS, 2006. Noma (cancrum oris). *Lancet* 368: 147–156.
10. Handler MZ, Patel PA, Kapila R, Al-Qubati Y, Schwartz RA, 2015. Cutaneous and mucocutaneous leishmaniasis: differential diagnosis, diagnosis, histopathology, and management. *J Am Acad Dermatol* 73: 911–926.
11. Bailhache A, Dehesdin D, François A, Marie JP, Choussy O, 2008. Rhinoscleroma of the sinuses. *Rhinology* 46: 338–341.
12. Navazo Eguia AI, Garcia Vicario F, 2010. Rhinoscleroma [in Spanish]. *Acta Otorrinolaringol Esp* 61: 160–162.
13. Mishra A, Kawatra R, Gola M, 2012. Interventions for atrophic rhinitis. *Cochrane Database Syst Rev* 2: CD008280.