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Case Report
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Review and Case Report: Treatment of an Atypical Manifestation of a Laryngeal Mycobacterial Infection

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Abstract

Objectives: We report 1 case of an atypical laryngeal mycobacterium infection through which we analyzed 10 cases of atypical manifestations of laryngeal mycobacteria infections in the literature to discuss diagnosis and therapeutic aspect of such infections.

Case Report: *Mycobacterium avium* Complex (MAC) infections of the larynx cause shortness of breath and stridor. Atypical mycobacterium infections of the larynx are rare, difficult to detect, and lack standardized treatment regimens. Initial treatment of patient did not succeed; thus, we aim to describe one possible treatment regimen. An 81-year-old woman presented with progressive stridor and dysphonia over the course of a year. Her medical history was significant only for osteoporosis and mild dementia, but was found to have glottic stenosis and decreased mobility of the true vocal folds bilaterally due to a posterior glottic scar band. Patient underwent direct microlaryngoscopy, tracheoscopy, biopsy, glottic balloon dilation, Potassium-Titanyl-Phosphate (KTP) laser-assisted lysis of stenosis, and Kenalog injection. Pathology reported numerous infiltrates with histiocytes containing multiple acid-fast bacilli, suggesting the presence of atypical mycobacterium and were positive for MAC. Antimicrobial therapy was initiated with azithromycin, ethambutol and rifampin.

Conclusion: We present the use of laser-assisted ablation of posterior glottic stenosis, in addition to long-term antibiotic therapy, as a possible sustainable treatment for atypical mycobacterium infections of the larynx.

Keywords: Atypical mycobacterium infection; Laryngeal disease; Larynx; *Mycobacterium avium* complex

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Introduction

Mycobacterium can be classified as either *Mycobacterium tuberculosis* complex or Non-Tuberculosis Mycobacterium (NTM). NTM infections are categorized according to the type of mycobacterium infection. Atypical mycobacterium can be categorized into either fast-growing or slow-growing, each with their own treatment regimens. Fast-growing mycobacterium include *M. fortuitum*, while slow-growing include *M. avium*, *M. kansasii*, *M. lentiflavum*, and *M. malmoense*. *Mycobacterium avium* Complex (MAC), a type of NTM, is composed of *Mycobacterium avium* and *M. intracellulare*. Mycobacterial infections usually originate from the environment, avian droppings, or animals such as cats, mice, or birds [1].

In rare cases, mycobacteria can cause infections within the larynx, with only nine cases documented worldwide [2-10]. The most common presentation of symptoms includes chronic cough, dysphonia, hemoptysis, fatigue, weight loss, fevers, and night sweats. Most cases of NTM infection experience near-complete resolution of symptoms after antibiotic treatment. Herein, we discuss our experience with a rare, NTM infection of the larynx and the implemented treatment regimen. Given there is no current standardized treatment regimen for such infections, we performed a review of the literature analyzing NTM laryngeal infections to elucidate management strategies.

The patient was diagnosed as following

An 81-year-old woman developed progressive stridor and dysphonia one-year prior to referral to our clinic. The patient denied a history of tobacco use, the use of steroids, or immunosuppression. Her medical history was significant only for osteoporosis and mild dementia. She was initially evaluated

by a community otolaryngologist who noted glottic stenosis and decreased mobility of the true vocal folds bilaterally. On presentation to our clinic, transnasal laryngoscopy demonstrated a posterior glottic scar band, hypomobility of the true vocal folds bilaterally, and a maximal glottic opening of approximately 3 mm (Figure 1). She had significant stridor at rest and moderate dysphonia. The patient reported that her breathing has been significantly worsening over the last week.

Given her worsening symptoms and limited airway, the patient was urgently taken to the operating room to undergo direct microlaryngoscopy, tracheoscopy, biopsy, glottic balloon dilation, Potassium-Titanyl-Phosphate (KTP) laser-assisted lysis of stenosis, and Kenalog injection. In the operating room, the scar tissue was remarkable for being atypically soft and friable (Figure 2). This posterior glottic stenosis was seen extending to the posterior membranous aspect of the left vocal fold. Frozen section analysis demonstrated findings of chronic laryngitis and the remainder of the tissue was sent for permanent sections and microbiology. KTP laser lysis of the posterior stenosis and balloon dilation resulted in significant improvement of the glottic airway.

Final pathology reported numerous infiltrates with histiocytes containing multiple acid-fast bacilli, suggesting the presence of atypical mycobacterium (Figure 3). Cultures were positive for MAC. Antimicrobial therapy was initiated with azithromycin, ethambutol and rifampin. The patient was seen back in clinic at 6 weeks at which point she reported near complete resolution in dyspnea, but only mild improvement with her dysphonia. Flexible laryngoscopy demonstrated significantly improved vocal fold abduction, but there was still evidence of infection within the posterior commissure (Figure 4).

One year after her first surgery and at the time of this writing, the patient continues to be treated with azithromycin, ethambutol, and rifampin. She has also required three additional balloon glottic dilation procedures to maintain an adequate airway in the setting of prolonged laryngeal MAC infection. At her fourth and most recent surgery, biopsies finally showed an absence of MAC organisms.

Materials and Methods

Data sources

A comprehensive search of the international medical literature from 1996-2021 was conducted by using databases from PubMed (US National Library of Medicine Database) and Google Scholar. Only articles written or translated to the English language were used.

Review methods

The following medical subject headlines were used ("larynx" or "laryngeal diseases") and ("Atypical mycobacterium" or "Atypical mycobacterial infections"). The PubMed search yielded 12 articles, with only eight specifics to NTM laryngeal infections. Google Scholar yielded 7 articles and only one specific to an NTM laryngeal infection. Out of the 19 total instances found, nine reported laryngeal NTM infections.

Results

Nine instances of laryngeal mycobacterial infections were identified and reviewed [2-10]. Table 1 summarizes patient characteristics and presents symptoms of each individual patient. The median age of patients was 45 years old. Seven patients were female (78%). Six patients endorsed dysphonia (67%), six endorsed cough (67%), and five endorsed fever (56%). Three patients used inhaled steroid medication prior to infection (33%) and one patient was immunocompromised (11%). Our patient was above the median age, without any underlying predispositions, inhaled steroid use, or immunocompromise.

Table 1: Patient characteristics and presenting symptoms of NTM laryngeal infections (n=9).

Variable	Value[a]
Age, yr, median (range)	45 (5-81)
Female gender, no. (%)	7 (78)
Presenting symptom, No. (%)*	
Dysphonia	6 (67)
Cough	6 (67)
Fever	5 (56)
Duration of presenting symptoms, months, median (range)	8.7 (2-24)
Possible predisposing factors, No. (%)	
Inhaled steroid use	3 (33)
Immunocompromised	1 (11)
ASTHMA	2 (22)
Exposure to bird droppings	3 (33)

[a]Numbers may sum to more than the overall total and percentages may sum to greater than 100%, as some patients met multiple criteria

Table 2: Clinical manifestations and diagnostic details

Characteristic	No. of Patients (%)[a]
Microlarnygoscopy findings (n=10)	
EXOPHYTIC MASS ON VOCAL FOLDS	6 (67)
LARYNGEAL EDEMA	4 (44)
Lesions on vocal folds	4 (44)
Laryngeal erythema	2 (22)
Positive culture for MAC [5]	2 (22)
Positive culture for *Mycobacterium fortuitum* [2]	1 (11)
Positive culture for *Mycobacterium lentiflavum* [3]	1 (11)
Positive culture for *Mycobacterium kansaii* [7-9]	3 (33)
Positive culture for *Mycobacterium leprae* [6]	1 (11)
Positive culture for *Mycobacterium malmoense* [10]	1 (11)
Unable to be determined [4]	1 (11)

[a]Numbers may sum to more than the overall total and percentages may sum to greater than 100%, as some patients met multiple criteria

Table 2 summarizes clinical manifestations and diagnostic details in the examined instances. The most common presentations included laryngeal edema (44%) and exophytic mass on the vocal folds (67%).

Patients who tested positive for NTM followed different treatment regimens case-to-case. Although all patients were placed on some form of antibiotic therapy, the type of antibiotic varied per case. The most common regimen used consisted of rifampin, ethambutol, and isoniazid to be taken daily. Interestingly, one patient with MAC was placed on an intense antibiotic regimen consisting of oral ciprofloxacin, clarithromycin, and doxycycline for six weeks.

Patients which presented with NTM, in general, saw full recovery after a prolonged course of treatment. It is important to note that one of the patients presented with a treatment regimen of oral ciprofloxacin, clarithromycin, and doxycycline did see a reappearance

Table 3: Individual case details.

Study	Gender	Age	NTM Type	Antimicrobial	Response
Yan et al. [2]	Female	45	*Mycobacterium fortuitum*	trimethoprim-sulfamethoxazole & moxifloxacin for 6 months	Complete resolution at 8 months
Hussin et al. [4]	Female	30	*Not Specified*	oral ciprofloxacin, clarithromycin, & doxycycline 6 weeks	Complete resolution at 6 weeks
Wang et al. [5]	Female	35	*MAC*	Unspecified "Antituberculosis Regimen"	Complete resolution. Timing not indicated.
Fwoloshi et al. [6]	Female	29	*Mycobacterium leprae*	dapsone, rifampicin, and clofazimine	Partial response at 1 month
Al-Zahid et al. [7]	Female	81	*Mycobacterium kansasii*	rifampicin, ethambutol, and clarithromycin; advised for 2 years	Patient died 2-3 after diagnosis after withdrawing care
Philip et al. [3]	Male	5	*Mycobacterium fortuitum*	rifampicin and clarithromycin for unspecified time	Complete resolution after 1 year
Lehman et al. [8]	Female	58	*Mycobacterium kansasii*	isoniazid, rifampin and ethambutol for 6 months	Partial response at 6 months
Khanna et al.	Female	81	MAC	azithromycin, ethambutol, and rifampin	Partial response at 1 year
Wray et al. [9]	Male	57	*Mycobacterium kansasii*	Rifater (rifampicin, isoniazid and pyrazinamide) and ethambutol	Complete resolution at 6 months
McEwan et al. [10]	Female	66	*Mycobacterium malmoense*	rifampicin, ethambutol, clarithromycin for 12 months	Complete resolution at 1 year.

Figure 1: In office flexible laryngoscopy prior to surgery. Exam demonstrates significant bilateral vocal fold hypomobility with posterior glottic stenosis.

Figure 2: Intraoperative view of the glottis. Star shows location of posterior glottic stenosis with MAC infection.

Figure 3: In office flexible laryngoscopy 6 weeks post-op. Exam demonstrates significant improvement in vocal fold mobility and size of posterior commissure.

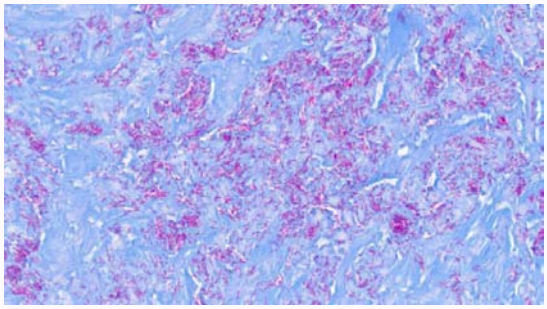

Figure 4: AFB stain - numerous mycobacteria (red elongated bacilli) were highlighted within the cytoplasm of macrophages. Biopsy revealed ulcerated mucosa containing dense histiocytic infiltrates. No necrosis and no well-formed granulomas were seen. The histiocytes contained numerous acid-fast bacilli, consistent with chronic mycobacterial laryngitis.

of MAC within two months of regimen. The patient was then treated with tracheostomy and microsurgery with laser removal in order to stop re-infection.

Discussion

In rare cases, atypical mycobacterial infections can cause laryngeal infection, such as the presented case. MAC is a bacterium found commonly in earthly reservoirs [5]. Most commonly, it is found in high abundance in pigeon droppings and can easily be inhaled into lungs. Laryngeal infection typically manifests as chronic sore throat, dysphonia, and fever. Atypical mycobacterial infections of the larynx can be life-threatening in immunocompromised patients.

Within the literature review, laryngoscopy and biopsy were used for diagnosis of laryngeal MAC. Gram staining and PCR were required to successfully identify the presence of acid-fast bacilli, specifically MAC, within a patient's tissue sample [5]. On reviewing prior publications of laryngeal NTM cases, summarized in Table 3, identified treatment regimens often include a combination of rifampin, ethambutol, and azithromycin. Although our patient has not yet completed treatment, she has been maintained on a regimen of rifampin, ethambutol, and azithromycin for over 1 year with biopsies showing a resolution of laryngeal MAC.

Our patient provided no history of smoking as well as no use of inhaled corticosteroids, which traditionally increases likelihood of

being infected with laryngeal MAC. Instead, she reported difficulty breathing for approximately one year and had been recommended a unilateral posterior cordotomy by outside provider, prior to diagnosis. Laryngeal MAC is important to have on one's differential for atypical laryngeal lesions or posterior glottic stenosis as culture and PCR testing are required for a diagnosis. PCR testing is more imperative when considering this diagnosis, as very often only trace amounts of acid-fast bacilli are detected. In the case of our patient, multiple biopsies were taken of the area showing chronic laryngitis and indeed, the mycobacterial smear returned positive. Due to the complexity of laryngeal MAC, based on our literature review a therapeutic approach of 10 mg/kg rifampin, 15 mg/kg ethambutol, and 300 mg isoniazid daily for 7 months yielded the best results in terms of treatment with complete vocal recovery. These patients must be followed up with regularly to monitor for progression of disease or clinical deterioration. Since MAC is more common than other species of mycobacterium, it should be considered more readily within differential diagnosis to reduce symptoms and likelihood of re-infection after treatment.

Conclusion

Laryngeal infection with atypical mycobacterial, specifically MAC, is a very rare diagnosis. A high index of suspicion is required, as these infections are often misidentified as laryngitis or other laryngeal infections. Biopsy, and often PCR, is required for an accurate diagnosis. Apart from antibiotic therapy, one possible treatment for sequelae of laryngeal MAC infections includes laser-assisted lysis of posterior glottic stenosis.

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