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Neisseria meningitidis Conjunctivitis Associated With Preseptal Cellulitis

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Abstract

Neisseria meningitidis (NM) is a gram-negative diplococcus causing varying clinical conditions, from asymptomatic colonization to life-threatening meningitis. We report a case of an unvaccinated woman with a history of systemic lupus erythematosus (SLE) who was diagnosed with conjunctivitis and periorbital cellulitis of the left eye due to NM following recent travel to Saudi Arabia for an Umrah pilgrimage. Diagnosis was made by computed tomography (CT) and confirmed by conjunctival fluid cultures. The present case represents a rare presentation of a serious bacterial infection that warrants consideration in at-risk individuals, such as returning travelers from high-risk areas.

Categories: Internal Medicine, Infectious Disease
Keywords: bacterial conjunctivitis, neisseria meningitidis, preseptal cellulitis, systemic lupus erythematosus, umrah pilgrimage

Introduction

Eye infections are classified by their location relative to the orbital septum, with infections anterior to the septum defined as preseptal cellulitis [1]. Incidence of preseptal cellulitis is highest in children, though increasing rates of infection have been identified in adults in recent years [2]. The majority of preseptal cellulitis cases are linked to staphylococcal species (mainly S*taphylococcus aureus)* and *Pseudomonas aeruginosa* [1]. Rarely, *Neisseria meningitidis* (NM) has also been associated with preseptal cellulitis, though with few reported cases in the literature [3,4].

NM is a gram-negative diplococcal bacterium that causes a spectrum of clinical conditions. Though commonly associated with meningitis, NM can cause a variety of clinical manifestations, including pneumonia and bloodstream infections [5]. In addition to symptomatic disease, about 10% of the population are carriers of the organism in the nose and upper airways [5]. Meningococci are further subcategorized by serogroup with variation in predominant strains by geography. Most invasive meningococcal disease is attributable to serogroups A, B, C, W, X, and Y [5,6]. NM is transmitted via inhalation of respiratory droplets or via direct contact with nasal or oral secretions. As such, close contact with infected individuals is often associated with transmission, and crowded conditions in association with international travel have been associated with outbreaks of infection [5,6].

The most severe form of NM infection is invasive meningococcal disease, and it often manifests as bacteremia and meningitis. However, localized infections, such as conjunctivitis, are also prevalent [7,8]. NM infection is a rare cause of conjunctivitis, though its true incidence is likely underreported as culture data are not collected in all cases of empirically treated disease [7]. Primary meningococcal conjunctivitis (PMC) refers to direct infection of the conjunctiva by NM, although conjunctivitis can also be a secondary manifestation of systemic meningococcemia [7]. PMC can also progress to invasive disease in some cases [7,8]. Several immune-related risk factors can contribute to the progression of invasive meningococcal disease. Reduced immunoglobulin quantity or function (e.g., in renal impairment or chronic lymphocytic leukemia) significantly increases susceptibility to invasive disease. Similarly, complement deficiency, often seen in conditions, such as systemic lupus erythematosus (SLE), is another recognized risk factor [6]. The optimal treatment for invasive meningococcal infection relies on parenteral antibiotics, whereas the treatment of localized infection such as conjunctivitis is less well established [7]. The risk for developing invasive meningococcal disease in contacts of patients with PMC is also unclear, though chemoprophylaxis is generally recommended for all close contacts of patients with localized or invasive disease [7].

Because of high rates of asymptomatic colonization, variable geographic distribution, and ease of spread via close contact, certain international events have been associated with NM outbreaks over the years, including pilgrimages associated with travel to Saudi Arabia [9,10]. Hajj and Umrah are pilgrimages to Mecca, Saudi Arabia that many members of the Islamic faith perform. The two events are similar, though Hajj is performed during a particular time of year, whereas Umrah can be performed at any time of year [10]. These pilgrimages have been associated with meningococcal disease and preventative public health efforts, including vaccination requirements and antibiotic prophylaxis for individuals from countries with high rates of NM, have been implemented to reduce transmission of NM among pilgrims [9]. However, the risk for

transmission remains elevated given variable adherence to preventative measures, communal living conditions with international travelers colonized with various serogroups of NM, and the fact that currently available vaccines do not cover all serogroups of NM [9-11].

Here we present one such case of NM infection associated with travel to Saudi Arabia. In this case, the patient was a returning traveler from an Umrah pilgrimage who presented with conjunctivitis and preseptal cellulitis, which was subsequently linked to NM cultured from conjunctival fluid.

Case Presentation

A 69-year-old woman with a history of SLE on hydroxychloroquine and methotrexate presented with upper respiratory symptoms and left eye swelling and discharge. Three days before this presentation, she had returned to the United States after having traveled with her daughter to Mecca and Medina in Saudi Arabia for an Umrah pilgrimage, where they stayed in large congregate settings. Moreover, they did not receive the recommended meningococcal ACWY vaccine before their travel. Two days before hospital presentation, she developed rhinorrhea, non-productive cough, and sore throat. The day before her hospital presentation, she went to a local urgent care where she tested negative for influenza, group A *Streptococcus*, and COVID-19. She was advised to continue home supportive care at that time.

The morning of hospital presentation, she developed left eye swelling with purulent drainage and a foreign body sensation in her eye. She denied any trauma or foreign exposures to the eye. No other household members were ill. She denied any headache, neck stiffness, changes to vision, eye pain, diplopia, fevers, or chills. That evening, she presented to an outside hospital for further evaluation. A computed tomography (CT) scan of her orbits with contrast noted pre-septal swelling and a small periorbital fluid collection without retro-orbital soft tissue swelling or enlargement of the extraocular muscles (Figure *1*). Conjunctival fluid cultures were taken about 15 minutes before receiving empiric antibiotics with intravenous vancomycin 1 g and ceftriaxone 2 g. Two sets of blood cultures were also collected 6 minutes and 11 minutes after antibiotic administration, respectively. The following day, she was transferred to our hospital for evaluation by ophthalmology.

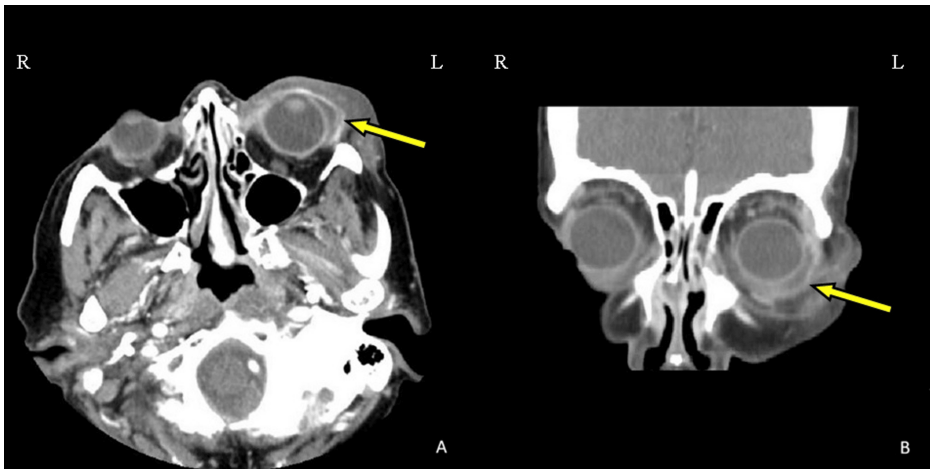


FIGURE 1: Axial (A) and coronal (B) CT orbits with contrast revealing an approximate 5 mm, crescent-shaped fluid collection at the anteroinferior aspect of the left globe (yellow arrow) with soft tissue swelling seen on the left periorbital space concerning for abscess

CT: computed tomography

Upon arrival, her oral temperature was 36.7°C, blood pressure was 150/89 mmHg, heart rate was 86 beats/minute, respiration rate was 18 breaths/minute, and the oxygen saturation was 98% on room air. Examination of her left eye was notable for erythema, soft edema, and a lateral redundant and boggy upper lid. The cornea showed scattered punctate epithelial erosions and a rapid tear break up time. Her visual acuity obtained by Snellen eye chart was 20/40 -3, PH 20/25 oculus sinister (OS) and 20/20 oculus dexter (OD). Admission labs are described in Table *1*, which revealed mild anemia, lymphopenia, a normal platelet count, and preserved renal function. On the same day as her presentation to our hospital, her conjunctival fluid culture was found to be growing gram-negative diplococci that later speciated to NM with a minimum inhibitory concentration (MIC) of 0.008 µg/mL for ceftriaxone, which was interpreted as susceptible based on Clinical and Laboratory Standards Institute (CLSI) guidelines. The organism was identified by soft ionization mass spectrometry (MALDI-TOF), and susceptibility testing was performed via

gradient diffusion (Epsilometer test). The positive result was reported to the Los Angeles County Department of Public Health. Infectious disease was consulted and she was continued on intravenous ceftriaxone 2 g daily and vancomycin 750 mg every 12 hours.

Category	Lab	Lab value	Reference range
Complete blood count	White blood cell count (1000/µL)	8.45	4.16-9.95
	Absolute neutrophil count (1000/µL)	6.95 (H)	1.80-6.90
	Absolute lymphocyte count (1000/µL)	0.79 (L)	1.30-3.40
	Red blood cell count (million/µL)	3.79 (L)	3.96-5.09
	Hemoglobin (g/dL)	11.0 (L)	11.6-15.2
	Hematocrit (%)	33.7 (L)	34.9-45.2
	Platelets (1000/µL)	280	143-398
Chemistry	Sodium (mmol/L)	135	135-146
	Potassium (mmol/L)	3.8	3.6-5.3
	Chloride (mmol/L)	106	96-106
	CO_2 (mmol/L)	21	20-30
	BUN (mg/dL)	21	7-22
	Creatinine (mg/dL)	0.72	0.60-1.30
	eGFR (mL/min/1.73 m^2)	>89	>89
	Calcium (mg/dL)	8.4 (L)	8.6-10.4

TABLE 1: Admission laboratory values

CO_2: carbon dioxide; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate

On hospital day 1 at our institution (about 24 hours from initial antibiotic administration), she was noted to have improvement in pain, chemosis, and the amount of purulent drainage from the left eye. Vancomycin was stopped on hospital day 3 (total four days of therapy), and she was continued on ceftriaxone 2 g daily. She remained hospitalized for four days with continued improvement in her symptoms and exam. She had not received topical ophthalmic antimicrobials during her hospitalization at either facility. On the day of discharge, her visual acuity had returned to baseline (20/20 OS), and chemosis and conjunctival injection had resolved. All previously noted lab abnormalities had normalized. Blood cultures were ultimately negative. She was discharged on intravenous ceftriaxone 2 g daily to complete seven days of therapy with outpatient ophthalmology follow-up, which the patient had ultimately declined to pursue.

Her daughter, who had accompanied her on this pilgrimage, remained asymptomatic in terms of upper respiratory or ocular symptoms. She was referred to an urgent care affiliated with our institution for a formal evaluation and received intramuscular ceftriaxone for post-exposure prophylaxis.

Discussion

Neisseria meningitidis infections have variable presentations ranging from the asymptomatic colonization of the nasopharyngeal tract to meningitis and bacteremia [3,5]. Presenting symptoms are often nonspecific and may include upper respiratory tract symptoms early in the course of the illness, as was seen in this case. Concurrent upper respiratory tract infections from other pathogens are also seen and can facilitate progression from asymptomatic colonization to invasive disease [6].

Dermatologic manifestations of *Neisseria meningitidis* infections are common and include petechiae, maculopapular eruptions, and in cases of meningococcemia, purpura fulminans [4,5]. However, cellulitis is a rare manifestation with fewer than two dozen cases reported in the literature [3,4]. Conjunctivitis and periorbital infections caused by NM are more frequently seen in pediatric populations [3,8]. In these cases, it is likely that conjunctivitis may spread to involve the periorbital tissues, as may have occurred in this case [4]. Among adult cases, comorbidities that affect host immune defenses are frequently identified [3]. In this

case, the patient had SLE managed with hydroxychloroquine and methotrexate. These treatments are not inherently associated with a significantly increased risk of NM infection [12]. More commonly, complement deficiency often mediates the risk of invasive meningococcal disease [6,13]. Importantly, SLE may confer increased risk of meningococcal infection from low complement levels or functional asplenia, though it is unknown if these conditions were present in this case [12-14].

While the source of this patient's NM infection is unconfirmed, outbreaks of NM have complicated Umrah pilgrimages for several decades [10,15,16]. The events undertaken during Umrah pose several risk factors for transmission of NM, including communal living conditions, exposure to large groups of people from many countries, and high rates of upper respiratory tract illnesses which may contribute to transmission [6,9,15-17]. Given the international exposure during Umrah, pilgrims are exposed to various serogroups of NM, though recent cases in returning travelers to the United States have been predominantly due to serogroup W [17]. While the lack of serogroup testing limits our ability to confirm this association conclusively, the onset of the patient's symptoms suggests exposure during her time in Saudi Arabia. Serogroup W is associated with a different spectrum of disease and a greater rate of atypical presentations with invasive disease, specifically with higher rates of conjunctivitis [18]. However, we cannot confirm that this relationship is definitively present in this case given the lack of serogroup testing.

Given the prevalence of disease among Umrah pilgrims, it is recommended that all travelers to Saudi Arabia who plan to perform Umrah receive the meningitis vaccine before travel, which this patient did not pursue [17]. Although Saudi Arabia officially requires pilgrims performing Umrah to obtain meningitis vaccination before travel, rates of vaccination remain low due to variable compliance and pilgrims not travelling to the country on an Umrah-specific visa [19]. Despite this suboptimal uptake, meningitis vaccination is associated with a significant reduction in NM carriage rates among pilgrims, with most cases of invasive disease occurring in unvaccinated individuals [11,19].

The management of preseptal cellulitis without high-risk features or previous treatment failure is typically performed in an outpatient setting with oral antibiotics [20]. However, the management of eye infections caused by NM is not well established, though it may involve administration of appropriate parenteral antibiotics, as was performed in this case [3,4,21]. Most reported cases appear to respond well to the antimicrobial therapies without further complications [4]. Antimicrobial prophylaxis for close contacts is also recommended [5,15].

Conclusions

This case describes a rare cause of conjunctivitis associated with preseptal cellulitis in a patient returning from an Umrah pilgrimage. Though primary periorbital infection with NM is an atypical manifestation, it should be considered in the differential diagnosis of patients who are at high risk, such as returning travelers from endemic areas. Transmission prevention efforts, such as vaccination requirements for travelers to Saudi Arabia for Umrah, have decreased rates of outbreaks, but symptomatic disease is still identified due to multiple factors, including low vaccination uptake. Management of conjunctivitis and preseptal cellulitis caused by NM should be individualized based on disease severity and potential for invasive disease because inadequate treatment can result in further disease progression and other complications. Prompt identification can also minimize disease transmission through antibiotic prophylaxis for close contacts.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Amit Levi

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Supervision: Amit Levi

Disclosures

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