Title

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Journal

Sexually Transmitted Diseases, 46(12)

ISSN

0148-5717

Authors

Adamson, Paul C

Judson, Seth D

Klausner, Jeffrey D

et al.

Publication Date

2019-12-01

DOI

10.1097/olq.0000000000001055

Peer reviewed

HHS Public Access

Author manuscript

Sex Transm Dis. Author manuscript; available in PMC 2021 April 27.

Published in final edited form as:

Sex Transm Dis. 2019 December ; 46(12): 813–815. doi:10.1097/OLQ.0000000000001055.

Neisseria gonorrhoeae as a Rare Cause of Preseptal Cellulitis

Paul C. Adamson, MD, MPH[*], **Seth D. Judson, MD**[†], **Jeffrey D. Klausner, MD, MPH**[*,‡], **Theodoros Kelesidis, MD, PhD**[*]

[*]Division of Infectious Diseases, David Geffen School of Medicine at UCLA

[†]Division of Internal Medicine, David Geffen School of Medicine at UCLA

[‡]Fielding School of Public Health, University of California, Los Angeles, CA

Abstract

Neisseria gonorrhoeae is a rare cause of preseptal cellulitis, but infections can be severe. Rapid diagnosis is critical and can be expedited by nucleic acid amplification tests. Contact isolation precautions are encouraged for hospitalized patients with gonococcal preseptal cellulitis and a prolonged course of antibiotics is recommended.

Neisseria gonorrhoeae is a very rare cause of preseptal cellulitis, with only 4 previous cases reported in the literature.[1–4] We describe a case of a 43-year-old woman who presented to the emergency room with acute onset, unilateral eye pain, swelling, mucopurulent discharge, and chemosis. She was diagnosed with conjunctivitis and preseptal cellulitis caused by *N. gonorrhoeae*. Here, we discuss transmission, diagnosis, and treatment considerations.

CLINICAL NARRATIVE

A 43-year-old woman presented with 36 hours of rapidly progressive left eye pain, purulent discharge, and swelling that limited eye opening. She denied recent upper respiratory tract infections, or trauma to the eye. She reported a low-grade fever the evening before presentation, as well as pain with urination during the previous week. She had 1 male sexual partner in the prior 6 months, denied any recent oral sex, and denied any recent sexually transmitted infections. On examination, she was afebrile and unable to open her left eye due to periorbital swelling. She had copious mucopurulent discharge, erythema of her upper and lower eyelids, mild ecchymosis over her lower lid, as well as severe tenderness with eye opening and with ocular movements. A slit lamp examination revealed chemosis with conjunctival injection, but with normal cornea and intraocular structures. A computed tomography scan of the orbit showed left periorbital preseptal soft tissue swelling without evidence of orbital inflammatory changes.

Correspondence: Paul Adamson, MD, MPH, Division of Infectious Diseases, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue CHS 37-121, Los Angeles, CA 90095-1688. padamson@mednet.ucla.edu.

Conflicts of Interest and Sources of Funding: None declared.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (http://www.stdjournal.com). DOI: 10.1097/OLQ.0000000000001055

A fourth-generation human immunodeficiency virus test was done (Roche Diagnostics, North America) and was negative. The gram stain of the left eye discharge done on admission showed rare gram-positive cocci in clusters. A nucleic acid amplification test (NAAT) (Cobas CT/NG; Roche Diagnostics, North America) for *N. gonorrhoeae* from a urine specimen obtained on hospital day 1, resulted positive on hospital day 2. Bacterial culture from the initial eye swab grew gram-negative diplococci on chocolate agar and Thayer-Martin media at 48 hours and was confirmed to be *N. gonorrhoeae* by MOLDI-TOF (Vitek MS version 3.0; Biomerieux, France) at 72 hours. On hospital day 3, we requested NAAT for *N. gonorrhoeae* from the initial swab of the left eye, which resulted positive later that day, around the same time of the culture results. Subsequently, a NAAT from a pharyngeal specimen was also positive. Blood cultures sent before antibiotics were negative.

She received intravenous (IV) cefepime and IV vancomycin, as well as 2 doses of IV piperacillin-tazobactam empirically. On hospital day 2, the eyelid swelling and pain continued, and she developed worsening ecchymosis over her lower lid. Once the urine NAAT for *N. gonorrhoeae* returned positive, she was started on ceftriaxone 1 g IV daily and received 1 dose of oral azithromycin 1 g to treat gonorrhea, as well as daptomycin 6 mg/kg IV daily for potential *Staphylococcus aureus* based on gram stain results. On hospital day 3, her eyelid swelling, pain, and discharge began to improve. Given the improvement to her eye discharge, a repeat eye swab was not performed. She was discharged on hospital day 5 after receiving 4 doses of IV ceftriaxone. She was discharged with oral cefixime 200 mg twice per day and tobramycin eye drops to treat gonococcal preseptal cellulitis and trimethoprim-sulfamethoxazole (TMP-SMX) 800 to 160 mg twice daily for potential S. *aureus* coinfection, based on initial gram stain, though culture results did not grow an additional pathogen. She completed a 10-day course of therapy, after which her pain, conjunctival injection, and swelling had entirely resolved (Supplemental Figure 2, http://links.lww.com/OLQ/A397).

DISCUSSION

N. gonorrhoeae is a well-known cause of conjunctivitis, most commonly presenting as *ophthalmia neonatorum* in neonates. In adults, gonococcal conjunctivitis is less common, but can present as a hyperacute, unilateral conjunctivitis.[5] Gonococcal conjunctivitis can be rapidly invasive, as *N. gonorrhoeae* can penetrate intact corneal epithelium, leading to corneal ulceration and blindness.[5]

Preseptal cellulitis is usually caused by *Streptococcus* and *Staphylococcus* species, including methicillin-resistant *Staphylococcus aureus* (MRSA). Infection typically arises from external sources of infection, with risk factors being recent trauma, sinusitis, upper respiratory tract infections, or dacrocystitis.[6] Preseptal cellulitis can be severe and increases the risk for infection extending into the orbit, which can lead to vision loss, cavernous sinus thrombosis, and meningitis.[6] Gonococcal infection leading to preseptal cellulitis in adults is rare, and only 4 cases have been reported in the literature, which are summarized in Supplemental Table 1 (http://links.lww.com/OLQ/A398).[1–4]

In adults, gonococcal conjunctivitis typically occurs in patients with urogenital infection and is thought to be caused by autoinoculation from the genital tract via contaminated hands. However, there is also evidence for alternative modes of transmission for gonococcal conjunctivitis, including sexual exposure, laboratory exposure, and transmission through fomites.[7] We suspect our patient developed the ocular infection through autoinoculation, as she had concomitant genitourinary infection. *N. gonorrhoeae* was also isolated from her pharynx which could represent an independent primary site of infection that developed after sexual exposure, though she denied recent insertive oral sexual exposure. The isolation of *N. gonorrhoeae* from 3 different anatomical sites, with the presence of ecchymosis around the left eye without preceding trauma, raised the possibility of disseminated gonococcal infection with involvement of the small blood vessels. Disseminated gonococcal infection presenting as vasculitis has been reported, and cutaneous vasculitis can be the sole manifestation of the disease.[8] However, there was no additional cutaneous involvement, tenosynovitis, or bacteremia to support disseminated gonococcal infection, and severe local inflammation likely accounted for the ecchymoses around the eye. Thus, autoinoculation was the most likely mechanism in this case.

Nucleic acid amplification testing is recommended for the diagnosis of urogenital gonorrhoeae.[9] However, NAATs have only been recently approved by the Food and Drug Administration for extragenital specimens and before this approval, laboratories provided gonococcal nucleic acid testing on rectal and oropharyngeal specimens after the performance of verification procedures.[10] For ocular specimens, there are no data on the performance of NAATs, thus culture remains the recommended diagnostic test.[9] Unfortunately, *N. gonorrhoeae* can take 3 to 5 days to grow in media, leading to delays in diagnosis of ocular infections. In our case, the turnaround time for the NAAT on the eye specimen was about 5 hours, which was also confirmed by bacterial culture. Given their high sensitivity and rapid turnaround time, NAATs offer advantages over traditional culture techniques and might serve a role in rapidly diagnosing severe eye infections. This is particularly important given the severity of infection. To our knowledge, this is the first report to demonstrate the utility of NAAT on an eye specimen to rapidly diagnose a severe *N. gonorrhoeae* eye infection in an adult.

The documented transmission of gonorrhea from contaminated hands and fomites raises important questions about the role for contact precautions. The United States Centers for Disease Control and Prevention (CDC) recommends only standard precautions for gonococcal conjunctivitis but contact precautions for acute viral conjunctivitis.[11] There have been outbreaks of nonsexually transmitted gonococcal conjunctivitis associated with household contacts[12]; a subsequent molecular analysis of one of these outbreaks did not identify a genitourinary reservoir for these infections.[13] Transmission through fomites has also been reported.[7] However, these cases were community-based outbreaks where hygiene practices may have been suboptimal, because many of these cases were among children. Nosocomial outbreaks of gonorrhea from contaminated hands and fomites have not been described. Thus, although this case report does not provide evidence to change approach to hospital infection control procedures, physicians should be vigilant about treating hospitalized patients with suspected gonococcal ocular infection and mucopurulent discharge.

In the United States, cases of gonorrhea are on the rise, and drug-resistance is a major treatment consideration. Gonococcal conjunctivitis is rare in adults, and treatment data are limited.[9] The 2015 CDC Sexually Transmitted Disease Treatment Guidelines recommend a single dose of 1 g intramuscular ceftriaxone plus 1 g oral azithromycin for treatment of gonococcal conjunctivitis. Treatment data are even more sparse for gonococcal preseptal cellulitis, but given the severity of the infection, a more prolonged course is likely needed. The previous cases reported in the literature utilized IV ceftriaxone for 5 to 7 days in combination with an oral macrolide or fluoroquinolone, with the exception of the initial case that was a penicillin-sensitive isolate1 (Supplemental Table 1, http://links.lww.com/OLQ/A398). Our patient experienced rapid improvement after 3 days of IV ceftriaxone. The patient ultimately received a total of 4 doses of ceftriaxone 1 gram IV daily and subsequently completed a 5-day course of oral cefixime 200 mg twice daily, tobramycin eye drops, and TMP-SMX twice daily and experienced good recovery. In the United States, antimicrobial susceptibility testing for *N. gonorrhoeae* isolates is not routinely performed, and when done, the turnaround time can be long. At our institution, susceptibility testing is coordinated through the county health department and the CDC, and the turnaround time can be several weeks, which limits the clinical use.

Preseptal cellulitis can be severe and increases the risk for infection extending into the orbital tissues, which can lead to vision loss, cavernous sinus thrombosis, and meningitis.[6] Clinicians must consider *N. gonorrhoeae* as a cause of acute, unilateral, purulent conjunctivitis, with or without preseptal cellulitis. In cases of preseptal cellulitis due to gonorrhea, a prolonged course of antibiotics is recommended. In Figure 1, we propose our clinical approach to an adult patient presenting with acute, unilateral, purulent conjunctivitis, with or without preseptal cellulitis.

Gonococcal conjunctivitis is uncommon in adults. *N. gonorrhoeae* is a very rare cause of preseptal cellulitis. However, clinicians must consider *N. gonorrhoeae* infection in sexually active adults presenting with acute, unilateral, mucopurulent conjunctivitis and preseptal cellulitis, as the infection can be severe, sight-threatening, and might progress to a more invasive infection. Rapid diagnosis is critical and currently relies on culture from an eye swab, though we propose NAATs might aid in the diagnosis. Contact isolation precautions are encouraged for patients with high clinical suspicion or diagnosed gonococcal conjunctivitis. For preseptal cellulitis, we suggest empiric antibiotics to cover MRSA, *Streptococcus* species, as well as *N. gonorrhoeae*, while awaiting microbiologic culture data. For gonococcal preseptal cellulitis, we recommend using at least 3 days of IV ceftriaxone before transitioning to oral antibiotics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

The authors would like to thank the patient for consenting to participate in this case report. The authors would also like to thank Leanne Mortimer, PhD for laboratory contributions. All authors declare no conflicts of interest.

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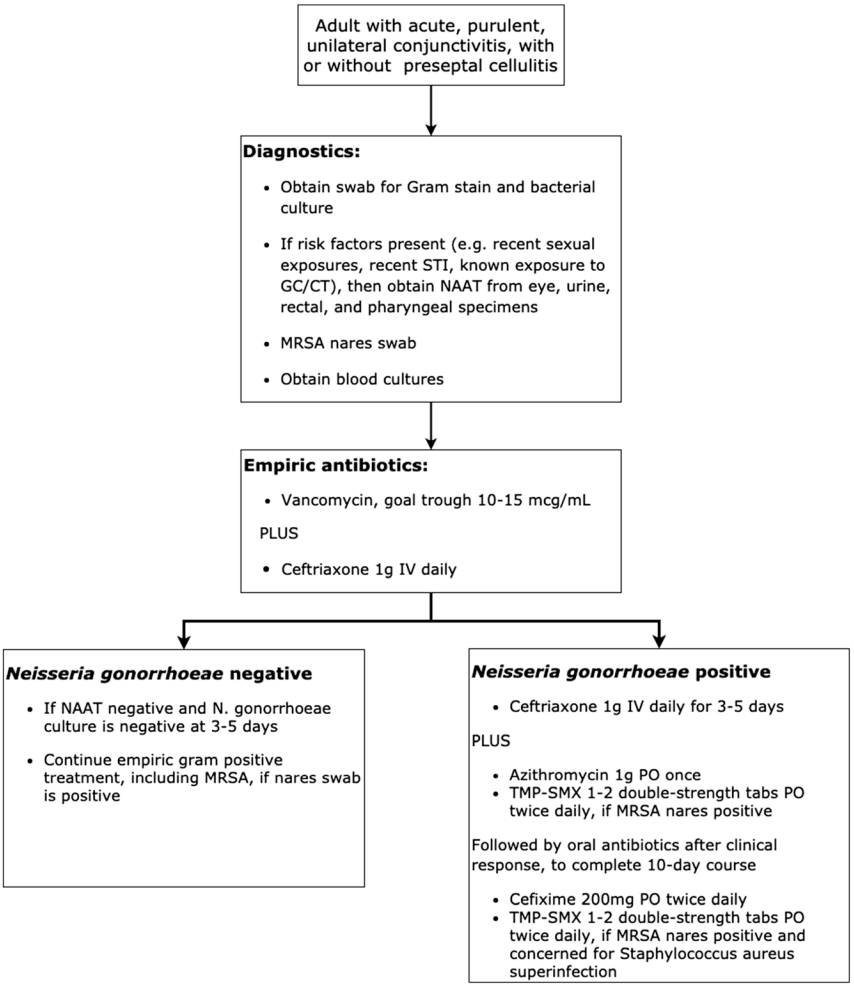

Figure 1.

A clinical approach for the presentation of acute, unilateral, conjunctivitis, with or without preseptal cellulitis in an adult. STI, sexually transmitted infection; GC, *Neisseria gonorrhoeae*; CT, *Chlamydia trachomatis*; TMP-SMX, trimethoprim-sulfamethoxazole.