



Index of Suspicion

1 Eye Discharge in a 10-day-old Neonate Born by Cesarean Delivery

Gagandeep Singh, MD,* Alvaro Galvis, MD,* Samrat Das, MD[†]

*Department of Pediatrics, University of Nevada School of Medicine, Las Vegas, NV

[†]Department of Pediatrics, Duke University School of Medicine, Durham, NC

EDITOR'S NOTE

We invite readers to contribute Index of Suspicion cases through the PIR manuscript submission system at: <https://mc.manuscriptcentral.com/pir>.

AUTHOR DISCLOSURE Drs Singh, Galvis, and Das have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

PRESENTATION

A 10-day-old boy presents with discharge from the left eye. It started at 3 days of age as a continuous, clear discharge and became copious and mucopurulent at 7 days of age. The mother reports swelling over the left eye, which started 2 days ago, and it worsened gradually so that he is not able to open his left eye today. The mother denies fever, trauma, sick contacts, recent travel, or rash. The patient was born at term via cesarean delivery. Maternal history is significant for a *Trichomonas vaginalis* infection during the second trimester, which was adequately treated. All other prenatal test results were negative. Review of the nursery records revealed that the patient received erythromycin prophylaxis for conjunctivitis.

On admission, he is afebrile and his vitals are stable. Physical examination shows a fussy neonate with eyelid swelling and erythematous conjunctiva with mucopurulent discharge from the left eye. The remaining physical examination findings are normal.

Initial laboratory evaluation shows a normal complete blood cell count and serum electrolyte levels. His human immunodeficiency virus (HIV) antibody test as well as rapid plasma reagin test results are negative. The cerebrospinal fluid (CSF) analysis results are normal. Additional evaluation leads to the diagnosis.

The Case Discussion and References appear with the online version of this article at <http://pedsinreview.aappublications.org/content/39/4/210>.

DISCUSSION

The differential diagnosis of injected conjunctiva with eye discharge (conjunctivitis) in the neonatal period includes chemical conjunctivitis, chlamydia conjunctivitis, gonococcal conjunctivitis, and trauma. Gram-stain of the discharge from the left eye of our patient showed gram-negative diplococci, which were confirmed to be *Neisseria gonorrhoeae* on culture. Chlamydia polymerase chain reaction was negative. Blood, urine, and CSF cultures were sterile.

The patient was initially started on intravenous ampicillin and cefotaxime pending culture results. The antibiotics were discontinued after 48 hours when the blood, urine, and CSF cultures were reported to be negative. However, after the culture result from the left eye was confirmed to be *N gonorrhoeae*, the patient was treated with a single dose of ceftriaxone and underwent scheduled irrigation of both eyes. The patient was evaluated by a pediatric ophthalmologist to ensure that he has not developed the complications of gonococcal conjunctivitis, and none were identified. The patient responded well, with complete resolution of the swelling and mucopurulent discharge. The mother and her partner were requested to get evaluated and treated for sexually transmitted infections (STIs).

The Condition

Ophthalmia neonatorum (ON), also called neonatal conjunctivitis, is a broad term and includes all forms of acute, mucopurulent infection of the eyes in the first 4 weeks of life. Up to 12% of newborns are affected by ON. In the past (before the 1880s), the term ON was used only for cases of

conjunctivitis caused by infection with *N gonorrhoeae* and was the primary cause of neonatal blindness. (Table)(1)

Epidemiology

Chlamydial infections are the most common bacterial cause of conjunctivitis in neonates, accounting for up to 40% of cases of neonatal conjunctivitis. *Streptococcus pneumoniae* and nontypeable *Haemophilus influenzae* have been estimated to account for 30% to 50% of cases of ON, whereas *N gonorrhoea* accounts for less than 1% of cases of ON in the developed world. In the United States, perinatal transmission occurs in 30% to 40% of patients with maternal cervical infection. (2) Intrauterine transmission is also possible after the rupture of membranes.

Gonococcal infection in neonates born by cesarean delivery is rare. The first case of gonococcal conjunctivitis after cesarean delivery was described by Thompson et al in a case series of 7 patients in 1974. (3)

A variety of mechanisms have been proposed to explain the transmission of gonococcal infection in newborns born via cesarean delivery, as discussed. (4) One of the suggested modes of transmission is spread of infection from the infected birth canal to the amniotic fluid during a period between rupture of membranes and birth of the neonate. It is also possible to have postnatal transmission of infection from maternal genitalia to neonatal eyes by person-to-person transmission. (4) In another study, Handsfield et al found neonatal orogastric contamination with *N gonorrhoeae*, suggesting intrauterine infection. (5)

Prophylaxis

Historically, the introduction of postnatal prophylaxis with 2% silver nitrate decreased the incidence of neonatal gonococcal conjunctivitis from 10% to 0.3%. (1) A need for prophylaxis is under debate because of the decreasing incidence of STIs, effective treatment for conjunctivitis, and risk of developing resistance to antibiotic agents. Currently, the standard of care in the United States is the use of topical erythromycin ointment for prophylaxis. However, although the use of postnatal prophylaxis decreases the incidence of transmission, it does not completely eliminate it. (1)

Microbiology and Pathogenesis

Neisseria gonorrhoeae is an intracellular gram-negative diplococci. The outer membrane of *N gonorrhoeae* contains lipooligosaccharide, phospholipid, and a variety of proteins, including the porin (PorB) protein. PorB is essential for bacterial viability because it mediates ion exchange between *N gonorrhoeae* and the environment. PorB has also

TABLE. Causes of ophthalmia neonatorum

• CHEMICAL	• VIRAL
• Bacterial	• Adenovirus
• <i>Chlamydia trachomatis</i>	• <i>Herpes simplex virus</i>
• <i>Neisseria gonorrhoeae</i>	
• <i>Haemophilus species</i>	
• <i>Streptococcus pneumoniae</i>	
• <i>Staphylococcus aureus</i>	
• <i>Staphylococcus epidermidis</i>	
• <i>Streptococcus viridans</i>	
• <i>Escherichia coli</i>	
• <i>Pseudomonas aeruginosa</i>	
• Other	

been implicated in being crucial for the pathogen to evade both the innate and adaptive immune systems. There are 2 alleles for PorB, known as PIA and PIB, that are associated with different phenotypes. The PIA strains are associated with disseminated disease because these strains are resistant to the bactericidal effects of human serum, and the PIB strains are associated with localized urogenital infections. (6)(7)(8) Initial attachment of gonococci to the surface of columnar epithelial cells is mediated by type IV pili. After attaching to mucosal cells, gonococci are engulfed in a process known as parasite-directed endocytosis, and the gonococci proceed to replicating intracellularly. The bacteria can then extend through lymphatics or can cause bacteremia, leading to disseminated disease.

Clinical Features

Infection usually is manifested 2 to 5 days after birth. It causes purulent conjunctivitis, with profuse exudate and swelling of the eyelids. If untreated, severe complications such as corneal scarring, blindness, and septicemia can occur.

Diagnosis

Gonococcal conjunctivitis is diagnosed by prenatal and perinatal history, physical examination, and microbiologic examination of conjunctival exudate. A Gram-stain of the conjunctival exudate should be examined for the presence of typical gram-negative intracellular kidney bean-shaped diplococci. For identifying *N gonorrhoeae* from nongenital sites, culture is the most widely used test. The patient should also be evaluated for chlamydia trachomatis, congenital syphilis, and HIV infections because of an increased incidence of coinfections with these pathogens. The mother's hepatitis B status should also be investigated. In addition, the patient's mother and her sexual partner should be evaluated for gonococcal and other STIs. (9)

Treatment

Infants suspected of having gonococcal ophthalmic disease should be hospitalized and observed for response to therapy and for disseminated disease (sepsis, arthritis, meningitis). After obtaining cultures (from eye, blood, urine, and CSF), empirical treatment should be started in patients in whom organisms are seen on Gram-stain or in those with negative Gram-stain but who are considered to be at high risk (eg, a mother with no prenatal care, history of STIs, or substance abuse). The current guidelines recommend treatment of neonatal gonococcal conjunctivitis

with a single dose of ceftriaxone 25 to 50 mg/kg, with a maximum of 125 mg given intravenously or intramuscularly. (9) Furthermore, patients require frequent irrigation of the eye with saline until resolution of discharge from the affected eye. (9) Topical antimicrobial therapy alone is not adequate to treat gonococcal conjunctivitis. Treatment of ON should be continued beyond the single treatment dose until all bacterial cultures are negative and systemic infection has been excluded, typically after 48 to 72 hours of therapy.

Lessons for the Clinician

- Clinicians should have a high index of suspicion for serious bacterial infections, such as infections with *Neisseria gonorrhoeae*, as the cause of neonatal conjunctivitis even in neonates born via cesarean delivery.
- Clinicians should start with systemic antibiotic drug treatment when gonococcal conjunctivitis is suspected.
- One should closely monitor neonates for ophthalmologic and systemic complications of gonococcal conjunctivitis.
- All newborns should be provided topical antibiotic drug prophylaxis at birth.

References

1. Recommendations for the prevention of neonatal ophthalmia. *Paediatr Child Health*. 2002;7(7):480-488
2. Bradley JS, Wassel RT, Lee L, Nambiar S. Intravenous ceftriaxone and calcium in the neonate: assessing the risk for cardiopulmonary adverse events. *Pediatrics*. 2009;123(4):e609-e613
3. Thompson TR, Swanson RE, Wiesner PJ. Gonococcal ophthalmia neonatorum: relationship of time of infection to relevant control measures. *JAMA*. 1974;228(2):186-188
4. Strand CL, Arango VA. Gonococcal ophthalmia neonatorum after delivery by cesarean section: report of a case. *Sex Transm Dis*. 1979;6(2):77-78
5. Handsfield HH, Hodson WA, Holmes KK. Neonatal gonococcal infection, I: orogastric contamination with *Neisseria gonorrhoeae*. *JAMA*. 1973;225(7):697-701
6. Fudyk TC, Maclean IW, Simonsen JN, et al. Genetic diversity and mosaicism at the por locus of *Neisseria gonorrhoeae*. *J Bacteriol*. 1999;181(18):5591-5599
7. Chen A, Seifert HS. Structure-function studies of the *Neisseria gonorrhoeae* major outer membrane porin. *Infect Immun*. 2013;81(12):4383-4391
8. Ram S, Cullinane M, Blom AM, et al. Binding of C4b-binding protein to porin: a molecular mechanism of serum resistance of *Neisseria gonorrhoeae*. *J Exp Med*. 2001;193(3):281-295
9. Kimberlin DW, Long SS, Brady MT, Jackson MA, eds. Gonococcal infections. In: *Red Book 2015: Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:356-366