

An Unusual Transmission of *Neisseria meningitidis*

Neonatal Conjunctivitis Acquired at Delivery From the Mother's Endocervical Infection

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Background: Primary meningococcal conjunctivitis is assumed to be due to the direct inoculation of *Neisseria meningitidis* into the conjunctival sac from an exogenous source. According to a literature review, no case of neonatal conjunctivitis infection acquired at delivery from maternal endocervicitis has been published.

Goal: To report a case of meningococcal neonatal conjunctivitis acquired at delivery because of the mother's endocervical infection and cross-transmission of the strain with her partner.

Study Design: Strains were characterized by bacteriologic and serologic methods including grouping (agglutination), typing, and subtyping (enzyme-linked immunosorbent assay). Molecular analysis was done by pulsed-field gel electrophoresis.

Results: The three strains (newborn infant, mother, partner) were of the same antigenic formula (C:NT:P1.NT) and exhibited similar *NheI* and *SpeI* pulsed-field gel electrophoresis patterns.

Conclusion: The identical phenotypic and genomic analysis of strains is the evidence for *N meningitidis* transmission at delivery from a maternal endocervical infection to the newborn infant and cross transmission between sexual partners.

NEONATAL CONJUNCTIVITIS is the most frequent infection during the first 6 weeks after birth, affecting 24% of the newborn infants in developing countries.¹

Neonate acute bacterial conjunctivitis transmitted at delivery is usually due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*. *Neisseria meningitidis* is an uncommon causative agent of acute conjunctivitis in both children and adults.

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Primary meningococcal conjunctivitis (PMC) has been reported even less frequently than secondary (endogenous) conjunctivitis. However, Barquet et al² described 9 of 84 cases of PMC that involved newborn infants. PMC is defined as acute or hyperacute purulent conjunctivitis with purulent exudate, clinically resembles gonococcal conjunctivitis, and can occur bilaterally or unilaterally. PMC is assumed to be due to the direct inoculation of *N meningitidis* into the conjunctival sac from an exogenous source.²

We describe a primary neonatal conjunctivitis caused by *N meningitidis* acquired at delivery from a maternal endocervical infection. Both the isolates from the cervix and from the neonate conjunctiva were confirmed to be the same strain. Two months later, this strain was also identified in the oropharynx of the mother's male partner. This may be the first confirmed case of meningococcal neonatal conjunctivitis infection acquired at delivery because no published case was found during the literature review.

An initial diagnosis of gonococcal ophthalmia was made because gram-negative intracellular diplococci were seen in the smear from the neonate conjunctiva and gram-negative diplococci, most of which were extracellular, in the mother's cervix. The isolates were submitted as *Neisseria spp* to the STD National Reference Center for identification and characterization because the appearance of the cultured colonies was atypical.

Case Reports

The sample collection and presumptive identification that included Gram stain, culture on selective modified Thayer-Martin and enriched media, and oxidase reaction³ were performed at the site where the mother and newborn infant were admitted (Ramon Santamarina Hospital).

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Case 1

A breast-fed newborn boy with a birth weight of 3150 g received conjunctival prophylaxis with NO_3Ag at birth. Two days after an uncomplicated vaginal delivery he presented an acute, purulent, and unilateral conjunctivitis with conjunctival injection, eyelid edema, and purulent discharge from the right eye. A conjunctival specimen was collected after washing out the excess of exudate with sterile saline, and the surface of the conjunctival sac was wiped with a sterile swab. The exudate disclosed gram-negative intracellular diplococci with a high rate of polymorph nuclear leukocytes in direct Gram smear. After 18 hours of incubation, smooth, round, and convex colonies were grown from the conjunctiva exudate in all cultures. The colonies were diplococci gram-negative and produced a positive oxidase reaction. Under the suspicion of gonococcal infection, the newborn infant was treated with erythromycin ophthalmic solution and 20 mg/kg/day ceftriaxone for 7 days, and was discharged the following day.

Clinical examination 3 days after treatment was normal. A nasopharynx specimen cultured for meningococci as a test-of-cure was negative. Medical controls were normal for the next 6 months. There were no general symptoms or signs of systemic meningococcal disease. No ocular complications occurred.

Case 2

The mother was a 16-year-old single woman with high-risk sexual behavior. She was primigravida and had antenatal care at the beginning of the third trimester. At that time, a Papanicolaou type II due to *Trichomonas vaginalis* colpitis was found and treatment was given. Serologic test results for syphilis, toxoplasmosis, and HIV were negative. The patient was admitted to the hospital at 36 weeks gestation while in labor with intact membranes, and gave birth 4 hours later without complications.

Two days after delivery, when the conjunctivitis of the newborn was detected, a bacteriologic study of cervix exudate was requested. Endocervical canal was swabbed after inserting the speculum and cleaning the cervix. The cervix showed an inflammatory process with purulent discharge, and a direct Gram stain and cultures were performed. The stain showed inflammatory reaction with a predominance of gram-negative extracellular diplococci. The cultures yielded diplococci gram-negative colonies with positive oxidase reaction. A pharyngeal specimen was not collected. The patient was empirically treated with 500 mg ceftriaxone IM for 7 days.

Case 3

The father was a 29-year-old truck driver who traveled frequently through Mercosur countries, and was absent

when the child was born. Two months later, he was notified of an appointment to complete epidemiologic studies. At this time, the man was asymptomatic and refused urethral study, but accepted an oropharynx sample. The sample was taken by swabbing the posterior pharynx and the region of the tonsillar crypts. Culture of the specimen in modified Thayer-Martin media showed growth of gram-negative, oxidase-positive diplococci. Serologic test results for syphilis and HIV were negative.

Discussion

To our knowledge, this is the first description of acute neonatal conjunctivitis caused by *N meningitidis* acquired at delivery. The index case was considered noninvasive PMC because clinical features of acute conjunctivitis were not followed by meningococcal septicemia or meningitis. Serologic tests for meningococcal antibodies are not performed in our country, which is unfortunate because the test had permitted us to assess the reasonable hypothesis of the newborn infants' immunity transmitted from the mother.

Confirmatory and molecular studies were performed. The three isolates fermented only glucose and maltose in CTA-1% carbohydrate media³ and belonged to *N meningitidis* serogroup C by slide agglutination with polyclonal antibodies. The isolates shown the same antigenic formula (C:NT:P1.NT) by enzyme-linked immunoabsorbent assay using whole cells and monoclonal antibodies.

The strains were found to be non β -lactamase producers by nitrocefin discs and showed identical susceptibility (MIC) to penicillin, ampicillin, ceftriaxone, rifampin, tetracycline, chloramphenicol, and ciprofloxacin when tested by agar dilution method.⁴ The isolates were susceptible to all the antibiotics assayed⁵ with the exception of penicillin (MIC, 0.125 $\mu\text{g}/\text{ml}$) and ampicillin (MIC, 0.250 $\mu\text{g}/\text{ml}$) which have been considered with decreased susceptibility. When the plasmid profile was analyzed,⁶ no plasmid was found among the strains (data not shown).

The strains recovered from the newborn child, mother, and father exhibited the same pulsed-field gel electrophoresis banding patterns with *NheI* and *SpeI* endonuclease digestion.⁷ Results of pulsed-field gel electrophoresis are shown in Figures 1 and 2. Figure 1 (lane 3, mother) has an extraband, but because this specimen was difficult to isolate and had to be subcultivate, that extraband could be caused by a punctual mutation. According to Tenover et al,⁸ one band of difference is considered closely related. Nevertheless, note that with *NheI* the pattern was identical in the three specimens (Figure 2). The identical phenotypic and genomic analysis of the strains reported suggests *N meningitidis* vertical transmission at delivery from an endocervical meningococcal mother's infection to her newborn.

Previous reports of meningococcal vertical transmission were found during the literature review. A case of premature

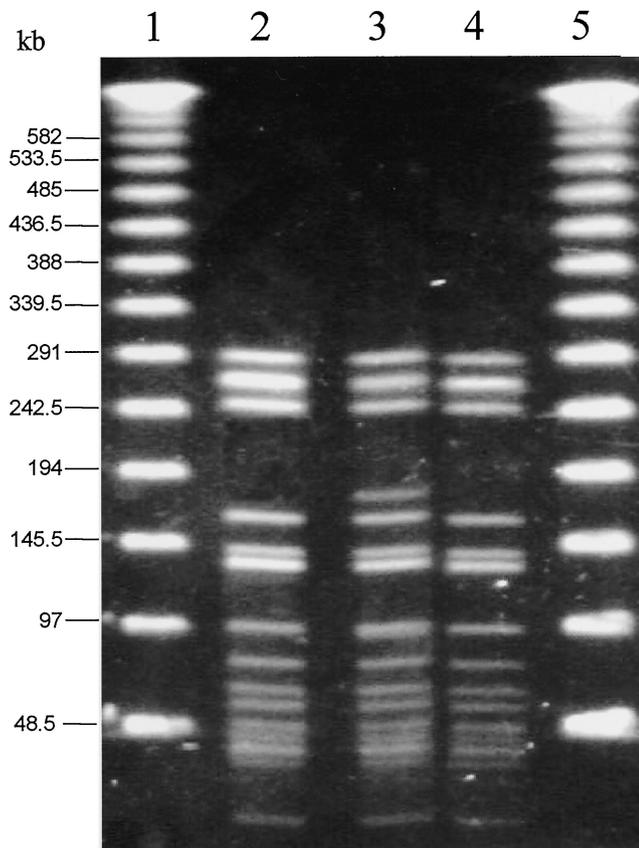


Fig. 1. Pulsed-field gel electrophoresis patterns of *N meningitidis* strains using *SpeI* digestion. Lane 1 and 5 = molecular size marker (Lambda ladder); lane 2 = Case 1 (neonate); lane 3 = Case 2 (mother); lane 4 = Case 3 (father). The extra band in lane 3 was considered nonsignificant.

delivery associated with a meningococcal endocervical infection in which early treatment avoided neonatal infection was described.⁹ Other previously reported cases described included a fatal intrauterine meningococcal infection caused by a severe maternal meningococemia¹⁰, a case associated with maternal vaginal infection and neonatal meningococemia,¹¹ and a case involving vaginal colonization that produced fatal neonatal meningococcal meningitis.¹²

We also demonstrated the cross transmission of this *N meningitidis* strain between the genital tract of the woman and her partner's oropharynx, because the relationship between the couple has been clearly established during epidemiologic investigation. The increase of orogenital practice has become an important transfer route of pathogens from the oral flora to the genitals.¹³⁻¹⁵ The identity of both strains was completely demonstrated by both phenotypic (serotyping) and genotypic (pulsed-field gel electrophoresis) methods. The meningococcal strain isolated from these patients had the same serosubtype as 30% of isolates that caused meningococcal disease in Argentina in the same year.

These *N meningitidis* isolates were submitted as *Neisseria spp* to the STD National Reference Center for identifi-

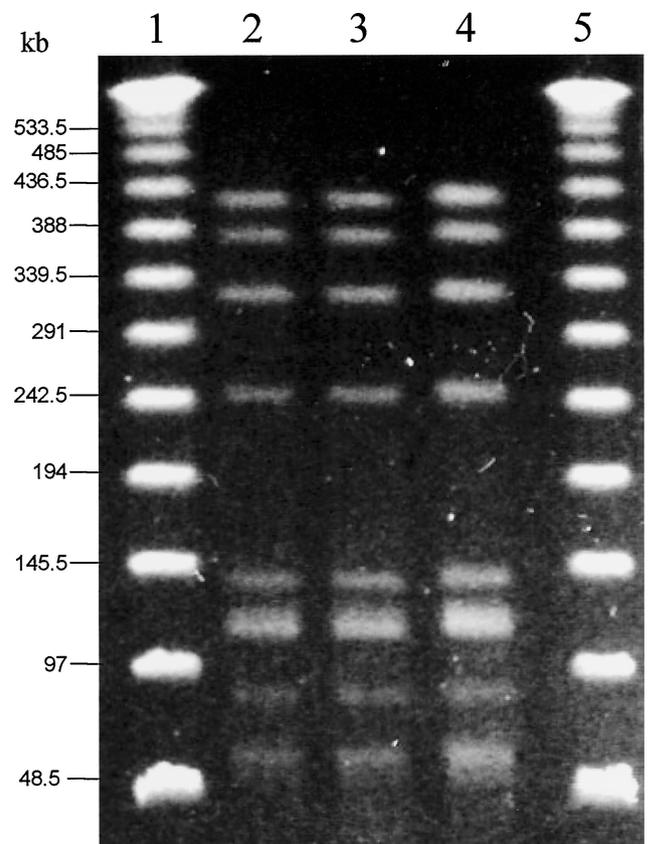


Fig. 2. Pulsed-field gel electrophoresis patterns of *N meningitidis* strains using *NheI* digestion. Lane 1 and 5 = molecular size marker (Lambda ladder); lane 2 = Case 1 (neonate); lane 3 = Case 2 (mother); lane 4 = Case 3 (father).

cation and characterization. At the hospital, gonorrhea infection was initially diagnosed and treated. The recent literature on this subject indicates that continuous attention to this misidentification is justified from a diagnostic, clinical, and epidemiologic point of view.¹⁶

Furthermore, we must be aware about diagnosis of meningococcal neonatal conjunctivitis, which may represent the portal of entry for invasive meningococcal disease.^{17,18} Because of the pathogenicity of *N meningitidis*, neonatal conjunctivitis caused by a gram-negative diplococci should be treated parenterally because the risk of developing systemic meningococcal disease is major when only topical therapy is used.

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