A Case Report of Meningococcal Disease in a Neonate
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INTRODUCTION
Meningococcal meningitis is a rare infection in the first 4 weeks of life. The causative agent is Neisseria meningitidis, an encapsulated gram-negative, aerobic, intracellular diplococcus. The spectrum of disease ranges from mild fever to fulminant septic shock, purpura fulminans, coma, and death.

In 1916, Koplik reported the first case of neonatal meningococcal meningitis (NMM) in a 3-day-old infant born after a prolonged labor. The baby survived, but later developed hydrocephalus. There have been 48 cases of NMM described since 1916. The incidence of NMM ranges from 0.8 to 1.3 per 100,000 in the US population. We present what is, to the best of our knowledge, the youngest documented case of NMM in the United States. This patient presented with fever and rash, progressed rapidly to purpura, uncompensated septic shock, multiple organ dysfunction syndrome (MODS), and died within 12 hours of presentation.

CASE PRESENTATION
A 40-week gestation male, with a birth weight of 3425 grams, was born in a referral hospital by normal spontaneous vaginal vertex delivery to a 24-year-old woman with 2 previous pregnancies resulting in 1 miscarriage and 1 live birth; this was her third pregnancy. Her prenatal screening tests (including gonorrhea, chlamydia, syphilis, rubella, group B streptococcus, and complete blood count) were unremarkable. Her labor was normal and uncomplicated, lasting 16 hours. She received 1 dose of intravenous ceftriaxone during her postpartum stay for fever. The infant’s Apgar scores were 7 and 8 at delivery, and he was discharged to home within 24 hours of birth.

The infant’s newborn genetic screen was normal. He had a normal well-child examination 4 days after discharge. His 11-month-old brother had left foot cellulitis and cold symptoms that were being treated with cephalexin at the time of this infant’s illness. Three days before onset of symptoms, the patient was taken to church for 2 hours, and several individuals held him, though none was reported as having been ill.

The patient’s mother called the nurse line, reporting a fever of 103.2°F, irritability, rash, poor feeding, moaning and crying for the past 2 hours. The mother reported that the infant had been doing well until that morning, when he would cry at feeding attempts. She described the rash as localized to the abdomen, with variably sized pink to dark pink spots. No respiratory problems were reported. She was advised by the nurse to take the infant to the nearest emergency department (ED).

The mother presented to the ED with the 12-day-old infant
within an hour of her call to the nurse line. The infant had a temperature of 101.8°F, and the rash had spread to his extremities, with petechial lesions in the groin that were purplish to black in color. He looked visibly ill, appearing ashen and sleepy with some grunting. On physical examination, his anterior fontanel was soft and open, but sunken, and his eyes appeared sunken. His lungs were clear without wheezes or rhonchi. His response to painful stimuli was decreased. He was given acetaminophen that reduced his fever to 99ºF. A complete blood count showed a white blood cell (WBC) count of 3500/uL, with 55% lymphocytes, 14% bands, 26% segmented neutrophils, and clumped platelets. Erythrocyte sedimentation rate, C-reactive protein, and electrolytes were normal. A chest radiograph revealed no acute pulmonary process and a normal cardiothymic silhouette. Blood and urine cultures were obtained, both of which eventually returned with no growth.

On admission to the pediatric floor, the infant looked visibly ill, was described as limp and hypotonic with prolonged capillary refill time, and petechiae and purpuric lesions covering his body. Ampicillin (200 mg/kg/day), gentamicin (5 mg/kg/day), and acyclovir (60 mg/kg/day) were given after lumbar puncture, within one hour of admission. He received a 30 cc normal saline bolus to treat hypotension (blood pressure 50/35 mmHg) and was transferred to the pediatric intensive care unit (PICU) due to his critical condition. An infectious disease specialist was consulted, and the antibiotic regimen was changed to ceftriaxone and linezolid. Because of respiratory failure, he was intubated 3 hours after arrival in the PICU. He continued to deteriorate, and the first cardiac arrest occurred 4 hours after PICU admission.

Laboratory results revealed disseminated intravascular coagulation (DIC) with D-dimer 5.00 µg/dl, fibrinogen 40 mg/dl, platelets 41000/ml, and INR 9.3 and severe metabolic acidosis with lactate >15 mmol/L and potassium 7.4 mmol/L. Cerebral spinal fluid (CSF) examination showed 3 WBCs/uL, 16 red blood cells/uL, total protein 76 mg/dL, and glucose 44 mg/dL. Initial gram stain of the CSF showed few neutrophils and no microorganisms, but it subsequently grew N meningitidis, serotype B. Herpes and entero viral polymerase chain reaction (PCR) tests were negative. The PCR test from a nasopharyngeal swab was negative for respiratory syncytial virus and influenza A and B. Subsequent blood and viral cultures were negative. Despite multiple boluses of saline, fresh frozen plasma, and infusions of dopamine, norepinephrine, and epinephrine, the infant died 12 hours after his mother’s phone call to the nurse advisor and 9 hours after hospital admission.

DISCUSSION

Although the incidence of meningococcal infection is relatively high in the first 2 years of life compared with other age ranges, the incidence in the first month of life is very low. From 1990 to 2002, there were 3335 deaths due to meningococcal disease reported in the United States, with the highest disease mortality rate reported in patients under 2 years of age. In the pre-antibiotic era, there were 11 cases of meningitis reported, with treatment consisting of anti-meningococcal serum given intravenously or intrathecally. With the use of antibiotics, the rate of complications has decreased to 16%. In 2003, a report of population-based surveillance data in the United States from 1990 to 1999 found a higher incidence rate of neonatal meningococcal disease than previously estimated, but a rate similar to that found in patients aged 6 to 23 months.

Since the advent of antibiotics, only 37 neonatal cases have been reported in the English language literature, with 18 of those reported in the United States; of these, 6 patients died due to either meningitis or uncompensated septic shock. One patient was a pregnant woman who was known to have meningitis before delivery. Her affected newborn developed petechial rash, uncompensated septic shock, and MODS, and the baby subsequently died.

Based on these reports, the case fatality rate is at least 50% in those who presented with severe purpura, MODS, and/or DIC. While the complication rate may be decreased with the use of antibiotics, the incidence of meningococcal infection has not changed.

The clinical spectrum and organisms that cause neonatal meningitis differ in infants from older children and adults. Neisseria meningitidis, a gram negative, encapsulated, intracellular diplococcus, is the causative organism for meningococcal meningitis. The serotypes responsible for neonatal meningitis may be B, C, Y as well as nongroupable serotypes. There are so few cases that virulence patterns are impossible to determine; however, serotype B was found to be the most common cause of meningitis in all age groups. While N meningitidis commonly causes sepsis and meningitis in children and adolescents, it rarely is associated with invasive infection in neonates. Leading causes of neonatal bacteremia, septicemia, and meningitis are group B streptococci, Escherichia coli, and Listeria monocytogenes. These pathogens commonly colonize the maternal rectovaginal area, and are thus most commonly associated with neonatal infection. Although N meningitidis may also colonize the female genital tract, it does so with much less frequency, and is therefore less often a cause for neonatal disease.

The two most common forms of meningococcal disease are meningitis and meningococcemia. The time from onset of fever until death in severe meningococcemia is often as short as 12 hours. Meningitis may initially present with fever, irritability, poor feeding, or poor activity with or without meningeal signs. Although the maculopapular rash is the distinctive sign of mening-
Meningococcal infection, it is seen in only 7% of cases.4 The rash may rapidly evolve into prominent petechiae and purpura and may progress to purpura fulminans, a necrosis of the skin and underlying tissues due to thrombosis. Meningococemia is a fulminant form of sepsis typified by severe septic shock, acidosis, DIC, and MODS. Despite rapid diagnostic testing, antibiotic treatment, and general support care in the PICU, mortality rates remain high. Patients with purpura fulminans, shock, acidosis, hyperpyrexia, DIC, and positive blood culture have a very poor prognosis, and most deaths occur within 24 to 48 hours of hospitalization.4 Meningitis can be complicated by empyema, cerebral abscess, obstructive hydrocephalus, and ventriculitis. The most common neurological sequela is deafness.

Diagnosis is made by isolation of N meningitidis from normally sterile body fluids.5 Spinal fluid cultures may be positive without pleocytosis, as described in our patient.12 Patients with CNS infection without CSF pleocytosis are at significantly higher risk of adverse outcomes such as death and limb loss than meningococcal bacteremia alone.14 Absence of CSF pleocytosis can be considered as a prognostic factor. Penicillin G or cefotaxime remain the initial drugs of choice.13 Duration of therapy depends on the patient’s clinical response, but a minimum of 10 days is indicated for a neonate. Before discharge, a brain sonogram should be done to assess for encephalomalacia, since neonatal meningitis can have profound implications for an infant’s neurodevelopment. Frequent sequelae include deafness, hydrocephalus, seizure disorders, speech disorders, and mental and motor disabilities. Because of the low incidence of this particular organism, it is difficult to specifically determine if there is more or less propensity for producing each of the common sequelae; however, neonatal meningitis in and of itself is a risk for poor outcome.11 Significant sequelae develop in up to 60% of surviving infants. In order to prognosticate, it is vital that a repeat LP be done at the end of therapy to demonstrate that the CSF is indeed sterile, and that imaging be done for the presence or absence of abscesses and/or thrombosis. The patient should be followed for long-term complications with developmental, neurologic, and hearing evaluations.

CONCLUSION
Meningococcal infection should be considered in the differential diagnosis of rash in the neonate, especially when rash is accompanied by other signs of illness such as fever, poor appetite, and abnormal appearance. Progression of the disease is more rapid than in other types of meningitis, and the first 24 to 48 hours are critical.

Rapid recognition of meningococcal infection, along with antibiotic treatment and supportive care, remain keys to successful treatment of invasive meningococcal infection. In most patients, the first sign of illness is fever that can be followed by decreased appetite, nausea, and vomiting. However, some investigations have found that the first signs of sepsis are fever, abnormal skin color, cold hands and feet, leg pain, and thirst (in patients old enough to describe this).

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REFERENCES
EDUCATIONAL OBJECTIVES
Participants in this CME should be able:

1. To recognize the various presenting symptoms and signs of meningococcal disease in the neonate.
2. To understand the appropriate evaluation and treatment of this disorder.
3. To understand the mortality rates and sequelae of this disorder.

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QUESTIONS
1. While Neisseria meningitidis is a frequent cause of sepsis and meningitis in children and adolescents, it rarely is associated with invasive infections in neonates.
   - True
   - False

2. The incidence of meningococcal infection in the first 2 years of life is relatively low but carries a higher mortality rate.
   - True
   - False

3. Neisseria meningitidis is an encapsulated gram negative, aerobic, intracellular diplococcus.
   - True
   - False

4. The clinical spectrum of meningitis due to meningococcal disease in the neonate differs from that in older children and adolescents and may present with only fever and poor feeding or decreased activity without meningeal signs.
   - True
   - False

5. Neonates without cerebral spinal fluid (CSF) pleocytosis may still have meningococcal meningitis, and this is a negative prognostic sign.
   - True
   - False

6. A maculopapular rash is a distinctive sign of meningococcal infection and is seen in the majority of cases.
   - True
   - False

7. If an infant survives meningococcal meningitis, the incidence of significant sequelae is relatively low.
   - True
   - False

8. Complications of meningococcal meningitis include empyema, cerebral abscess, and obstructive hydrocephalus.
   - True
   - False

9. The case fatality rate of neonatal meningococcal disease for those infants who present with severe purpura and multisystem organ failure is at least 50%.
   - True
   - False

10. The leading causes of neonatal bacteremia, sepsisemia, and meningitis are:
    a. Neisseria meningitidis
    b. Group B streptococci
    c. Listeria monocytogenes
    d. Escherichia coli
    e. Staphylococcus species
    - All of the above
    - A, B, C, and D
    - A, C, and E
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