Consultant360 Multidisciplinary Medical Information Network

CASE IN POINT

PEER REVIEWED

Late-Onset Spontaneous Meningitis in an Infant

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A 2-month-old girl presented to the emergency department (ED) for evaluation of fever, fussiness, poor oral intake, and nasal congestion for 1 day. The mother reported that the infant had been well until the day of presentation, when she had become difficult to arouse and had increased work of breathing. Two days prior, she had had loose, watery stools for 1 day. Her father had had abdominal pain and cramping 2 weeks ago; however, all of his symptoms had since resolved. The patient was not in day care.

History. The infant had been born via spontaneous vaginal delivery at 33 weeks of gestation secondary to severe maternal preeclampsia and suspected abruption. The 34-year-old, gravida 3, para 2 mother had tested negative for group B streptococcus, HIV, syphilis, gonorrhea, chlamydia, and hepatitis B antigen. The child's Apgar scores were 8 and 8 at 1 and 5 minutes, respectively. The patient had been admitted to the neonatal intensive care unit for poor feeding and had been discharged home 3 weeks later after an uncomplicated course.

Physical examination. On initial examination in the ED, the infant appeared drowsy and pale. Her vital signs were as follows: rectal temperature, 38.1°C; heart rate, 226 beats/min; blood pressure, 117/16 mm Hg; and oxygen saturation, 100% on room air. She appeared distressed, with grunting, and was placed on oxygen via high-flow nasal cannula. Her anterior fontanelle was open, soft, and full. The remainder of physical examination findings were normal, other than a small hemangioma on the thoracic region of her back.

Diagnostic tests. Laboratory evaluation demonstrated respiratory acidosis, leukopenia, and anemia. Electrolytes and liver enzymes were within normal limits. Blood and urine cultures were drawn. Cerebrospinal fluid (CSF) showed a white blood cell (WBC) count of 431/μL with 86% neutrophils, and a red blood cell (RBC) count of $3.4 \times 10^6/\mu$L; no protein or glucose values were obtained. CSF and blood Gram stains and cultures led to the diagnosis.

The patient's blood culture results were positive for *Enterococcus faecalis* within 1 hour via rapid diagnostic techniques using multiplex polymerase chain reaction (PCR); CSF cultures also grew the organism.

Discussion. *Enterococcus* species are Gram-positive bacteria found in the gastrointestinal tract as colonizing organisms. Common presentations of enterococcal disease in infants include bacteremia, intra-abdominal infection, and urinary tract infection, with meningitis being rarely reported.[1,2] Enterococcal meningitis accounts for approximately 0.3% to 4% of all cases of bacterial meningitis cases in infants.[3] *E faecalis* is most often reported, although meningitis due to *Enterococcus faecium* can occur in hospitalized neonates as a complication of nosocomial bacteremia where high antibiotic resistance in a hospital setting contributes to its pathogenicity.[2,4] The mortality rate for enterococcal disease ranges from 6% to 8% depending on the age of the infant at the time of disease onset.[4]

The typical presentation of enterococcal meningitis is rapid onset of fever, altered mental status, signs of meningeal irritation such as poor feeding and irritability, and seizures. Data on predisposing characteristics are sparse, although risk factors for development of enterococcal sepsis include preterm birth before 37 weeks, cesarean delivery, small for gestational age, Apgar score less than 6, endotracheal intubation, and umbilical catheterization.[4,5] Based on case reports, some factors associated with meningitis from *Enterococcus* species include CSF shunts for hydrocephalus, umbilical catheter, neurosurgical procedures, or malformations such as myelomeningocele.[6,7]

Our patient is unique in that she was a healthy infant who developed spontaneous community-acquired meningitis.

Common causes of bacterial meningitis in a young infant should be included in the differential diagnosis, since most cases are clinically indistinguishable regardless of the etiologic pathogen.

Gram-positive organisms include *Streptococcus pneumoniae* and Group B streptococcus. Gram-negative organisms such as *Escherichia coli* or *Enterobacter* species are rare outside of infancy. *Citrobacter* species can present with brain abscess in neonates. In an infant with clinical signs of bacterial meningitis but negative Gram stain results, pleomorphic bacteria such as *Mycoplasma* and *Ureaplasma* species should be considered.

Treatment for *E faecalis* meningitis depends on the susceptibility of the isolate. The Infectious Diseases Society of America guidelines recommend ampicillin plus gentamicin for ampicillin-sensitive species or vancomycin plus gentamicin for ampicillin-resistant strains.[8] Case reports in adults have reported some success with linezolid for ampicillin- and vancomycin-resistant species, since rising rates of drug resistance have posed a challenge in determining the best treatment.[2,8,9] Most cases of *E faecalis* infection in young infants have been ampicillin-sensitive, although vancomycin-resistant *E faecium* has been described primarily in the neonatal intensive care unit population.[5] Duration of antimicrobial therapy should be individualized based on the patient's clinical response but is generally 14 to 21 days. Lumbar puncture should be repeated at the end of therapy prior to discontinuing antibiotics to demonstrate clearance of the organism, or earlier if the infant is slow to improve, which may suggest the development of antimicrobial resistance.[5]

Outcome of the case. Our patient was initially treated with cefotaxime and vancomycin prior to organism speciation but was transitioned to ampicillin and gentamicin after testing confirmed the presence of ampicillin-sensitive *E faecalis*. Initial blood and CSF cultures were both positive for *E faecalis*, with repeated cultures negative after 1 and 10 days. She completed a total of 21 days of antimicrobial therapy after her first negative blood culture result.

Given the increased risk of seizures, a neurologist was consulted for further recommendations. The patient's brain and spine magnetic resonance imaging results were normal with no ventriculitis, subdural collections, or spina bifida occulta. An initial electroencephalogram was negative for seizure activity; however, she developed clinical seizures later in her hospitalization and was started on twice-daily oral levetiracetam, with no additional seizure activity thereafter. Her hearing screen results at the end of therapy were normal. The infant was discharged home in stable condition with twice-daily oral levetiracetam and plans to repeat a hearing screen 6 months postdischarge.

At 5 months of age, the infant had had no recrudescence of meningitis or other serious infections and was developmentally appropriate for her age.

The take-home message. A thorough history and physical examination is essential when evaluating an infant for bacterial meningitis. Laboratory evaluation results may show leukocytosis or leukopenia, neutrophilia, anemia, and either thrombocytosis or thrombocytopenia. CSF often demonstrates pleocytosis, elevated protein, and low glucose.[1]

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Gram stain may demonstrate gram-positive organisms in pairs or chains, which can be confused with streptococcal species, and routine culture is the gold standard for diagnosis. Newer molecular techniques such as multiplex PCR may provide more rapid organism identification.

Enterococcal meningitis should be considered in healthy infants who present with rapid onset of fever, altered mental status, ill appearance, and meningeal symptoms and who fail to improve on empiric therapy. Treatment varies by patient, should be based on susceptibility testing of the identified pathogen, and includes ampicillin plus gentamicin, vancomycin and gentamicin, or linezolid.

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