Early Onset Neonatal Sepsis and Meningitis

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Received November 15, 2013; accepted December 12, 2013; electronically published February 6, 2014.

CASE PRESENTATION

Brief History of the Present Illness
A 6-day-old female with septic shock was admitted to the hospital in the fall. Two days before admission, she had developed a macular rash on her face and extremities that was attributed to a normal newborn rash. She also had difficulty with breastfeeding, and her mother started formula supplementation upon suggestion by her pediatrician. Over the next 48 hours, the baby became lethargic and the rash became generalized. The patient returned to the pediatrician’s office, and the physician noted that she was listless, her oxygen saturation was 48% in room air, and she had a heart rate of 72 beats per minute. An arterial blood gas analysis showed a pH of 7.08 and a pCO2 of 96 with a base deficit of −1. The patient was apneic with occasional periodic breathing and seizure-like activity. She was intubated, volume-resuscitated with 8 mL/kg normal saline as well a continuous infusion of D10W at 4 mL/kg per hour. She was given ampicillin, gentamicin, and phenobarbital. She was then transferred to the Pediatric Intensive Care Unit.

Past Medical History
The patient was born at 37 weeks to a 38-year-old G1P1, via spontaneous vaginal delivery. Her birth weight was 2.58 kg (5 lbs, 11 oz). She received hepatitis B immune globulin and hepatitis B vaccine because of a maternal history of chronic hepatitis B infection. She had an uneventful nursery stay.

Key Medications
The patient received no key medications.

Maternal Epidemiological History
The patient’s mother was originally from South Korea but has resided in the United States for over 10 years. Her mother had travelled to South Korea at 34 weeks of gestation for a family emergency. While there, the mother reportedly consumed fish and multiple vegetables, including cabbage and soups made with meat stock or boiled bones as well as kimchi (a spicy mixture of radishes, cucumbers, and cabbage). Her mother also consumed multiple strawberries, cantaloupe, yogurt, cottage cheese, apples, oranges, bananas, and kiwis after her return to the United States.

Her mother developed a febrile illness at 35 weeks gestation, upon her return from South Korea, with body aches, headaches, and fever that resolved at 36 weeks of gestation.

Physical Examination
On admission, the infant’s height, weight, and head circumference were less than the 3rd percentile. She received mechanical ventilation. Initial vital signs included a blood pressure of 74/56 mm Hg, a pulse 158 beats per minute, a temperature of 36.9°C, and a respiratory rate of 52 beats per minute. A faint diffuse rash consisting of 1–2 mm blanchable papules was noted mainly over her lower extremities. Her anterior fontanelle was soft and flat. The examination otherwise revealed no focal abnormalities.

Initial Laboratory and Radiographic Studies
The infant’s white blood cell count was 17.6 × 10³ mcL (normal range, 5–21 × 10³ mcL) with 60% bands and 28% segmented neutrophils. Platelet count was 46 × 10³ mcL (normal range, 150–450 × 10³ mcL), C-reactive protein was 10.8 mg/dL (normal range, 0-1 mg/dL), and D-dimer was 1.68 (normal range, ≤0.49). Her liver enzymes were normal.

A chest radiograph and a head ultrasound were normal. An echocardiogram showed a moderate-sized patent ductus arteriosus with left-to-right flow and normal systolic function.

Clinical Course Prior to Diagnosis
The patient’s rash quickly resolved by the next hospital day. After initial resuscitation with fluid boluses, she
remained hemodynamically stable. She had no additional seizure activity.

DISCUSSION

Diagnostic Procedure(s) and Result(s)

A cerebrospinal fluid (CSF) examination was initially deferred because of the neonate’s instability. A lumbar puncture that was performed on the second hospital day after 24 hours of antibiotics was insufficient for cell count and chemistries. The Gram-stained smear revealed Gram-positive rods suspicious for the organism of concern (Figure 1 and Figure 2). However, the bacterium was not isolated in culture. Additional congenital infection studies for enterovirus, herpesvirus, parechovirus, lymphocytic choriomeningitis virus, toxoplasma, syphilis, and cytomegalovirus were negative.

A repeat lumbar puncture on the 3rd hospital day revealed 239 red blood cell/mcL and 794 white blood cells/mcL with 32% segmented neutrophils, 4% lymphocytes, and 64% monocytes, 24 mg/dL glucose (normal range, 50–80 mg/dL), and 558 mg/dL protein (normal range, 20–72 mg/dL).

A brain magnetic resonance image (MRI) showed small scattered foci of restricted diffusion in the bilateral cerebral hemispheres suggestive of small vessel ischemia, infection, or postinflammatory demyelination, without abscess (Figure 3 and Figure 4).

Figure 1. Gram-stained smear of cerebrospinal fluid. Gram-positive rods are observed in this stain.

Figure 2. Gram-stained smear of cerebrospinal fluid. Gram-positive rods are observed in this stain.

Figure 3. Magnetic resonance image brain diffusion imaging. Small scattered foci of restricted diffusion in the bilateral hemispheres.

Figure 4. Magnetic resonance image brain diffusion imaging. Small scattered foci of restricted diffusion in the bilateral hemispheres.
Diagnosis
The patient’s blood culture, obtained on admission, revealed *Listeria monocytogenes* after 48 hours. Her diagnosis was early-onset neonatal sepsis and meningitis caused by *L. monocytogenes* based on her CSF gram stain, blood culture results, and clinical presentation.

Treatment and Follow-Up
Ampicillin and cefotaxime were initiated until blood culture results were known. The cefotaxime was stopped and ampicillin and gentamicin were continued for a total of 21 days. The patient was extubated on the 6th hospital day. By 4 months of age, her head circumference was at the 99th percentile. A head ultrasound showed significant enlargement of her lateral and third ventricles. She had a ventroperitoneal shunt placed for hydrocephalus (Figure 5), which resolved by 7 months of age. She initially had delayed developmental milestones, but by 7 months of age her development was appropriate for her age. The Neurosurgery Clinic continues to follow her progress.

Brief Discussion of Differential and Major Teaching Points of Case
This case describes a near-term neonate presenting in early-onset septic shock with seizures and rash. *Listeria monocytogenes* is a Gram-positive rod that replicates intracellularly. Long recognized as a foodborne pathogen, this organism causes serious invasive disease in pregnant women, neonates, the elderly, and immunocompromised adults [1]. Neonatal listeriosis, especially in cases of early sepsis, is acquired transplacentally. In mothers, *Listeria* infection often causes a flu-like illness. In a review of 222 cases of pregnancy-associated listeriosis, 29% of pregnant women were asymptomatic and the rest presented with nonspecific signs [2]. The perinatal fatality rate is reported at 14.3%. In a study of the cases reported in the United States between 2004 and 2007, 74% of the pregnancies resulted in live births [3].

The most common clinical manifestations in the newborn include bacteremia, meningitis, and pneumonia. Nonspecific radiographic findings may be seen in *Listeria* pneumonia. The presence of a papular rash, which has been termed “granulomatosis infantisepticum,” has been described in severe neonatal infection. The rash is often transient, as in our patient, but should raise concern for possible listeriosis. Granulomatous lesions may also be seen in the liver, spleen, adrenal glands, and lungs.

Data reported to the Foodborne Disease Active Surveillance Network between 2004 and 2009 demonstrate that laboratory-confirmed listeriosis cases continue to occur across the United States, and the highest rates occur in adults over 50 years and pregnant women [4]. Dietary risk factors for listeriosis have been identified and include exposure to a wide range of ready-to-eat foods such as hot dogs and delicatessen meats, but risk factors have also been linked to melons, cantaloupes, and Mexican-style soft cheeses made from unpasteurized milk [3]. Between 1998 and 2008, there have been 24 confirmed listeriosis outbreaks related to foods, which lead to 359 illnesses, 215 hospitalizations, and 38 deaths [5]. The last large outbreak in the United States was reported in 2011 and was linked to cantaloupes. It resulted in 147 invasive cases with 143 hospitalizations, 33 deaths, and 1 miscarriage in 28 states [6]. In the last 2 years, the US Food and Drug Administration has alerted consumers to the risk of *Listeria* colonization in commercially produced kimchi, resulting in removal of such products from produce shelves [7].

Treatment of central nervous system (CNS) disease consists of ampicillin as the preferred agent with aminoglycosides in synergy for at least the 1st week of treatment. Trimethoprim-sulfamethoxazole is the treatment of choice in patients with penicillin hypersensitivity. Vancomycin failures in patients with CNS disease have been reported [8].

There are specific prevention recommendations for pregnant women regarding the avoidance of high-risk foods as well as specific handling, storage, and cooking instructions on ready-to-eat foods, uncooked meats, poultry, and vegetables [9]. Although the incidence has declined in the last 2 decades, *Listeria* remains an important cause of neonatal infection. Empiric treatment for suspected serious bacterial infection in neonates should continue to include ampicillin plus gentamicin. Neonatal listeriosis is rare, but when it does occur it can lead to serious infections and fatality.

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Figure 5. Noncontrast computed tomography head at 4 months of age. Significant lateral and third ventricular enlargement.
Acknowledgment

We thank Dr. Steven Welch (Assistant Professor of Radiology, UMKC School of Medicine, Kansas City, MO) for contributing to this study.

References