CASE 9.7
Meningitis | Level 3

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1. What subjective and objective evidence supports the diagnosis of bacterial meningitis in this patient?

SUBJECTIVE FINDINGS: The patient presented with a chief complaint of fever (39.1°C) and irritability for the past 3 days. Early this morning, she vomited and became lethargic and is now difficult to arouse. Young children with meningitis often present with nonspecific symptoms, which can lead to misdiagnosis.

OBJECTIVE FINDINGS: On physical exam, she is febrile (39.7°C in ED), lethargic, and irritable during examination, particularly during the neck exam. The lumbar puncture results that are suggestive of bacterial meningitis are hazy color, low glucose (cerebrospinal fluid [CSF] to serum ratio ≤0.4), elevated protein, and leukocytosis with a predominance of neutrophils. This patient has evidence of a traumatic spinal tap (RBC >100,000/mm^3), which can cause xanthochromia and falsely elevate the protein and WBC count in the CSF sample. For every 1,000 RBCs in the CSF caused by a traumatic tap, there is an artificial increase of one WBC and 1 mg/dL of protein. After correcting for these values in this patient, the WBC and protein counts are still elevated and suspicious for bacterial meningitis. Other laboratory features that suggest a serious bacterial infection in this patient include hyperglycemia, metabolic acidosis, an elevated peripheral WBC count with a left shift, an elevated procalcitonin, and an elevated C-reactive protein.

Key diagnostic information used to elucidate the cause of meningitis is the Gram stain and culture of the CSF. Because this child's symptoms are consistent with meningitis, a CSF sample was obtained. The CSF Gram stain was negative, and the culture is pending. It should be noted that this patient received three doses of amoxicillin prior to the lumbar puncture obtained in the emergency department. Antibiotic pretreatment, whether oral or parenteral, can affect the positivity rate of blood and CSF cultures in children with bacterial meningitis, whereas Gram stain results do not appear to be significantly affected. However, Gram stain has a fairly low sensitivity rate (67%) for detecting bacterial meningitis and cannot be used alone to exclude infection. Other tests that may be performed to determine the cause of infection include latex agglutination and polymerase chain reaction, particularly in children who have been pretreated with antibiotics before a CSF sample was obtained or whose Gram stain and culture results are negative.

2. Develop a treatment plan for this patient's meningitis.

It is important to distinguish between bacterial and viral meningitis in order to minimize morbidity and mortality while avoiding unnecessary antibiotic use. Once it is determined that bacterial meningitis is present or until it can be ruled out when a bacterial cause is suspected, empiric antibiotic therapy is required as soon as clinically possible. The empiric regimen that is selected should be based on patient age and other clinical characteristics, such as predisposing conditions, immunization status, medication allergies, and geographical antimicrobial susceptibilities. In children 1 to 23 months of age, the most common bacterial pathogens are *Streptococcus pneumoniae*, *Neisseria meningitidis*, *H. influenzae*, *Streptococcus agalactiae*, and *Escherichia coli*, where the latter two are less common after 2 months of age. Universal childhood immunizations introduced in developed countries have nearly eradicated *H. influenzae* type b (Hib) meningitis and dramatically reduced invasive disease caused by vaccine serotypes contained in the 7-valent pneumococcal conjugate vaccine (PCV-7). Non-PCV-7 serotypes are now the leading cause of bacterial meningitis in this age group; however, PCV-7 was replaced by the 13-valent pneumococcal conjugate vaccine (PCV-13) in 2010. Its use may impact the prevalence of pneumococcal meningitis, and its effect must be monitored through epidemiologic surveillance studies. In young children, meningococcal meningitis is most commonly caused by serogroup B for which no currently licensed vaccine is available in the United States but is approved for use in Europe, Australia, and Canada. Outbreaks of serogroup B meningococcal disease at the University of California, Santa Barbara, and Princeton University in 2013 and 2014 prompted the FDA to allow emergency use of the meningococcal B vaccine for at-risk students and staff.

Based on this child's age and lack of vaccinations, the most likely causative organisms are *S. pneumoniae* and *N. meningitidis*. Although she has not been vaccinated against Hib, near complete eradication of this pathogen in the United States and protection from herd immunity make this organism a less likely cause of her infection. In addition, she has a recent history of AOM, which can lead to meningitis, particularly when caused by pneumococci. Therefore, she should receive empiric antibiotic therapy that covers both pneumococci and meningococci. The Infectious Disease Society of America (IDSA) treatment guidelines recommend initiation of parenteral vancomycin plus either cefotaxime or ceftriaxone in order to provide adequate coverage for potentially drug-resistant pathogens. Ceftriaxone is contraindicated in neonates who are hyperbilirubinemic or who require calcium-containing intravenous (IV) fluids, and it should be used with caution in patients with concurrent hepatic dysfunction and significant renal disease or patients with presence of or risk factors for biliary stasis or sludging. The goals of treatment are to eradicate the infecting organism and to prevent or manage complications. This patient should be monitored for improvement (normalization of vital signs, return to baseline mental status and behavior, and normalization of laboratory values including WBC count, procalcitonin, and C-reactive protein [CRP]) and the development of complications such as seizures and hearing loss. She should also be monitored for medication adverse reactions including hypersensitivity and renal dysfunction. Repeat lumbar puncture is recommended if there is a lack of improvement or worsening after 48 hours of appropriate antibiotic therapy, in patients with pneumococcal meningitis caused by penicillin- or cephalosporin-resistant strains (particularly if dexamethasone was administered), and in neonates with meningitis caused by gram-negative bacilli.

For this patient, IV vancomycin 15 to 20 mg/kg/dose (150 mg) every 6 hours and IV ceftriaxone 50 mg/kg/dose (480 mg) every 12 hours can be initiated. If CSF culture and sensitivity results allow, antimicrobial therapy can be narrowed to treat the specifically identified pathogen. If vancomycin therapy will be continued for more than 48 hours, a target vancomycin trough of 15 to 20 mcg/mL is recommended. The duration of antibiotic therapy is dependent on the causative pathogen: a 7-day treatment course is recommended for meningococcal and *H. influ-*