BENDING THE VALUE CURVE

To Spinal Tap or Not To Spinal Tap, That Is the Question

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CASE PRESENTATION

Marcia is a 35-day-old, previously healthy girl who presents to the emergency department (ED) for "feeling warm." Marcia has been feeding well with a normal amount of wet diapers. There are no other symptoms, including no fussiness, rash, rhinorrhea, diarrhea, vomiting, cough, or respiratory distress. Marcia had been alert and happy at home, but this evening she felt warm to her mother's touch. Marcia's birth history was unremarkable; she was born at term via vaginal delivery without complication and after appropriate prenatal care. She enjoys a diet of breast milk and has been growing and developing well.

In the ED, Marcia's vital signs are as follows: rectal temperature is 101.9°F, heart rate is 140 beats per minute, respiratory rate is 45 breaths per minute, blood pressure is 76/51, and pulse oximetry is 99% on room air. She is well appearing with no significant findings on physical examination. A complete blood count, procalcitonin, blood culture, urinalysis, and catheterized urine culture are obtained and sent for analysis. Her laboratory values are notable for a peripheral white blood cell count of 10 000 cells/μL with an absolute neutrophil count of 7000 cells/μL and no band cells. Her procalcitonin is 0.25 ng/mL, and the urinalysis is negative for leukocyte esterase and nitrites with no leukocytes on microscopy. A lumbar puncture is performed, and on the third attempt, cerebrospinal fluid (CSF) is obtained with results as follows: white blood cell count is 20 cells/μL, red blood cell count is 14 000 cells/μL, protein is 71 mg/dL, and glucose is 60 mg/dL. Because of the CSF pleocytosis, Marcia is admitted to the general pediatrics floor after receipt of ampicillin and ceftriaxone at meningitic dosing. She is hospitalized on intravenous antibiotics for 36 hours. During the hospital stay, her intravenous line infiltrates after her second dose of antibiotics, which leads to the placement of a second intravenous line after multiple attempts. Marcia is ultimately discharged from the hospital with outpatient follow-up and instructions to return if she becomes ill appearing. Her urine, blood, and CSF culture results remain negative for 5 days.

WHAT IS THE VALUE OF CSF TESTING IN FEBRILE INFANTS?

Evaluation and management of the febrile infant <90 days of age is a common scenario for general pediatricians, emergency medicine physicians, and hospitalists.[1] Although the prevalence of serious bacterial infection (SBI) in febrile infants is ~10%,[2,3] most of these infections are urinary tract infections. Bacterial meningitis is rare, with an overall prevalence of ~0.6% in febrile infants,[4] and is even lower among well-appearing febrile infants >28 days of

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age.[1,5,6] This low prevalence of meningitis coupled with the risks and costs of lumbar puncture and resultant hospitalization warrants the ongoing discussion about the value of CSF testing in a well-appearing febrile infant.

WHAT ARE CURRENT PRACTICE PATTERNS?

With numerous risk stratification criteria and algorithms available for reference,[3] the percentage of febrile infants who undergo lumbar puncture varies widely across institutions and clinicians.[1,7] However, the percentage of febrile infants who undergo lumbar puncture is lower for infants evaluated in the office setting compared with the ED.[1,5,7] By using clinical judgment when deciding to perform invasive testing, primary care practitioners identify a similar proportion of infants with bacterial meningitis compared with those using a more strict adherence to established criteria. In a study of over 3000 febrile infants in an office setting, only 40% of infants underwent lumbar puncture. Among the 63 infants with bacteremia and/or bacterial meningitis in the cohort, there was only 1 infant with a delayed diagnosis of bacterial meningitis, and this infant was reported to have done well.[5] In a recent study at Kaiser Permanente, researchers found that up to one-third of febrile infants did not have any bacterial cultures obtained, including 24% of infants 7 to 28 days old, without associated poor outcomes or increased return visits. Furthermore, there was no delayed identification of bacteremia or bacterial meningitis in the cohort.[1] These outpatient investigations are in contrast to studies of management in the pediatric ED that have revealed that neonates ≤28 days of age routinely undergo lumbar puncture and hospitalization, whereas ∼50% of infants 29 to 56 days have CSF testing performed.[7–9]

ARE THERE RISKS WITH ROUTINE VERSUS SELECTIVE CSF TESTING?

One can argue that febrile infants managed in the primary care office are fundamentally different from those evaluated in the ED, particularly in regard to reliable follow-up. Although this may partially explain the differences in management, the potential downsides to strategies that use routine versus more selective lumbar puncture must also be identified. For well-appearing febrile infants who are otherwise low risk for an SBI, the risk of not performing a lumbar puncture is a delay in diagnosis of bacterial meningitis. The following risk stratification algorithms do not include CSF testing: the Rochester criteria,[10] the modified Philadelphia protocol,[11] and the Step-by-Step approach.[6] Although these algorithms differ in their age cutoffs and in the specific laboratory tests used to define low risk, infants who are older than 28 days, well appearing, and have reassuring urine and blood test results have a risk of meningitis as low as 0%; however, the small number of cases of meningitis make this risk estimate imprecise.[6,10,11] In addition, although meningitis is associated with mortality and neurologic morbidity in young infants,[12,13] the few infants who were deemed low risk through stratification strategies but were ultimately diagnosed with meningitis have had reportedly good outcomes.[3] However, there is a paucity of data on these infants given the very small number of infants in the published literature that were initially stratified as low risk and then subsequently diagnosed with meningitis; therefore, the absolute risk of an adverse outcome is unclear.[3] What is clear is that the prevalence of bacterial meningitis is very low among these otherwise low-risk infants.

The reverse side of the coin is the potential downside to routine performance of lumbar punctures. First, the results of the CSF testing can be ambiguous. As in our patient, traumatic lumbar punctures can cloud the use of risk stratification criteria. Approximately 14% to 18% of lumbar punctures attempted are either traumatic or unsuccessful.[14,15] Additionally, certain factors may increase the probability of a traumatic or unsuccessful lumbar puncture in a febrile infant, such as performance of the procedure by a less experienced provider, absence of local anesthetic use, and advancement of the spinal needle with the stylet in place.[16] Given the inherent difficulty in the interpretation of CSF results, traumatic lumbar punctures lead to more hospitalizations,[14] which in turn result in higher costs.[8] This increased resource use occurs despite a similar prevalence of bacterial meningitis in these infants compared with those with nontraumatic lumbar punctures.[14,15] In addition to unnecessary hospitalization, traumatic lumbar punctures may also lead to repeat procedures, which amplifies the risk of iatrogenic morbidity. Furthermore, a higher proportion of positive CSF culture results represents contaminants rather than true pathogens,[17] which can result in prolonged hospital stay and longer duration of intravenous antibiotics.

It is also important to note the potential "downstream" effects of lumbar puncture and hospitalization. The performance of lumbar puncture with subsequent hospitalization is highly stressful and anxiety provoking for parents.[18] Additionally, hospitalized infants may be exposed to nosocomial infections and iatrogenic complications that carry risks and associated costs. Specifically, up to 20% of febrile infants have been reported to experience a complication during the hospitalization, which range from the infiltrated intravenous line in our case to uncommon but more serious adverse events.[3,19] Lastly, hospitalized infants often receive empirical intravenous antibiotic therapy,[7] and antibiotic use in early infancy is linked to asthma and pediatric obesity, each with potential morbidity.[20–22]

RISK TOLERANCE

Weighing all of these factors, the decision to perform a lumbar puncture and hospitalize a febrile infant is often based on tolerance of risk. Given the low prevalence of bacterial meningitis in low-risk febrile infants, particularly by using newer algorithms such as the Step-by-Step approach,[6] many well-appearing febrile infants >28 days of age do not require a lumbar puncture and hospitalization. The decision on whether to perform a lumbar puncture should take into account not just the physician's tolerance for risk and confidence in the examination of young infants but also the risk tolerance of the

parents through a shared decision-making process.[23] The decision will also depend on the ability to ensure close follow-up and, therefore, engagement of the primary care physician may also be of benefit. Implementation of evidence-based protocols for management of febrile infants, such as the care process model implemented in the Intermountain Healthcare system, can also improve resource use and diagnosis of SBI while simultaneously lowering costs.[24] Further studies are still needed to assess outcomes for infants who experience a delayed diagnosis of SBI, particularly meningitis, as well as to evaluate the outpatient management without lumbar puncture for low-risk neonates 7 to 28 days of age.[3] Ultimately, outpatient observation without lumbar puncture for low-risk febrile infants is a cost-effective, value-based management strategy for this patient population.

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