

The Cost of a Culture and Doctoring at a Distance

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A term infant at a community hospital was noted to be apneic with thick meconium at birth. She required intubation for respiratory distress and had an initial axillary temperature of 38.27°C (100.9°F). Blood culture was drawn, umbilical catheter was placed, and ampicillin and gentamicin were started for presumed sepsis. The C-reactive protein (CRP) level at birth was 12.3 mg/L and rose to 30.8 mg/L on day of life (DOL) 2. Cerebrospinal fluid (CSF) was drawn, but the fluid had too many red blood cells for a reliable white blood cell count. The CSF was sent for culture, which remained negative. The NICU team trended CRP levels, and on DOL 3, the CRP fell to 20 mg/L. The neonate continued to do well clinically and on DOL 3 was transitioned to room air. On DOL 7, she was ready for discharge, but the care team decided to obtain another CRP before discontinuation of antibiotics. It was then 88 mg/L. Because of the elevated CRP, peripheral blood and CSF cultures were again obtained while the infant remained on antibiotics administered via umbilical catheter. The blood culture grew *Klebsiella pneumoniae* that was sensitive to gentamicin. The CSF culture was negative. The NICU team wanted to treat the infection appropriately and called the infectious diseases service at the regional referral hospital for advice on antibiotic choice. The infectious diseases team suggested that either ciprofloxacin or a carbapenem would be appropriate given the resistance pattern. Still, the infectious diseases team thought that bacteremia in an infant who was otherwise clinically ready for discharge was surprising. They suggested consideration of an endovascular source and an ultrasound of the umbilical vein given the concurrent presence of an umbilical line and the growth of a gentamicin-susceptible organism during gentamicin therapy. The radiology department at the community hospital was reportedly unable to obtain neonatal endovascular ultrasound, and therefore the NICU team requested that the infant be transferred to the regional children's hospital. The infant was switched to intravenous ciprofloxacin, and the umbilical line was removed before transfer.

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On arrival, the infant was well appearing. The ultrasound did not reveal an endovascular thrombosis. Additional blood cultures drawn on DOL 10 and 11 remained negative. On the basis of direct evaluation of the patient and her medical records, in addition to the conversations with the NICU team regarding her well appearance at the time of CRP check, neither the primary nor infectious diseases services were sufficiently convinced of bacteremia to commit the infant to a long course of antibiotics and hospitalization. Specifically, the infant's clinical course was incongruent with the development of Gram-negative rod bacteremia, the culture was positive only once, and the organism was cultured on the seventh day of antibiotics to which it was susceptible. The decision was made to discontinue antibiotics and monitor the infant. The infant remained well appearing for several days, and a blood culture drawn 36 hours after discontinuation of antibiotics was sterile.

The question of value and effectiveness of health care delivery is highlighted in several aspects of the patient's clinical management: the decision to trend CRP, the decision to initiate a second septic workup due to the elevated CRP, and, most important, the decision to discontinue treatment. The case also highlights telemedicine and advice by telephone, which is limited by an inability to evaluate the patient and thoroughly review medical records.

In neonates, the identification of sepsis remains difficult given that clinical signs and symptoms may be subtle and nonspecific. Many NICUs routinely obtain CRP levels as a screening tool for sepsis.¹ Most data regarding CRP measurements and the probability of neonatal bacteremia focus on diagnosis at the onset of symptoms. CRP is generally considered to be specific, but not sensitive, in the initial detection of neonatal sepsis.²⁻⁵ Several studies have shown that serial determinations of CRP levels increase the sensitivity of detecting the onset of sepsis, and serial normal CRP levels have been shown to have high negative predictive value.^{1,2,6-8} Although this infant's fever

and apnea guided her initial cultures and therapy, the NICU team drew cultures on DOL 7 only because of an elevated CRP. This response to an elevated CRP is reasonable, but the decision to obtain a repeat CRP at the end of therapy in an otherwise clinically well infant warrants further consideration. There is some evidence that a normal CRP at the end of treatment may be indicative of effective treatment.¹⁹ Ehl et al⁹ evaluated 176 newborns with suspected sepsis and found that CRP values often peaked, then decreased after 16 hours, and a value that remained negative >24 hours after initiation of antibiotics had a negative predictive value of 99%, provided that initial culture results were negative.⁹ Serial negative CRP levels have been used as evidence to consider discontinuing treatment⁹; however, there are no data to show that elevation in CRP at the end of treatment of a non-culture-proven sepsis justifies extension of antibiotic therapy. As a result, if therapy is otherwise complete and the infant is clinically well, it is unclear what value a final CRP adds to the care of the child.

Management was further complicated in this case when the blood culture obtained in response to the CRP grew a multidrug-resistant organism. When faced with a positive blood culture, regardless of clinical status, clinicians must decide whether the result is clinically significant. Rates of contamination generally range from as little as 0.6% to 6%.¹⁰ *K pneumoniae*, the organism isolated in this case, is typically not considered a contaminant.¹¹ It is reasonable for anyone to treat *Klebsiella* spp isolated from the blood, and it is more often unreasonable not to treat it. Arguing for the validity of the culture was the presence of an umbilical line. However, in the setting of a clinically well-appearing infant who was ready for discharge, the growth of a gentamicin-susceptible organism on the seventh day of gentamicin treatment was discordant. The decision to discontinue treatment and monitor the infant was a difficult one, but it was weighed against risks of continued treatment. Specifically, central catheter placement has known risks of central line-associated infections and thrombotic

complications, and prolonged antibiotics are associated with antimicrobial resistance, candidal superinfections, and growing concerns of effects on the gut microbiome and subsequent health outcomes.¹²⁻¹⁵ There is much uncertainty regarding the value of care provided in this case due to potentially incomplete data from the referring hospital and limited evidence in the literature to support the decisions to trend CRP values and repeat the blood culture. However, the decision to discontinue antibiotics and spare the infant prolonged hospitalization and antibiotic therapy was certainly high value care.

Finally, this case highlights the role of telemedicine in health care delivery. Telemedicine is becoming common in the medical community and is thought to have potential to contribute to cost-effective delivery. However, the evidence demonstrating the efficacy of telemedicine is still limited.¹⁶⁻¹⁸ In 1 study, there was a 20% reduction in subspecialty referrals in a practice that used an electronic consult system.¹⁹ Another study showed that videoconferencing in nursing homes reduced unnecessary hospital readmissions and led to significant savings by the nursing homes.²⁰ However, our case demonstrates limitations of subspecialty communication by phone, where the subspecialty services lack the ability to examine the patient and medical records. They must rely on the findings and information provided and therefore cannot give the caliber of advice that would be possible in person. Many may therefore be more comfortable with the provision of general recommendations when providing advice over the phone. In this case, the infectious diseases team provided an answer to the question of antibiotic coverage and expressed surprise about the culture result but felt that more specific advice regarding reconsideration of antibiotic use was not appropriate without examining the patient and reviewing the full records. This limitation was highlighted in a study that compared care decisions when the same set of physicians was provided information via electronic visits or office visits. For some conditions, physicians providing care via electronic

visits were more likely to prescribe antibiotics.²¹ The lack of in-person contact may lead to additional tests or procedures that would otherwise have not been ordered if the provider was able to fully examine the patient and medical records. This may not always be beneficial to the patient and can increase health care costs. Therefore, although telemedicine has potential to provide high-quality care and increase value, it needs to be used in the right way to result in cost-effective outcomes.

As with many encounters, both high- and low-value care was provided to this patient. This well-appearing neonate underwent a potentially unnecessary second septic workup, but the cascade of testing and treatment was arguably ended earlier than it might have been. As Schroeder et al²² discusses, “Doing more feels safer, because it alleviates uncertainty, particularly when the stakes are high.” This case illustrates that “more” care is not always higher-value care, especially when it is difficult to decide when it is actually safe to do less.

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