BREASTFEEDING MEDICINE
Volume 10, Number 10, 2015

DOI: 10.1089/bfm.2015.0146

Mother's Milk as a Source of *Enterobacter cloacae* Sepsis in a Preterm Infant

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Dear Editor:

We would like to report a case of late-onset sepsis with *Enterobacter cloacae* in a preterm infant fed expressed mother's milk, which grew the same organism on repeated cultures. The male infant was born at 26 weeks of gestation and was tolerating continuous feeding with expressed mother's milk. The milk, stored at −4°F, was prepared by the patient's nurse in a dedicated nutrition room by adding liquid human milk fortifier to make 24 kcal/ounce. Following unit protocol, the milk was discarded and replaced every 4 hours. On Day of Life 40, the infant developed sepsis with respiratory failure and shock. Cultures drawn from the peripherally inserted central catheter, a peripheral vein, and urine grew *E. cloacae*. The infant was treated with antibiotics and rapidly improved.

Because of the sudden onset of severe sepsis in this previously stable infant, a sample of the mother's milk was sent for culture (a drop of milk streaked in four quadrants on blood, chocolate, and MacConkey agars). It was positive for 2+ *E. cloacae* and 1+ *Staphylococcus aureus.* The antibiotic susceptibility pattern of the *E. cloacae* found in the milk matched that from the infant. The mother was re-educated on hygienic collection techniques, and over the next 7 days, two subsequent fresh milk cultures were collected using new sterile pump kits. These were positive for *E. cloacae*, *S. aureus*, and *Staphylococcus epidermidis*. The mother had no breast lesions or symptoms of mastitis. She was treated with ciprofloxacin 500 mg by mouth twice daily for 7 days, and breastmilk expressed during this period was discarded. After treatment, a repeat fresh milk culture was positive only for *S. epidermidis*. The infant was subsequently fed his mother's milk, had an unremarkable hospital course, and was discharged home.

The challenge in this case is to properly evaluate and manage pathogens in human milk. Maternal milk is generally protective in nature, and the presence of bacteria is not unusual. Schanler et al.[1] reported nearly all milk samples have bacterial growth, but even when Gram-negative organisms sporadically appear in the milk, the associated risk of infection is low. Nevertheless, there have been reports describing infections acquired from human milk.[2] Identifying the bacterial content in human milk that might pose risk to a premature infant is problematic. Routine screening of an infant's own mother's milk for bacteria is not recommended[3]; it does not seem to prevent neonatal infections due to a poor correlation between bacteria found in maternal milk and pathogens cultured from corresponding neonates.[1] The World Health Organization recommends breastmilk cultures to aid in the diagnosis and management of mastitis.[4] Members of the Human Milk Banking Association of North America culture pasteurized milk and discard batches with bacterial growth,[5] and some have also recommended prepasteurization bacterial screening.[6] Interpretation of such cultures, however, is difficult as the Clinical and Laboratory Standards Institute offers no standards for human milk culture, and there is no established definition for unsafe human milk.[7]

Several factors present in this case may have shifted the risk–benefit toward infection, including decreased gastric acid secretion, the presence of *S. aureus*, and frozen storage. Even without acid suppression, preterm infants spend much of the time with gastric pH >4,[8] which could increase the risk of acquiring an infection from ingested bacteria. Furthermore, continuous feeding may have prevented the re-acidification that normally occurs after bolus feeding.[8] *S. aureus* is a known human pathogen whose virulence factor, alpha-toxin, has been shown to increase permeability of human intestinal epithelium.[9] The presence of *S. aureus* alpha-toxin may have reduced cell–cell adhesion, allowing for translocation of *E. cloacae* from the intestinal lumen into the bloodstream. Finally, frozen storage has been shown to reduce the antibacterial properties of human milk. When compared with fresh milk, concentrations of lysozyme, secretory immunoglobulin A, and lactoperoxidase are lower, muramidase and peroxidase activities are lower, and bacterial proliferation is greater in frozen milk.[10]

Although each of these factors is common in the neonatal intensive care unit, it stands to reason that the combination of these factors might have contributed to this infant's susceptibility to infection when persistently exposed to *E. cloacae* in his mother's milk. Although this case is remarkable because the same pathogen was repeatedly identified in the mother's fresh milk over the course of 7 days despite using multiple sterile collection kits, we still cannot definitively establish that the mother's milk was a direct cause of the infant's sepsis. Both mother and infant might have acquired the pathogen from the shared neonatal intensive care unit environment. However, it is feasible that repeated exposure to *E. cloacae* in the mother's milk contributed to a microbiome

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so abundant in *E. cloacae* that the developing immune system was overwhelmed when translocation occurred.

We are not aware of any case precedents or studies of whether or not to treat mothers whose breastmilk cultures grow pathogenic bacteria with antibiotics. In our case, we treated the mother because we wanted to support the mother's desire to breastfeed her infant, but we were concerned that re-exposure to the *E. cloacae*–containing milk could lead to recurrent sepsis. Maternal colonization appeared to be eliminated after treatment, and there were no further episodes of bacterial sepsis during the hospitalization. Although bacteria found in the mother's milk is generally beneficial to neonates, this case illustrates that mother's milk can be a reservoir for pathogenic bacteria, and unpasteurized human milk may be a potential source for infection in extremely premature neonates. Additional research is needed to determine what maternal, environmental, and neonatal factors increase the risk of developing infection.

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