

## Post-Viral Non-ESBL *Klebsiella Oxytoca* Bacteremia in an Infant

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### INTRODUCTION

*K. Oxytoca* is a gram-negative rod that usually infects newborns and children by nosocomial spread in neonatal intensive care units (NICU) or via community acquisition.<sup>1</sup> After colonization of mucosal surfaces, primarily the gastrointestinal tract, and given the right conditions, this organism can lead to severe infections of multiple sites, bacteremia, septic shock and death.<sup>2</sup> Underlying disease, immunosuppression, prematurity, and the use of prophylactic antibiotics in the context of respiratory distress in the NICU all contribute to colonization/infection with this organism in this setting.<sup>3</sup> We present below a case of a six-week old male diagnosed with an acute co-infection with respiratory syncytial virus (RSV) and corona virus infection who developed non-ESBL *Klebsiella Oxytoca* bacteremia concomitantly within the same illness. We then explore maternal/child, host, and organism specific factors that may have contributed to this sequence of events for this patient.

### CASE PRESENTATION

Our patient was a male born full-term via normal spontaneous vaginal delivery to a 36 year-old group B Streptococcus negative G2P1001 mother who had an unremarkable pregnancy, no infectious risk factors, and smoked two cigarettes a day while pregnant. Respiratory distress was noted thirty minutes after birth and the patient was transferred to the NICU where a right-sided pneumothorax was detected on chest x-ray. Continuous positive airway pressure (CPAP) ventilatory support followed by high flow nasal cannula (HFNC) were implemented successfully and re-inflation of the right lung was documented-the patient was discharged home on day five of life after weaning from respiratory support. Of note, the patient was treated with intravenous ampicillin and gentamycin for the first forty-eight hours of life. Additionally, the patient was exclusively formula fed in the hospital and after wards as well.

At six weeks of age he presented to the emergency room with a two-day history of cough and increased work of breathing, post-tussive vomiting and decreased oral intake. He was afebrile, nontoxic in appearance, with a respiratory rate between 36-40 breaths per minute, copious nasal secretions, intercostal retractions and only transmitted upper airway sounds audible on pulmonary auscultation. His oxygen saturation on room air was 96-98% and a complete blood count was remarkable for an elevated white blood cell count of 15.6 thousand cells per cubic millimeter (nl 4.8-10.8 th/mm<sup>3</sup>) with 29 percent neutrophils (nl 42.2-75.2%), 61 percent lymphocytes (nl 20.5-51.1%), and seven percent monocytes (nl 1.7-9.3%), and a platelet count of 671 thousand per cubic millimeter (nl 130-400 th/mm<sup>3</sup>). A chest radiograph was significant for diffuse bilateral hazy opacities. A respiratory virus panel (RVP) was obtained. After receiving a 20 cubic centimeter per kilogram bolus of normal saline and three normal saline nebulizer treatments, the patient's respiratory rate rose to a

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sustained 60-70 respirations per minute, and a prolonged expiratory phase with wheezing was now noted on respiratory exam—he was then admitted to the Pediatric Intensive Care Unit (PICU) with a presumptive diagnosis of bronchiolitis. The patient was started on HFNC, intravenous fluids, albuterol nebulizer treatments as needed, and nasogastric tube. Oral feedings were initiated. The patient clinically improved over the next three days- respiratory support was weaned off and full oral findings were resumed. The respiratory virus panel was positive for both RSV and HKU1 coronavirus. During his PICU stay till now, the only new abnormality noted was spiking fever once a day ranging from 101.2 to 102.6 degrees Fahrenheit without any other associated findings.

On day four of admission, as downgrading of the patient's status to the floor was being contemplated, the patient became irritable, refused oral intake, and became persistently febrile at 104 degrees Fahrenheit. A full sepsis workup was performed—his white blood cell count was 5.14 thousand per cubic millimeter with immature granulocytic predominance at 9.3% (nl 0.1-0.3%), with marked thrombocytopenia of 30 thousand per cubic millimeter, and anemia with a hemoglobin of 8.8 grams per deciliter (down from 10.3 grams per deciliter on admission). Cerebrospinal fluid (CSF) analysis showed 60 red blood cells per cubic milliliter, 30 white blood cells per cubic milliliter (60% neutrophils, 30% lymphocytes, 10% macrophages), clear and colorless fluid, with a glucose of 54 milligrams per deciliter (nl 45-75mg/dl) and an elevated protein at 90.1 milligrams per deciliter (nl 15-45mg/dl). His urinalysis, liver function tests, peripheral smear, and head ultrasound were all normal. Transfer to the floor was cancelled, and the patient was empirically started on intravenous ampicillin, cefotaxime, and acyclovir.

Upon being informed that the blood culture was growing gram negative rods the next day, the antibiotic regimen was changed to piperacillin-tazobactam, and gentamycin.

By day six, the patient's respiratory status had improved markedly as did his oral intake, and one 15 cubic centimeter per kilogram packed red blood cell transfusion was given for a hemoglobin nadir of 6.7 grams per deciliter associated with persistent tachycardia. The urine culture, CSF culture and herpes virus polymerase chain reaction were negative at 48 hours—the acyclovir was discontinued.

On day seven, the organism in the blood was identified as *Klebsiella Oxytoca*, resistant to ampicillin only. The antibiotics were switched to ceftriaxone and were continued for fourteen more days via peripherally inserted central catheter— the patient was discharged home in good health and no sequelae of this infection have occurred to date.

## DISCUSSION

Given the resistance pattern of the strain of *K. Oxytoca* (not K55 or K72) that affected our patient, and that no other cases of infection with this organism occurred in this NICU, the likelihood of a nosocomial mechanism of acquisition is very low. Vertical transmission is a possible mechanism of transfer of this organism, although babies born vaginally generally acquire a bowel flora that is much less replete with gram-negative organisms. It is possible that exclusive formula feeding may have mitigated the protective effects of vaginal delivery and aided in producing a gram-negative predominant or gram-negative friendly microbiome that allowed for *K. Oxytoca* to exist.<sup>4</sup> This is in addition to baseline higher permeability of the gastrointestinal and respiratory epithelium and the relative paucity of pathogen killing proteases and peptides in infants in general.<sup>4</sup> *K. Oxytoca* also preferentially expresses a fimbrial adhesin MrkD which binds to type V collagen, thus enhancing attachment to the basement membrane of bronchial epithelial cells.<sup>5</sup>

In light of the above, the portal to the bloodstream for this organism was most probably the respiratory tract, colonization of which was achieved via the mechanisms cited above plus possible microaspiration. Additionally, the desquamation known to occur within the respiratory tree after a viral insult, especially RSV, conforms well with the timing of the fevers and subsequent detection of the bacteremia in our patient. Finally, our patient had

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no other manifestations post-discharge of findings consistent with a Toll-like receptor 4 defect, an immune defect known to confer susceptibility to *K. Oxytoca* infections in particular.<sup>6</sup>

In summary, we hypothesize that brief administration of prophylactic antibiotics during a short NICU stay and formula feeding allowed colonization of our patient with *K. Oxytoca* via vertical transmission. The combination of prior colonization, microaspiration, and a desquamating respiratory tract infection led to portals of entry of the organism resulting in subsequent bacteremia. It may have been possible to avoid this and other similar cases of neonatal bacteremia by encouraging more judicious use of antibiotics in the NICU setting and/or promoting and facilitating breast feeding of all infants.

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