Case Report

Burkholderia cepacia Sepsis in a Previously Healthy Full-Term Infant

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1.Introduction

Burkholderia cepacia (Bcc) is an aerobic, catalase-producing, Gram-negative bacillus not considered part of normal human flora but typically of low virulence. It can severely affect immunocompromised children such as those with malignancy, congenital heart disease, or a history of prematurity. Pediatric cases describe severe bacteremia in children with cystic fibrosis (CF) and chronic granulomatous disease (CGD) [1].

Immunocompetent individuals are not commonly affected; however, nosocomial infections have been observed due to contaminated medications, fluids, antiseptics, and medical equipment. Examples include contaminated sodium chloride, distilled water, 5% dextrose, and even ultrasound gel. Nebulization, flushing orogastric tubes, and humidification of oxygen delivery devices are the vehicles of transmission [2, 3].

Two of the earliest known case reports involving Bcc sepsis in neonates were in preterm infants. One was an ex-24-weeker with extremely low birth weight who developed thrombocytopenia to 26,000 at 24 days of life and despite ceftazidime + imipenem, died from an ileocutaneous fistula and necrotizing enterocolitis. The other patient was an ex-22-weeker who grew Candida albicans and was treated with amphotericin and flucytosine, and by day 62 of life, the patient had thrombocytopenia. A positive culture for Bcc was resulted, and ceftazidime appropriately cleared the infection [2]. Patra el al. described a cohort of 12 neonates in India whose gestation ranged from 29 to 41 weeks and primarily had lethargy, tachypnea, or poor feeding. Bcc was
isolated from blood cultures, and neonates were treated with piperacillin-tazobactam, ciprofloxacin, and cotrimoxazole either singly or in combination to result in an eventual sterile repeat culture [4]. Chandrasekaran et al. identified a group of 59 average full-term neonates in India where most (59%) had Bcc early-onset sepsis with predominantly respiratory, hemodynamic instability, and abdominal distension. Over 95% either had a previous peripheral IV line used or IV antibiotics administered, and only 29% had maternal risk factors. Piperacillin-tazobactam was the empirical first-line antibiotic [5].

2. Case Presentation

We describe a case of Bcc sepsis in a previously well 5-week-old ex-full-term infant. He was admitted to an outlying hospital for fever of one day duration. After two days of antibiotic treatment with minimal improvement, he was transferred to our hospital for further management.

He was delivered by cesarean section due to failure to progress at 39 weeks of gestation. The mother was a 22-year-old Hispanic woman gravida 1 para 1 with an unremarkable prenatal history including a negative group-B Streptococcus screen. The infant had respiratory distress after birth requiring continuous positive-pressure support and oxygen for a short duration. Sepsis evaluation at that time was negative, and he was discharged home after a two-day hospital stay. He did well at home with no exposures to daycare, animals, or travel outside the country. No family history of chronic disorders, recurrent infections, or known immunodeficiency was found.

At the outlying hospital, the review of systems was significant for decreased appetite. Rhinorrhea and sneezing preceded 1.5 weeks prior to the ER visit. Vital signs recorded a temperature of 102.7°F, respiratory rate of 45 breaths/min, and pulse of 190 beats/min. Physical exam revealed a well-appearing infant with normal cardiopulmonary and abdominal exams but with a faint erythematous maculopapular rash throughout the chest and legs. There was no stomatitis, perianal abscesses, or other signs of skin infections. Laboratory evaluations showed a white blood cell count of 10,000 μL and a band count (16.5%). Chest radiograph showed “focal airspace opacity projecting over the right midlung zone, probably pneumonia” (Figure 1(a)). Ampicillin and gentamicin were started after full sepsis workup was performed. Blood and urine cultures were negative after 48 hours. Respiratory viral panel including influenza and respiratory syncytial viruses were also negative. Cerebrospinal fluid (CSF) was described as cloudy and negative after 48 hours. Respiratory viral panel including coinfection. No viral cytopathic changes were visualized. Hepatomegaly and splenomegaly were identified with areas of acute and granulomatous necrotizing inflammation. Because of the rapid downhill course, no immunological tests were done before death such as immunoglobulin or T cell subsets. No neutrophil oxidative burst or dihydrodiamnine assays were performed. Further genetic testing was advised to the family. Even though these tests were not performed, CGD remained as the most probable cause of this patient’s multiorgan granulomatous disorder. There were no other associated pathogens identified or other probable disorders based on history and autopsy findings to explain the granulomatous findings. What is known is that defects in the oxidative burst can lead to severe infections particularly Staphylococcus aureus, Aspergillus species, and Bcc [6].

3. Discussion

Bcc is a rare cause of sepsis in newborns, and its transmission involves human contact with heavily contaminated medical devices and disinfectants. It most commonly presents with respiratory tract, urinary tract, and blood stream infections [4]. Of the few reports describing Bcc sepsis in neonates, the prenatal course is typically significant for certain hospital exposures or family history of an immunodeficiency. There are risk factors like prematurity, surgeries, or instrumentation [3]. Contributing maternal risk factors such as poor intrapartum or postnatal infection control practices are also
noted [7]. Our patient did not have any risk factors such as
prolonged mechanical ventilation, chronic nebulized
treatments, multiple bronchoscopies, or being on previous
antibiotics [3]. His postnatal course consisted of needing
some continuous positive airway pressure momentarily
without having to go to the neonatal intensive care unit.

The chief initial presentation of fevers and congestion
were unusual and not reported as most present with res-
piratory distress, lethargy, and/or emesis [4]. Although less
likely, a nosocomial infection could not be completely ex-
cluded. After discharge home, the patient had one visit to the
hospital two weeks prior to presenting with fevers for an
abdominal X-ray which only showed mildly distended loops
of bowel with stool throughout. Aside from this exposure,
the patient may have acquired the infection via the noso-
comial route from being transported from one hospital to
another. Even though Bcc has an incubation period of 1–21
days [8], this is less likely considering the patient already
presented to the first ER with a right lower lobe opacity.

Even without respiratory distress or hypoxia, pneumonia
was the leading diagnosis as the opacity appeared to improve
with antibiotics. Neuroblastoma was suspected; however,
homovanillic and vanillylmandelic acid urine studies were
normal. Congenital cardiac defects were unlikely based on a
normal echocardiogram. Absent pulmonary cystic struc-
tures or active respiratory distress made congenital pul-
monary airway malformation or bronchopulmonary
sequestration unlikely. Immunodeficiencies like CF or a
hemoglobinopathy were unlikely given the normal infant
screen. CGD was never suspected since patients typically
have recurrent, life-threatening bacterial and fungal infec-
tions in the first year of life [9], and the median age of
diagnosis is 2-3 years [10]. Additionally, there were no
findings on physical exam. Also, the patient did not possess
skin abscesses, have a history of otitis media, or was con-
sidered failure to thrive. Family also reported a healthy
background without immunodeficiency.

Microbial diagnosis for Bcc is made following blood
culture collection using Bcc-selective agar, Pseudomonas
capsae agar, or oxidation-fermentation polymyxin bac-
tracin lactose agar. Bcc-selective agar is superior to others as
it enhances the growth of Bcc while suppressing the growth
of other organisms [11]. Overall, Bcc is difficult to culture,
can initially be negative, and, once collected, can prove
challenging to properly identify [2, 9, 12]. This was seen with
our patient as the first blood culture taken at the outside
hospital on admission was negative despite the patient’s
symptoms of being febrile. Inappropriate microbial expertise
in preparing the blood sample in the specific agars may have
resulted in a false negative the first time around.

For the second set of blood cultures taken from the
intensive care unit, the susceptibilities for Bcc resulted
postmortem for levofloxacin, cefazidine, and cefepime to
name a few (Table 1). Unfortunately, the patient had been on
ceftriaxone, metronidazole, and vancomycin, and so, the
antibiotics could not be further tailored to improve coverage.
Sputum cultures resulted positive +1 for Bcc, Steno-
trophomonas maltophilia, and Enterobacter cloacae complex,
respectively, which were listed in Table 2.

Even though our patient did not have formal immuno-
logic testing done due to rapid patient decline, there are many
findings to strongly suggest that the patient had CGD which
go beyond pure speculation. To name a few examples, there
were the autopsy findings of a widespread granulomatous
process with Bcc and coinfection with fungal elements in
addition to positive blood and sputum cultures. There was a
consistent presentation with what is described in the literature
of a patient with Bcc who had CGD with a primary pre-
sentation of pneumonia (being the most common site of
infection) followed by lymphadenitis, subcutaneous abscess,
liver abscess, and sepsis [10]. The patient’s end of his life
mirrored previous case reports of newly diagnosed CGD in
patients with Bcc sepsis. Lacy et al. [12] described findings
including hepatomegaly, splenomegaly, ascites, disseminated
intravascular coagulation, and granulomas within the lungs,
liver, and spleen. The autopsy report not only confirmed the
granulomas however made mention of hepatosplenomegaly,
scattered microthrombi in multiple organs, and a collection of
ascitic fluid upon starting the exam.

With these findings and concerns for their future health
and offspring, the parents were advised to seek genetic
testing for oxidative burst activity. This would assist with
future family planning and determining if other family
members had to be evaluated. Testing is critical because

**Figure 1:** (a) Chest radiograph showing focal airspace opacity projecting over the right midlung zone. (b) Lateral CXR of "well-defined right lower lobe opacity interpreted as pneumonia versus mass."
mutations can be either X-linked or autosomal recessive; individuals may unknowingly have a decrease in the percentage of positive stimulated granulocytes compared to healthy controls [10, 12].

In the presence of an infant with a previously healthy background not following the typical course for pneumonia, it is important to have a broad differential diagnosis including immunoglobulin or complement deficiencies. If the patient has findings of pneumonia, sepsis, skin abscess, lymphadenitis, or hepatosplenomegaly, then Bcc should be considered and confirmed with appropriate testing. Multiple blood cultures may need to be drawn as this organism is difficult to isolate. If initial broad-spectrum antibiotics like ceftriaxone are not effective, more empiric drugs like ceftazidime or meropenem may be beneficial to initiate until further microbe identification. It may not be a priority to conduct a primary immunodeficiency workup in the midst of a fulminant disease course; however, it must be kept in mind early on as it can help with understanding the pathophysiology of the patient’s clinical trajectory.

| Table 1: Blood culture susceptibilities. |
|----------------------------------------|
| Microreports | Susceptibilities | Specimen | Action list |
|---------------|-----------------|-----------|-------------|
| 1             | *Burkholderia cepacia complex* | MIC dilutn | MIC interp |
| 2             | Amikacin        | ≥64       | R           |
| 4             | Cefepime        | 2         | S           |
| 5             | Ceftazidime     | 2         | S           |
| 6             | Gentamicin      | ≥16       | R           |
| 7             | Levofloxacin    | 1         | S           |
| 8             | Meropenem       | ≥16       | R           |
| 9             | Piperacillin/tazobactam | ≥128     | R           |
| 10            | Tetracycline    | 4         | S           |
| 11            | Tobramycin      | ≥16       | R           |
| 12            | Trimethoprim/sulfa | ≤20      | S           |

| Table 2: Sputum culture susceptibilities. |
|------------------------------------------|
| Enterobacter cloacae complex             |
| Cefepime                                 |
| ≥64                                      |
| ≤0.25                                    |
| ≤1                                       |
| ≤0.12                                    |
| 1                                        |
| ≥128                                     |
| 4                                        |
| ≤20                                      |
| Stenotrophomonas maltophilia             |
| Ceftazidime Etest                        |
| S                                        |
| —                                        |
| —                                        |
| —                                        |
| Minocycline Etest                        |
| S                                        |
| —                                        |
| —                                        |
| —                                        |
| Trimethoprim/sulfa                       |
| S                                        |
| —                                        |
| —                                        |
| —                                        |
| Stenotrophomonas maltophilia             |
| Ceftazidime                              |
| ≥64                                      |
| ≤0.25                                    |
| ≤1                                       |
| ≤0.12                                    |
| 1                                        |
| ≥128                                     |
| 4                                        |
| ≤20                                      |
| —                                        |
| —                                        |
| —                                        |
| —                                        |

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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