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Case Report

Neonatal Listeriosis Resistant to Ampicillin: A Case Report

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Received: May 23, 2023; **Published:** May 31, 2023

Abstract

Background: Perinatal listerial infection is the most common clinical syndrome caused by *Listeria monocytogenes* and includes abortion, still birth, neonatal sepsis, and meningitis. Listeriosis is caused by the foodborne pathogen *Listeria monocytogenes*. It can present as a maternal-neonatal infection.

Case Presentation: A female newborn with birthweight of 750 grams was delivered vaginally at 25 weeks of gestation. Both the 1- and 5-minute Apgar scores were 4. Respiratory distress and bradycardia necessitated the insertion of an endotracheal tube and the initiation of ventilation assistance. Newborn infection was resistant to ampicillin and was then treated with vancomycin and gentamycin. However, the infant's condition suddenly deteriorated the next day, and the baby ultimately passed away due to cyanosis and bradycardia.

Conclusion: *Listeria* in newborn is rare, yet some cases has been addressed in the literature. Early detection and treatment might lead to good outcomes. However, resistant strains are emerging making the management more difficult and worsen the outcome. Mothers' are advised to avoid foodborne infection with *Listeria* during pregnancy as this severely affect the pregnancy outcome as reported in the current case.

Keywords: *Neonatal Listeriosis; Resistant to Ampicillin*

Introduction

The infection caused by the gram-positive, motile bacteria *Listeria monocytogenes* is known as listeriosis.

Listeriosis may cause moderate illness (febrile gastroenteritis) in otherwise healthy people, but it can cause serious illness and even death in the very young, the very old, those with impaired immune systems, and pregnant women [1]. In the first week of life, neonatal listeriosis may present as bacteremia, meningitis, or pneumonia and is thought to be spread via the placenta or the birth canal by a mother who is already infected with the bacteria [2,3]. Meningitis is the most prevalent symptom of late-onset newborn listeriosis, which may arise after day 7 of life can be caused by transplacental infection, delivery-related exposure, or environmental factors [4]. Research on

patients with documented dietary exposures suggests that the incubation time of listeriosis varies with clinical manifestation, from 1 to 12 days for bacteremia, 1 to 14 days for central nervous system illness, and 17 to 67 days for pregnancy-associated listeriosis (including neonatal disease) [5].

In addition to being effective against L. and Group B *Streptococcus* (GBS), ampicillin is also effective against *S. monocytogenes* [6-9]. In light of this, GBS and L are routinely included in empiric antibiotic treatment for sepsis in young newborns. ampicillin with gentamicin (for the first month only) or ampicillin and cefotaxime (or ceftriaxone after the first month) for monocytogenes and *E. coli* [10-12]. Recent retrospective cross-sectional investigations in the United States, however, found no cases of L that could be confirmed by culture. 375 babies less than 90 days old with fever were tested for monocytogenes bacteremia [13-15]. Various additional studies have shown that L. is rare: 4 instances out of more than 21,000 newborns 90 days old with severe bacterial infections (SBI) of *Listeria monocytogenes* [16,17]. This has led some to question whether or not ampicillin should be included in empiric antibiotic regimens for children of any age who are running a fever in addition to cefotaxime or ceftriaxone. This research was unfortunately retrospective and limited to a single nation (the USA). Evidence-based empiric antibiotic recommendations and evidence-based clinical management for sepsis in infants need population-based, multinational data on listeriosis in infants.

The current paper presents a case of listeriosis in a newborn infant with resistant to ampicillin.

Case Presentation

A female newborn with birthweight of 750 grams was delivered vaginally at 25 weeks of gestation. Her mother suffered a flu-like sickness and got her second dose of the COVID-19 vaccination only eight days before she went into birth. This baby was born while being transported to the hospital, and she was flat when she was brought to the emergency room; she was given two cycles of neonatal resuscitation program (NRP) before being picked up. Both the 1- and 5-minute Apgar scores were 4. Respiratory distress and bradycardia necessitated the insertion of an endotracheal tube and the initiation of ventilation assistance. An X-ray of the chest revealed reticulo-granular infiltrations on both sides. Leukocytes (12.9/mm^3) were within the usual range in hematograms.

On day one, a dosage of 300 mg/kg/day q8h of ampicillin and a dose of 100 mg/kg/day q12h of cefotaxime were given. An ultrasound of the brain performed on the second day revealed a grade 4 intraventricular hemorrhage, moderate ventriculomegaly, and left paraventricular hemorrhage. On day 1, *L. monocytogenes* was isolated from a blood culture (Figure 1). With reports of resistance to ampicillin, cefotaxime, and meropenem, but sensitivity to vancomycin and gentamycin, antibiotic coverage was switched to high dosage ampicillin and gentamycin on day 4. However, due to the patient's poor state, a CSF culture was not performed.

Figure 1: *L. Monocytogenes colonies on blood agar.*

Conventional mechanical ventilation was performed in order to provide the patient with the necessary level of respiratory support, the ventilation mode was changed to high frequency ventilation. The infant's condition suddenly deteriorated the next day, and the baby ultimately passed away due to cyanosis and bradycardia.

Discussion and Literature Review

Meningitis, or bacterial meningitis, is an infection of the membrane linings that surround and protect the brain and may affect people of any age. A demographic that is especially vulnerable is neonates. Up to one in two thousand live births in wealthy countries may be affected by bacterial meningitis, but the prevalence of this disease is much greater in developing countries [18,19]. Meningitis has the highest rates of morbidity and death among the major bacterial infections of infancy. If ignored, bacterial meningitis almost always results in death due to the continuous inflammation that may cause irreparable harm to the underlying parenchyma, thrombosis of arteries, and consequent ischemia/infarction, hearing loss, vision loss, intellectual incapacity, and physical handicap. Newborns' early symptoms are often vague and include fever, irritability, excessive crying or drowsiness, and difficulties with feeding, but older children and adults generally appear with fever, neck stiffness, headache, and disorientation. Infrequently, a doctor may suspect a central nervous system infection in a child because of posturing, seizures, or an abnormally stiff, sensitive, or bulging fontanelle [18,19].

CSF taken via an LP may swiftly and accurately indicate concerns for bacterial meningitis, despite clinical symptoms that may be indistinguishable from those of other dangerous bacterial illnesses in the neonate [20]. Hypoglycorrhacia is characterized by abnormally low glucose levels in the CSF due to severe inflammation of the meninges, which disrupts glucose transport across the blood-brain barrier and increases metabolic activity by the invading bacteria and white blood cells (WBCs). An increase in CSF protein levels results from the recruitment of many activated macrophages and neutrophils, as well as from capillary leak and acute inflammatory mediators. Pleocytosis, hypoglycorrhacia, and increased CSF protein are the traditional triad of symptoms in bacterial meningitis, which our patient had. Such a trend is unusual in cases of viral meningitis [20]. The criteria for defining bacterial meningitis include Gram staining and culture of cerebrospinal fluid (CSF) taken prior to the administration of antibiotics, which is adequate to identify the causal organism in up to 85% of suspected cases [20]. Gram staining of cerebrospinal fluid (CSF) alone has a varying sensitivity (from 20% to 93%) that depends on the organism being tested for [21]. Acridine orange's sensitivity has been found to be 21% greater than that of Gram staining, making it a promising supplement when a Gram stain is negative or as a first-line screening test [22]. Despite highly suggestive laboratory evidence of bacterial meningitis and CSF obtained prior to antibiotic administration, cultures remained negative in our patient's case, presenting a diagnostic conundrum. The yield of CSF cultures can significantly decrease, up to 41%, in patients treated with antibiotics prior to LP, whereas the yield of CSF Gram staining pretreatment decreases only slightly [21].

Meningitis may be caused by a wide variety of bacteria, and the most often seen organisms change with patient age and comorbidities. Approximately seventy percent of all instances of bacterial meningitis in infants less than one year old are caused by Group B *Streptococcus* and *Escherichia coli* [18,19]. Other Gram-negative enteric species and enterococci make up the bacterial etiologic agents. Meningitis caused by *L. monocytogenes* occurs in 0.5 to 3 of per 100,000 births, making it an uncommon but clinically important cause of illness [18,19].

Listeriaceae is a family of microorganisms found in a variety of habitats, including soil and water, and contains a number of distinct species. Since *L. monocytogenes* can infect animals, including humans, it is the only important human pathogen in the family. It can survive in environments with low temperatures, high salinity, and alkalinity, and it can do so in refrigerated unpasteurized or contaminated foods as well [23]. One way to separate *Listeria* species from other bacteria is by cold enrichment. Approximately 1,600 cases and 260 fatalities per year are attributed to *L. monocytogenes* as a food-borne disease in the United States. When exposed to the bacteria, the vast majority of healthy people either show no symptoms at all (asymptomatic) or exhibit very moderate symptoms (abdominal cramps and self-limiting diarrhea). Pregnant women, babies less than 2 months old, the elderly, and those with immunodeficiencies, especially those with impairment of T-cell activity like those with HIV/AIDS, are at the highest risk for severe illness. It has been hypothesized that the higher risk of invasive illness in pregnant women is due to the loss in T-cell function that is necessary to make room for the baby [23].

L. monocytogenes is a gram-positive, non-spore-forming rod or coccobacillus that exhibits tumbling motility in broth incubated between 18 and 25°C when grown in the lab. When temperatures are lower or higher, this action weakens. Positive catalase and hippurate tests, as well as the presence of a small zone of beta-hemolysis on BAP, provide further evidence for the identification of *L. monocytogenes* beyond the gram stain results and the confirmation of tumbling motility [24]. *Listeria* spp. are notoriously difficult to recover from clinical specimens and food samples without a pre-enrichment process and selective medium. *Listeria* spp. have a broad temperature range for growth (1 to 45°C), although they do best at 37°C. Although incubating agar at 4 degrees Celsius for a long time will enhance yield, this process can take weeks, and it won't let you isolate damaged bacterial cells since they won't grow when subjected to stress [25]. Commercial identification systems, 16S rRNA sequencing, and matrix-assisted laser desorption ionization-time of flight mass spectrometry are all viable alternatives for identifying *L. monocytogenes*. Broad-spectrum cephalosporins are a beta-lactam medication class widely used to empirically treat sepsis and meningitis of unknown cause; nevertheless, *L. monocytogenes* is inherently resistant to these antibiotics.

The ability to correctly de-escalate or optimize antimicrobial treatment depends on the correct identification of *Listeria* spp. However, obtaining useful information from clinical samples is not always easy. There needs to be a more sensitive diagnostic technique since only 83% of CSF cultures and 64% of blood cultures of materials from individuals with suspected *L. monocytogenes* meningitis grew the organism [26]. Harmful culture results may have negative consequences, since they may lead doctors to wrongly rule out bacterial meningitis, in which case they may stop administering antibiotics too soon or use inadequate empirical antibiotics. Empirical treatment may also be maintained needlessly if it is not possible to tell the difference between a false-negative and a true-negative outcome. Molecular panels now provide a way to supplement conventional methods. The time it takes to get a diagnosis from testing is far less than it would be with traditional culture, and it can detect many viruses that conventional testing could miss. Within 1 hour, the Film Array ME panel can identify 14 different common bacterial, viral, and yeast pathogens that have been linked to CNS illnesses. This assay has been authorized by the Food and Drug Administration (FDA). The panel was tested in 1,560 clinical samples from many centers, and the results showed a sensitivity and specificity anywhere from 85.7% to 100%, depending on the outcome being sought [27]. In a separate analysis of 342 adult and pediatric patients, the Film Array ME panel achieved overall positive agreement levels of 92.9 and negative agreement levels of 91.9%. Only 57% (6/14) of the cryptococcal antigen-positive specimens correlated with the panel findings. Furthermore, there were no culture findings, and further confirmation testing using sequencing was similarly negative [28]. Because *L. monocytogenes* infections are so uncommon, neither research found any. Most significantly, no false-positive cases were found [27-28].

As approved After the 1960s, that ampicillin or amoxicillin in combination with aminoglycosides were considered as the treatment of choice for Listeriosis. In our case the isolated *L. monocytogen* from blood culture was resistant to ampicillin using the disc diffusion method of susceptibility, and resistant to meropenem as well with MIC of 8 mg/L. In such case, alternative therapy with different antibiotics is needed. The second line of treatment is TMP/SMX (trimethoprim-sulfamethoxazole) that is contraindicated in less than 2 months of age. A Study was done in Russia over 3 different periods of time (1950–1980;2000–2005, and 2018–2021) that was looking for Susceptibility of 117 *L. monocytogenes* strains isolated to 23 antibiotics was tested by the disk diffusion method. In total, 59 strains (51% of the total amount of strains) were resistant to one or more antibiotics. All strains resistant to penicillin G, ampicillin, tetracycline, tylosin, and chloramphenicol were isolated in 1950–1980 or 2000–2005 but not later. Resistance to carbapenems and ciprofloxacin was found in strains isolated after 2000 only. Clindamycin resistant strains were found among isolates obtained in all periods studied. No ampicillin resistant strains and only one gentamicin-resistant strain were found among 544 strains isolated in Germany. Less than 3% of the strains showed resistance to ampicillin and gentamicin among 118 L. monocytogenes isolates from meat in Spain.

Vancomycin used for treatment of *L. monocytogenes* bacteremia, but not for meningitis. In a report by E.M.Jones and collogues in 1995,that vancomycin has poor CNS penetration and advocated for not using it in case of *L.Monocytogenes* meningitis.

Finally, *L. monocytogenes* is a major reason for meningitis, thus a correct diagnosis is necessary for optimizing antimicrobial treatment. Traditional culture methods for diagnosing listeriosis in the laboratory have its limitations. Novel molecular tests may improve detection

of *L. monocytogenes* and other infections typically associated with bacterial meningitis, and hence have an immediate effect on patient care.

Conclusion

Listeria infection during pregnancy often manifests in the first trimester, whereas complications manifest in the third. Low birth weight and other newborn complications are common effects of this condition. Serious complications for pregnant women include miscarriage, stillbirth, and premature delivery due to infection. Trans-placental transmission, inhalation of contaminated amniotic fluid, and colonization through the mother's gastrointestinal tract or genital tract are all potential routes of transmission of neonatal listeriosis. This case presents a preterm delivered newborn with listeriosis resistant to ampicillin and ended with death.

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Volume 12 Issue 6 June 2023