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Case report

Neonatal listeriosis: an cause of neonatal sepsis

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ABSTRACT

Although *Listeria* is an uncommon cause of neonatal sepsis and meningitis, perinatal listerial infection is the most common clinical syndrome caused by this organism. Foodborne outbreaks associated with consumption of dairy products and processed meat have been known in the past. Infected mother may present with flu-like symptoms, and premature labor and still births are known to occur in perinatal listeriosis. Neonates may acquire the infection either transplacentally or by aspiration of infected amniotic fluid. Early-onset infection is associated with overwhelming sepsis and high risk of mortality. High proportion of late-onset infection presents with meningitis. Ampicillin in combination with an aminoglycoside is the preferred treatment for neonatal listeriosis. It should be kept as a part of the differential diagnosis while investigating for neonatal sepsis. Preliminary reports of gram-positive rods may help in making a presumptive diagnosis of listeriosis.

1. Introduction

Listeria monocytogenes, a gram-positive intracellular rod, has the ability to trigger cytoskeletal changes in host cells which help in the entry of the organism in a variety of host cells. Although it is a rare cause of illness in general population, it can be responsible for life-threatening bacteremia in certain high-risk population such as pregnant women, neonates, transplant recipients, and immunocompromised individuals.[1] Listeriosis is a foodborne disease often associated with intake of unpasteurized milk, processed meat, soft cheese, and melons exposed to room temperature.[2] Worldwide, it is the third leading cause of neonatal septicemia and meningitis, ranking next to *Escherichia coli and Streptococcus agalactiae*. Reporting of perinatal listeriosis in India is very limited.[3,4]

2. Case summary

An early-term small for gestational age baby born to a primigravida mother by lower segment caeserean section (LSCS) in view of meconium-stained liquor was admitted to Sir Gangaram Hospital Neonatal Intensive Care Unit for postresuscitation care. The baby was born limp and required positive pressure ventilation for 1 min [appearance, pulse, grimace, activity, respiration (APGAR) score of 2 and 9 at 1 and 5 minutes, respectively] after which the baby was shifted to nasal continuous positive airway pressure in view of respiratory distress. Cord arterial blood gases were as follows: pH, 7.2; lactate, 5.2 mmol/l; and base deficit, 8.1 mmol/l. The baby remained asymptomatic till 8 hours of life; when low random blood sugar was documented, the baby was managed with glucose infusion rate of 6 mg/kg/minute. Soon after this, the baby had one episode of apnea, and the baby responded to stimulation. At this point, sepsis workup was performed and intravenous (IV) antibiotic was started empirically. The baby was provisionally managed as a case of hypoxic ischemic encephalopathy. Simultaneously, the baby was also noted to have purulent eye discharge. The baby had to be on high-flow nasal cannula, and one saline bolus was also given in view of poor perfusion. Later, at around 12 hours of life, the baby had one episode of abnormal movement associated with desaturation and apnea, after which the baby was loaded with levetiracetam. On the second day of life, there was severe conjunctival congestion associated with discharge for which topical antibiotics were used.

Sepsis screening results were negative except for a raised C-reactive protein, −46 mg/l. Gram's staining performed on blood sample and eye swab culture showed gram-positive bacilli [Fig. 1]. Culture revealed growth of small gray beta-hemolytic colonies [Fig. 2] which were later identified by matrix-assisted laser

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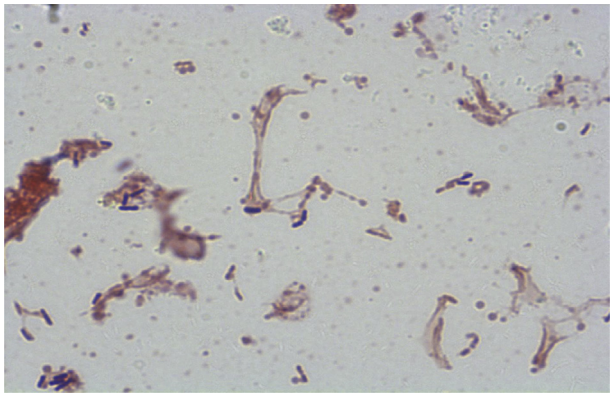

Fig. 1. Gram-stained smear of blood showing gram-positive rods.

Fig. 2. Small gray beta-hemolytic colonies of *L. isteria monocytogenes* growing on blood agar.

desorption ionization–time for flight mass spectrometry (MALDI-TOF MS) as *Listeria monocytogenes*. Concurrently, eye swab cultures also showed growth of *Listeria monocytogenes*. The strain was sensitive to ampicillin. Cerebrospinal fluid (CSF) culture was sterile (see Fig. 3).

Antenatal history was again reviewed for possible transmission. There was no history of maternal pyrexia, diarrhea, backache, myalgias, and leaking or bleeding per vaginum. There was no history of possible consumption of food items [unpasteurized milk, hot dogs, refrigerated smoked sea food, processed meat, soft cheese, raw sprouts, and old cut melons] listed in centers for disease control and prevention (CDC) guidelines that could lead to foodborne listeriosis. There was no history of pets in the family and any other animal contact. Blood culture and vaginal swab culture of the mother did not show any yield for the organism.

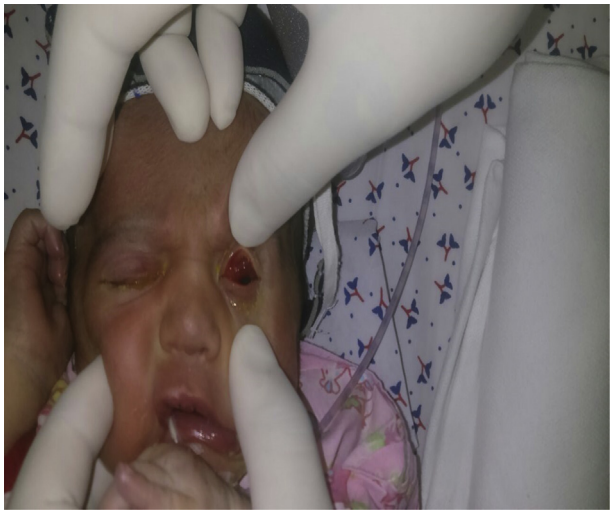

Fig. 3. Purulent conjunctivitis in the new born.

Later, IV ampicillin was started after antimicrobial susceptibility testing showed isolate to be sensitive to ampicillin. The baby showed significant improvement within 48 hours of starting ampicillin. Tube feeding was resumed after 24 hours, and was continued in view of reduced activity and respiratory distress.

The baby was weaned off from oxygen support to room air on day 6 of life, and direct feeds were started on day 7, which the baby tolerated very well. IV ampicillin was continued for a total duration of 10 days. On discharge on day 14, the baby was hemodynamically stable and neurological examination was normal.

3. Discussion

The incidence of listeriosis is 20-fold higher among pregnant women than among general population.[5] Maternal listeriosis has a benign presentation and may show mild flu-like symptoms. *Listeria* may infect the fetus via infected birth canal or transplacentally. Abortion or still births are common, depending on the time of acquiring infection.[6] The occurrence of pathogenic *L. monocytogenes* in cases of spontaneous abortions is 3.3%; an important determinant was plcA gene expression.[7] In a study from North India, the incidence of neonatal listeriosis is reported to be 2.2% in meconium-stained babies and 0.2% in total births.[3] *L. monocytogenes* has been isolated from the genital tract of 14% of women with bad obstetric history in Mumbai and 1.34% of women in Delhi.[8,9] There are a total of 14 cases of human listeriosis reported in India, of which 4 were cases of neonatal listeriosis. Out of the 4, three cases presented as early-onset disease (Gupta et al.[10], Srivastava et al.[11], and Mokta et al.[12]), whereas one case presented in the late neonatal period (Khan et al.[13]). Although neonatal listeriosis is mostly seen in preterm babies, the one in our case was a term baby.

Neonatal listeriosis occurs as early-onset (<7 days) and late-onset diseases (>7 days) Early neonatal infection (contacted *in utero*) accounts for most cases (62%) and presents mostly as a septicemic illness.[14] Case fatality rate for early-onset illness is reported to be high and ranges from 14 to 56%.[15] In contrast, late-onset infections present as meningitis and probably are due to cross-infections in hospitals.[16] Neonatal listeriosis is also associated with pneumonia, cellulitis, lymphadenitis, endocarditis, and conjunctivitis. In our case, the baby had conjunctivitis.

Although rare, a pathognomonic feature in neonatal listeriosis is a rash called granulomatosis infantisepticum, characterized by widespread microabscesses and granulomas. The case reported in this study did not have this characteristic rash. In the 222 cases of maternal infection reported in the literature and reviewed by Mylonakis et al.,[17] 94 infants were infected. Of these, 59 (62.8%) recovered completely, 23 (24.5%) died, and 12 (12.7%) had neurologic sequelae or other long-term complications. Meningitis alone or in combination with bacteremia/sepsis or pneumonia was associated with the worst prognosis.

Although neonatal listeriosis is mostly seen in preterm babies, our case was a term baby. There are very few reports from India and other parts of the world wherein term neonates presented with symptoms of early neonatal listeriosis.

Limited reporting from India could be attributed to a low carriage rate or lack of awareness and noninclusion of selective

media for *Listeria* in plating of blood cultures. The identification of *L. monocytogenes* can pose a diagnostic challenge because in a clinical specimen, *Listeria* may appear gram-variable and be mistaken for diptheroids, streptococci, or enterococci. It is imperative to rule out *L. monocytogenes* whenever gram-positive bacilli are isolated from blood or CSF before discarding it as a contaminant. Despite a battery of routine biochemical tests, cold tolerance and typical tumbling motility the diagnosis of *Listeria* are often missed. MALDI-TOF MS technique, which was used for identification in this case, is currently the most preferred method of identification. MALDI-TOF MS technique is increasingly being used in clinical laboratories and helps in the identification of pathogens that were previously misidentified or ambiguously identified by conventional methods. It yields identification results within minutes from the time the isolate is grown in culture. Timely identification in this case helped direct antibiotic therapy, facilitating recovery. Early diagnosis and treatment of listeriosis in high-risk patients is important because the outcome of untreated infection has shown devastating statistics with a very high mortality rate. Mortality among newborns ranges from 30 to 50%.[18] Even among treated babies, overall mortality accounts for 30%. Traditionally, neonatal septicemia in developing countries is treated with a combination of aminoglycosides such as gentamicin and third-generation cephalosporins such as ceftriaxone. Notably, such a regime proves ineffective in cases of listeriosis because *L. monocytogenes* is known to be not sensitive to cephalosporins.[18] Hence, possibility of listerial etiology should be ruled out in every case of neonatal sepsis and ampicillin ought to be included in the regimen. Pregnant women with listeriosis may have only mild symptoms of the infection, but for those with fever or signs of sepsis, blood and urine samples should be obtained for culture and sensitivity. High vaginal swab culture is less satisfactory. In pregnant women with suspected listeriosis, empiric therapy including ampicillin should be started for coverage of *Listeria* infection. Although the incidence at present may be low, it is a potential threat in near future, making it worth to look out for the possibility of listeriosis in cases of neonatal sepsis.

4. Conclusion

Neonatal listeriosis is an important cause of neonatal sepsis, and even a single occurrence of *Listeria* infection in a nursery may be related to a large outbreak. However, it is underreported in our country due to lack of awareness and suspicion while investigating sepsis. Therefore, we need to obtain a detailed history of exposure and try to retrieve the organism by culturing of specimens taken from different body fluids.

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Conflict of interest

None declared.

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