

Well-known but rare pathogen in neonates: *Listeria monocytogenes*

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Abstract. – *Listeria monocytogenes* is a very important life-threatening bacteria in certain risk groups such as neonates, pregnant women, elderly people, transplant recipients and others with impaired cell-mediated immunity. However, its infections are very rare in healthy children. Reports of listeriosis in newborn period are limited. We report a case of neonatal listeriosis with erythematous rash, intractable convulsions, severe early neonatal sepsis, disseminated intravascular coagulation, multiple organ dysfunction syndrome and death. Although an empirical antibiotic therapy including ampicillin (semisynthetic penicillin) and aminoglycoside combination is effective by the means of a probable *Listeria* infection, the progression of the very early-onset disease may be fatal, despite vigorous treatment efforts as in our case.

Key Words:

Listeria, Newborn, Sepsis.

Introduction

Listeria (L.) monocytogenes is a Gram-positive foodborne pathogen which is often found in diverse environments such as soil, water, various food products, animals, and humans¹. It is a very important life-threatening bacteria in certain risk groups such as neonates, pregnant women, elderly people, transplant recipients and others with impaired cell-mediated immunity. However, its infections are very rare in healthy children². Any infection during pregnancy can cause miscarriage, sepsis, and premature birth, as well as amnionitis, disseminated abscess accompanied by sepsis, granuloma, and late-onset meningitis, conjunctivitis, and pneumonia³. In addition, *Listeria* can cause suppurative arthritis, osteomyelitis, and liver abscess⁴. The source of infection is usu-

ally acquired from animals through undercooked meat or chicken⁵. Neonates acquire infection by transplacental spread, aspiration of infected meconium or in rare instances of cross-contamination in newborn nurseries. Even with appropriate treatment, the overall mortality with listeriosis is 30%⁶.

Herein, we report a case of neonatal listeriosis with erythematous rash, intractable convulsions, severe early neonatal sepsis, disseminated intravascular coagulation, multiple organ dysfunction syndrome and death.

Case Report

A male preterm baby weighing 1520 g was born via cesarean section due to fetal distress at a gestational age of 31 weeks. The mother had subfebrile fever and moderate abdominal pain within 3 days prior to the delivery. In the laboratory investigation of the mother, a leukocyte count of 40000/mm³ was detected, she was started an empirical treatment of ceftriaxone and metronidazol after obtaining a blood culture.

At delivery, findings of endometritis, meconium-stained amniotic fluid and yellow-green umbilical cord mimicking funicitis (Figure 1) were noted. The 1- and 5-minute Apgar scores were 0 and 4, respectively, and resuscitation and endotracheal intubation was performed immediately in the delivery room. Therefore, the infant was transferred to the neonatal intensive care unit (ICU), and he was put on mechanical ventilation. Physical examination on admission revealed depressed activity, severe hypotonia, pallor and poor peripheral perfusion, tachypnea, subcostal retractions, and cutis marmoratus. Erythematous maculopapular rashes were noted over the chest and extremities (Figure 1). Severe respiratory distress syndrome (RDS) was noted



Figure 1. Erythematous maculopapular rashes on the trunk and extremities.

on his chest radiography, surfactant was given for two doses and ventilator support was continued. His blood pressure was within normal limits with continuous direct invasive monitoring. In whole blood count analysis hemoglobin, leukocyte and platelet counts were 14.1 g/dl, 5600/mm³ and 96000/mm³, respectively. C-reactive protein was 6.84 mg/dL and procalcitonin was 2.4 ng/ml. An empirical antibiotic treatment with ampicillin (100 mg/kg/day q12h) and netilmicin (4 mg/kg/day q36h) was started initially for neonatal sepsis after a blood culture was sent to the microbiology laboratory. Fresh frozen plasma was also given. Subtle and clonic seizures were noted on the first day and phenobarbital was administered as the first antiepilep-

tic agent. However, as the seizures persisted, phenytoin, midazolam and pyridoxine were given respectively. However, no response was achieved with these therapies, and continuous midazolam infusion was administered for persistent seizures. Cranial ultrasonography was normal. An echocardiography revealed a pulmonary artery pressure of 60 mmHg (moderate to severe pulmonary hypertension). On the second day of life, fever, desaturation and spoiling of skin color developed, and a repeated laboratory investigation demonstrated increased leukocyte count, C-reactive protein and procalcitonin values (22.000/mm³, 15 mg/d L and 32 ng/ml, respectively) and decreased platelet count (46000/mm³). Therefore, fresh frozen plasma and platelet transfusions were given, and his antibiotic treatment was changed to meropenem, amikacin and teikoplanin because of clinical and laboratory deterioration. At the 48th hour the patient was oliguric, oxygen requirement and pulmonary hypertension increased, and the patient expired at the 60th hour of life with multiple organ dysfunction syndrome despite vigorous treatments with high frequency oscillation plus inhaled nitric oxide, packed red cell and platelet transfusions.

Blood culture obtained on admission yielded *L. monocytogenes*. However, blood culture resulted after the infant died. His mother's blood culture also yielded *L. monocytogenes*. Pathologic examination of the placenta and umbilical cord disclosed chorioamnionitis and funicitis (Figure 2).

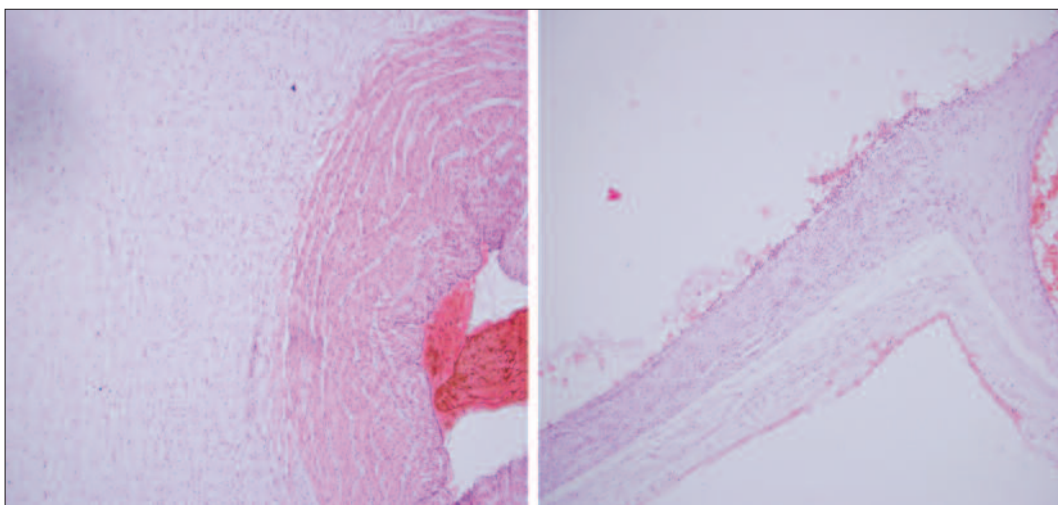


Figure 2. Pathologic findings of funicitis and choriomnionitis in the umbilical cord (right) and placenta (left) (x 100, Haematoxylin Eosin).

Discussion

Listeriosis is a severe foodborne disease characterized by bacteremia and meningoencephalitis in individuals with impaired cell-mediated immunity, including neonates, pregnant woman, elderly persons, and immunosuppressed patients. The prevalence of listeriosis is rather low but the outcome is much more severe and often fatal. In fact, it represents one of the most fatal bacterial infection with a mortality rate of 20-30% despite early antibiotic treatment⁷.

Listeria monocytogenes enters into the immune system cells and other tissue cells, by phagocytosis and invades into the phagocytic vacuole, and multiplies inside the cell. *Listeria* forms a structure that is surrounded by actin filament from the host cell in the protoplasm. This results in a protrusion which is facilitating bacterial transmission among cells. As a result, listeria can hide inside the host cell and be protected from the immune reaction of host cells, enabling the spread of infection⁸. This invasion can cause severe damage sequelae by affecting white blood cells and stimulating an inflammatory reaction in whole body⁹.

Very few cases of invasive listeriosis have been reported as individual case reports from Turkey^{10,11}. False determination of culture results due to its coccobacilli shape and changeable Gram-positive stain may be one of the impacting factors in its incidence detected lower than expected¹². Obstetricians rarely examine materials and take cultures from placenta and fetus in abortus, which may also result in misdiagnosis of perinatal infection, and thus many cases of neonatal listeriosis may remain as undiagnosed. It is, thus, difficult to calculate the exact prevalence of perinatal infections. Although pregnancy-associated listeriosis may occur during any stage of gestation, most cases are detected during the 3rd trimester. The organism establishes itself in genital tract leading to chronic infection and infects products of conception in successive pregnancies¹³. In our case, the mother manifested some symptoms including malaise, fever and lower abdominal pain which started 3 days before delivery. Also, meconium-stained amniotic fluid and chorioamnionitis were determined at the time of delivery. Therefore, maternal history including signs of nonspecific infections and chorioamnionitis might be a clue for considering Listeriosis.

Early-onset listeriosis that occurs in the first 7 days of life is often associated with maternal illness and preterm delivery. Septic-like syndrome

may predominate but acute respiratory distress and pneumonia may also be observed. Our case had findings of respiratory distress, and surfactant was given with the clinical and radiologic diagnosis of RDS. Meningitis and myocarditis are relatively rare in the early-onset disease¹⁴. *L. monocytogenes* often pass into the meninges and blood-brain barrier by the means of macrophage phagocytosis of the bacteria and then spread to and grow within the central nervous system in preterm infants¹⁵. We did not perform lumbar puncture in our case as the disease presented very early in the first minutes of life, the clinical status of the patient was not very stable (intubated and thrombocytopenic) and the infectious window of the clinical picture was not predominating.

Laboratory diagnosis requires isolation of *L. monocytogenes* from normally sterile clinical specimens and identification through standard microbiologic techniques. In clinical specimen, the organism may be Gram-variable and look like diphtheroids, cocci or diplococci and because of this reason, laboratory misidentification is common. The isolation of Gram-positive bacilli or coccobacilli from blood or CSF should not be commented as contaminants unless *Listeria* is ruled out¹⁶. *Listeria monocytogenes* is sensitive to penicillin, chloramphenicol, aminoglycosides, tetracyclines, and erythromycin. It is uniformly resistant to cephalosporins. Treatment of choice for listeriosis is high dose of penicillin or ampicillin, preferably in combination with aminoglycoside¹⁷.

Listeria infections should be considered in infants who present with erythematous rash, respiratory distress and nonspecific findings of early neonatal sepsis. Although an empirical antibiotic therapy including ampicillin (semisynthetic penicillin) and aminoglycoside combination is effective by the means of a probable *Listeria* infection, the progression of the very early-onset disease may be fatal despite vigorous treatment efforts as in our case. Pathologic examination of umbilical cord and placenta may be helpful in rapid diagnosis of such cases.

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