

PERINATAL ASPHYXIA ASSOCIATED WITH EARLY NEONATAL SEPSIS WITH *LISTERIA MONOCYTOGENES* – CASE PRESENTATION

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ABSTRACT

Listeria monocytogenes is a gram-positive bacillus with a low incidence of diagnosed infections that can cause maternal, fetal and neonatal listeriosis by vertical transmission from the mother. In adults, the infection is mild with gastrointestinal or flu-like symptoms, sometimes it may even be asymptomatic. In contrast, in newborns it can cause early or late neonatal sepsis, endocarditis, meningitis, neurological complications. Neurolisteriosis is the most serious form of neonatal disease with an increased rate of perinatal mortality. We present a case of a term newborn with early neonatal sepsis with *Listeria monocytogenes* that associated severe perinatal asphyxia.

Keywords: perinatal asphyxia, early neonatal sepsis, *Listeria monocytogenes*

INTRODUCTION

Listeria monocytogenes is a gram-positive bacillus that is transmitted through the ingestion of contaminated foods (milk, cheese, meat), with a low incidence of diagnosed infections but in the last years an increase is expected, especially for women of Hispanic origin (1). It can cause maternal, fetal and neonatal listeriosis by vertical transmission from the mother (transplacental, vaginal birth, ascending). Invasive infections with *Listeria* are divided into 3 forms: sepsis, neuro-listeriosis and maternal-fetal infection (2).

Infection during pregnancy causes miscarriage, preterm birth, fetal death in utero or chorioamnionitis, and is often underdiagnosed (3). In adults, the infection is mild with gastrointestinal or flu-like symptoms, sometimes it may even be asymptomatic. In contrast, in newborns it can cause early or late neonatal sepsis, endocarditis, meningitis, neurological complications (4,5).

The neonatal diagnosis of *Listeria* infection is challenging because of the low specificity of the blood cultures or of the cerebrospinal fluid cultures for *Listeria*. Depending on the stage of development of the bacterium, they can appear in the form of coccoids and can be difficult to detect in Gram staining, requiring serial cultures. Being such a rare infection, the test rate for *Listeria* is very low (6).

Clinical manifestations reported in neonatal cases were of early or late neonatal sepsis, congenital pneumonia, respiratory distress and fever. Other symptoms include neurological signs, rash and jaundice. Neurolisteriosis is the most serious form of neonatal disease with an increased rate of perinatal mortality. Respiratory distress at birth determines severe perinatal asphyxia and grade II or III hypoxic-ischemic encephalopathy (7).

In 2017, the MONALISA study was conducted in which the risk factors and the prognosis of infections with *Listeria monocytogenes* are presented. In the case of neonatal listeriosis, the prognosis has

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not improved in recent years due to the few studies, but if there is a highly suspicion of the diagnosis, paraclinical investigations should be performed as soon as possible and the correct treatment started immediately to reduce the bacteremia (8).

CASE PRESENTATION

We present the case of a newborn transferred to our clinic at 5 hours of life for treatment with controlled hypothermia. Coming from a monochorial-diamniotic twin pregnancy, partially investigated, with a urinary tract infection in the third trimester of pregnancy with *Listeria monocytogenes*. The 38-year-old mother third time pregnant, primiparous with no significant personal pathological history, normal BMI, non-smoking, no exposure to toxic environment, normal blood pressure, normal blood sugar levels. The pregnancy was not followed in our clinic but the paraclinical investigations performed showed negative TORCH, the usual analyzes within normal limits and a positive uroculture in the third trimester of pregnancy with *Listeria*. Fetal morphology ultrasounds were within normal limits for gestational age.

The pregnancy had normal evolution without complications. Labor began spontaneously at 37 weeks of gestation with the rupture of membranes and painful uterine contractions. She was admitted in a second degree maternity where it was decided to terminate the pregnancy by caesarean section and were extracted two live newborns, twin I a female of 2,300 grams (10-25% percentile) AS 2/4/6/7, twin II also female of 2,200 grams (10-25% percentile) AS 9/9.

The amniotic fluid was green and the morphopathological examination of the placenta was not available, the lochia culture harvested a few days after birth was positive for *Listeria monocytogenes*. The mother followed antibiotic therapy with favorable evolution.

At birth, the newborn I required complex resuscitation maneuvers (ventilated with positive intermittent pressure on the bag and endotracheal tube, adrenaline IV). It required volume and metabolic balance, vasopressor therapy with dopamine IV, antibiotic therapy with Cefuroxim and Gentamicin. In the first hours of life he presented generalized tonic-clonic seizures for which phenobarbital i.m.

loading dose and Midazolam in continuous infusion were administrated. In contrast, the second newborn did not require resuscitation and presented a favorable adaptation.

They were transferred to the "Filantropia" Hospital for initiation of treatment with controlled hypothermia in twin one. They were admitted to the neonatal intensive care unit. Twin I presented severe general condition, intrarectal temperature 36.2 Celsius degrees, acrocyanosis, intubated and mechanically ventilated, breath sound present bilaterally without crackles, rhythmic cord without murmurs, HR 160 bpm, blood pressure 50 mmHg, hypotonic, hyporeactive (sedated), without seizures at the time of transfer. Controlled hypothermia was started immediately at 33.5 Celsius degrees intrarectal temperature, mechanically ventilated initially in the high-frequency oscillator system and volume-targeted and then conventional ventilation and noninvasive mechanical ventilation for 11 days. Patient needed fresh frozen plasma transfusion, antibiotic therapy with Meronem and Vancomycin and sedatives. For the seizures continuous infusion with Midazolam was administrated, subsequently phenobarbital.

Paraclinical investigations met the criteria for controlled hypothermia (ph 6.89, pCO₂ 75 mmHG, BE -19), associated leukocytosis with neutrophils and intensely positive inflammatory samples, without anemia, without thrombocytopenia, coagulation samples within normal limits. The peripheral cultures harvested at birth did not isolate pathogenic germs, but blood culture was positive for *Listeria monocytogenes*. The neurological examination at the time of admission included stage II Sarnat hypoxic ischemic encephalopathy, the cranial ultrasonography was normal. aEEG was recorded during the controlled hypothermia and in the first hours it was with microvoltage without identifying seizures, then normalized.

After 72 hours of controlled hypothermia, the warming began with 0.5 Celsius degrees at 2 hours without any complications, stable hemodynamic without seizures. The evolution of the newborn was favorable with the improvement of the functional respiratory syndrome (it allowed extubation at 8 days of life but remained oxygen dependent for 11 days), the axial hypotonia was maintained, without repeating seizures.

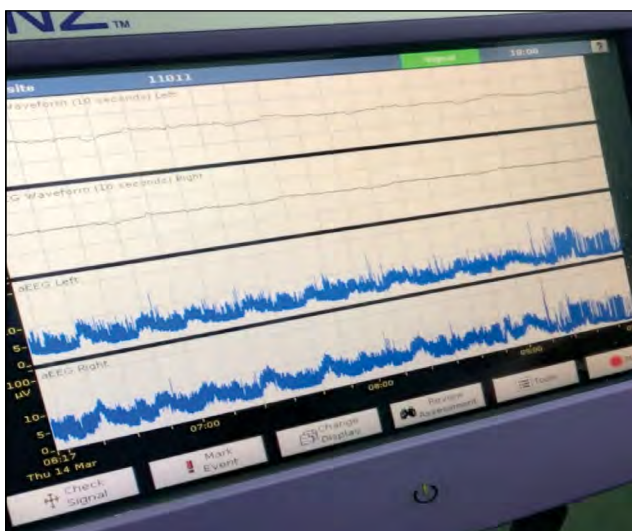


FIGURE 1. aEEG monitoring – microvoltage aspect without seizures

Twin II has presented from the beginning of hospitalization in the neonatal intensive care unit with overall satisfactory condition, acrocyanosis, balanced cardio-respiratory, HR 140-50 bpm, rhythmic heart without murmurs, blood pressure 52 mm Hg, breath sound present bilaterally without crackles, SpO₂ > 96% in atmospheric air, supple abdomen, liver, spleen within normal limits, good tone and reactivity. Paraclinical investigations have shown leukocytosis with neurophilia, without anemia, without thrombocytopenia and positive blood culture for *Listeria monocytogenes*. Cranial ultrasonography with normal appearance and neurological examination without pathological changes. Antibiotic therapy was started with Meronem and Vancomycin. The evolution was favorable with good general condition, balanced cardio-respiratory, good digestive tolerance, ascending weight curve, tone and reactivity within normal limits.

At 13 days of life, they were transferred to the premature compartment where the evolution was favorable for both twins. They were released at 19 days of life with good general condition, only twin I maintained axial hypotony, without seizures.

DISCUSSIONS

Listeria infection is a rare and most commonly undiagnosed condition in both mother and newborn (9). In 30% of cases the infection is asymptomatic (10). In this case, although the mother was asymptomatic, *Listeria* was isolated in the routine urine

culture during the third trimester of pregnancy and followed a complete course of antibiotic therapy according to the antibiogram. Despite the antibiotic treatment, the infection was transmitted to the fetuses (positive blood cultures) and twin I was with severe symptoms at birth. The mother's lochiaculture was positive for *Listeria*, blood culture wasn't performed due to low sensitivity (11).

Pregnancy being monochorionic-diamniotic associated maternal-fetal infection of both fetuses. In the present case, although *Listeria* was isolated in both blood cultures of the twins, but only one of them developed severe hypoxia at birth, the other being without clinical symptoms (12). In the absence of proper antibiotic treatment we cannot say whether the second twin would have developed a clinical form of *Listeria* infection.

Neonatal listeriosis associated with neurological complications has a high rate of perinatal mortality (5). In the presented case, the treatment with controlled hypothermia performed during the first 6 hours of life and the combination of the antibiotic therapy determined a favorable evolution of the newborns without the neurological sequelae.

Treatment of hypoxic-ischemic encephalopathy with controlled hypothermia of the whole body initiated within the first 6 hours after birth and continued for 72 hours, until complete reheating, decreases the mortality rate and neurological sequelae at term newborns (13). Twin I met the criteria for achieving controlled hypothermia and thus the subsequent neurological evolution was favorable without the sequelae.

In recent years studies have focused on identifying as early as possible the infection with *Listeria* and testing all women in endemic areas, even asymptomatic ones, to prevent transmission to the fetus (14). They have developed protocols to identify alarm signs that might be present in *Listeria* infection.

Inadequate management, lack of timely diagnosis and improper treatment during pregnancy causes neonatal complications. In pregnant women, the complications are minimal with the remission of the symptoms after the antibiotic treatment. In contrast, complications in newborns are severe with the association of increased rates of perinatal mortality (15).

CONCLUSIONS

Following the presentation of this case, we can say that although the pregnancy was a monochorionic-diamniotic twin, the clinical symptoms were present only in one of the fetuses, respectively the

twin I. The diagnostic and treatment administered in the first hours of life for the twin I helped her not develop serious neurological complications with subsequent sequelae.

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