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Relevance of microbiological cultures of cord blood and placental swabs in the rapid diagnosis of preterm newborn infection due to *Listeria monocytogenes*: A case report

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ABSTRACT

Listeria monocytogenes (*Lm*) is a Gram-positive bacterium causing listeriosis, a rare but severe foodborne infection, particularly impactful during pregnancy. Maternal-fetal transmission can lead to adverse fetal outcomes, yet symptoms in mothers may be nonspecific, delaying intervention. Despite the severity, the mechanisms of vertical transmission remain unclear. This report describes a case of rapid *Lm* diagnosis in a preterm newborn using cord blood and placental swabs. A 31-week pregnant woman presented with abdominal pain, diarrhea, and reduced fetal movements after consuming raw sushi. Laboratory findings indicated infection, and she vaginally delivered a live infant with placental and fetal abscesses. Cultures confirmed *Lm*, with swift diagnosis aided by molecular syndromic testing. The neonate received appropriate antibiotics and was asymptomatic by the end of treatment. This case underscores the need for the rapid diagnosis of maternal-fetal listeriosis, as it poses significant risks during pregnancy, including preterm birth and neonatal complications. Current diagnostic methods often delay treatment. This report emphasizes the use of innovative molecular techniques for early diagnosis, which is crucial in managing neonatal infections, especially in preterm newborns.

1. Introduction

Listeria monocytogenes (*Lm*) is a Gram-positive facultative intracellular bacterium responsible for causing listeriosis, a rare yet severe foodborne infection. *Lm* is commonly found in the environment and can contaminate a variety of unprocessed and processed foods of both animal and plant origin. Most outbreaks have been linked to unpasteurized dairy products but meat products and ready-to-eat foods also cause outbreaks. Other food sources, such as caramel apples or soybean sprouts, have also been associated with listeriosis. For these reasons, expectant mothers are advised to avoid consuming raw cheeses, fish, and other uncooked foods [1,2].

Listeriosis can manifest as a self-limiting gastroenteritis in immunocompetent individuals, but also as bacteremia and central nervous system infections, primarily in immunocompromised individuals and the elderly, and maternal-neonatal listeriosis in pregnant women [3]. Pregnancy represents a significant risk factor for listeriosis, with an estimated incidence in this group that is 10 to 100 times higher than that in the general population [4,5]. Listeriosis during pregnancy can exhibit a wide range of nonspecific symptoms, including fever, flu-like symptoms, gastrointestinal issues, premature contractions, and preterm labor [6]. It tends to be more prevalent during the second and third trimesters [4,5]. After ingestion, *Lm* can actively penetrate the intestinal barrier, spread through the bloodstream, and eventually cross the placental barrier, resulting in placental and fetal infections [7]. It thrives and spreads intracellularly, causing invasive disseminated disease affecting various organs, including the liver, spleen, central nervous system, and, in pregnant women, the placenta [8]. When *Lm* infections involve the maternal-fetoplacental unit, they can lead to adverse outcomes for the fetus, such as chorioamnionitis, premature labor, neonatal sepsis,

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meningitis, and neonatal mortality [9–11]. Therefore, during pregnancy, vertical transmission of the infection from mother to fetus can have devastating consequences. However, fetal complications often arise even when the mother does not exhibit obvious symptoms, delaying medical intervention [6].

Despite the significant impact of microbial infections on fetal development, there is still a lack of evidence regarding how these pathogens breach the placental barrier to achieve vertical transmission during pregnancy. To understand vertical transmission, it is crucial to comprehend the structure of the human placenta. By the 10th to 12th weeks of gestation, the maternal circulation changes the formation of spiral arteries, and the placenta becomes hemochorial, allowing direct contact between maternal blood and the chorion. This arrangement acts as a protective barrier for the fetus against pathogens present in maternal blood. Syncytiotrophoblasts provide defense against infection through effector mechanisms that operate in a paracrine manner. The invasion of non-phagocytic cells is facilitated by two bacterial surface proteins, internalin A and internalin B [7].

Maternal listeriosis continues to be one of the infections associated with the highest rates of fetal and neonatal morbidity, leading to fetal loss in up to 20% of cases [12]. For these reasons, the rapid detection of *Lm* infection during pregnancy is of utmost importance. This report details a case of rapid diagnosis of *Lm* infection in a preterm newborn by microbiological cultures of cord blood and placenta swabs.

2. Case Presentation

A pregnant woman at 31 weeks of gestation presented to the maternity unit with severe abdominal pain and diarrhea. She had no underlying health conditions or known allergies to medications and had received the COVID-19 vaccine. Her obstetric history included two uncomplicated full-term vaginal deliveries. Toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex (TORCH) screening was negative for acute infections. She mentioned that she had consumed raw salmon sushi. Additionally, she had been experiencing reduced fetal movements for the past 24 h. General physical examination was unremarkable, and vital signs were within normal limits. During abdominal and speculum examinations, a soft gravid uterus and brown vaginal discharge were noted. The cervical os was closed, and there were signs of spontaneous rupture of the membranes with the presence of black meconium. Laboratory tests revealed an elevated white blood cell count (16.3×10^9/L), increased C-reactive protein levels (223 mg/L), and elevated lactate levels (2.0 mmol/L). All serological tests (also for *Lm* antibodies) were negative. Blood cultures were negative. Her clotting parameters were within normal limits.

Suddenly, the patient experienced acute abdominal pain, perineal pressure, and an urge to push, which led to the vaginal delivery of a live infant. Examination of the placenta's cut surface revealed white-grey abscesses, while the membranes exhibited signs of severe acute chorioamnionitis. The microscopic evaluation reported intracytoplasmic rods were evident in the amniocytes within the membranes. Some areas of the membranes displayed calcification, and the placental parenchyma showed multiple intervillous abscess formations, diffuse villus swelling, and focal necrosis in the basal decidua. Additionally, there was a focal increase in trophoblastic giant cells and evidence of focal chorionic plate thrombosis. Cultures of umbilical cord blood and swabs from the placenta's maternal and fetal sides were conducted. Both cultures tested positive for *Lm*. In particular, cord blood resulted positive after only 6 h of incubation in the blood culture system (Bactec, Becton Dickinson). Gram-positive rods were detected by microscopic examination. An aliquot of cord blood sample was taken from the positive bottle, and a molecular syndromic test for positive blood cultures (BCID2 panel, Biofire, Biomerieux) was applied, giving a positive result for *Lm* after only 8 h from the delivery. Positive cultures for *Lm* were also assessed from placenta swabs. The *Lm* strain was susceptible to ampicillin, erythromycin, and meropenem, while it was resistant to trimethoprim/sulfamethoxazole, using the Kirby-Bauer method (antibiotic discs from Liofilchem), and the susceptibility profile was interpreted by EUCAST criteria.

The newborn was hospitalized in the neonatal intensive care unit, where antibiotic therapy was started with ampicillin and gentamicin for 14 days. Upon completion of the pharmacological treatment cycle, the infant had a negative swab test and was completely asymptomatic.

3. Discussion

Lm is a small, facultatively anaerobic, Gram-positive, flagellated, linear motile rod that can survive within human cells. It was initially documented by Hulphers in Sweden in 1911, following its discovery as a causative agent of liver abscesses, monocytosis, and septicemia in rabbits [13]. The first reported case in humans dates back to 1929 [14]. Its current name, "Listeria", was officially adopted in 1940 in honor of Lord Joseph Lister [15]. *Lm* has an incidence rate of 4–7 cases per million in the population [3].

Listeriosis is an uncommon but severe foodborne infection [1,2] that can affect both mothers and neonates, often resulting in fetal loss and neonatal infection. There is an increased susceptibility of the fetus to *Lm* after the first trimester, indicating potential gestational age-specific differences in vertical transmission or deficiencies in cell-mediated immunity [2,8]. It rarely causes invasive disease in immunocompetent individuals and is symptomatically shed by only 1% of healthy individuals [3]. The median incubation period is approximately 21 days, reflecting the time required for maternal sepsis, placental infection, and fetal infection to develop. Maternal infection typically presents with a wide range of nonspecific symptoms, such as fever, decreased fetal movements, and signs of threatened preterm labor, including abdominal pain and vaginal bleeding. Gastrointestinal and flu-like symptoms may also be among the initial presenting symptoms [8]. A cohort study [6] reported uterine contractions, labor, or abnormal fetal heart rate in 75% of cases and fetal loss in 21% of affected women. Fever is not always present and has been reported in 10%–80% of cases [16]. Acute hepatitis is an uncommon manifestation.

Neonatal listeriosis can occur through vertical transmission, inhalation of infected amniotic fluid, transplacental transmission from the maternal circulation, or ascending colonization from the vagina [7]. Hematogenous spread is also possible. Cutaneous eruptions, such as

Table 1
Summary of clinical findings and investigations for listeriosis in pregnancy.

Maternal clinical findings	Fever, flu-like symptoms (general malaise, muscle aches), gastrointestinal symptoms (nausea, vomiting, diarrhea), abdominal pain, premature uterine contractions, reduced fetal movements
Maternal investigations	Physical examination (vital signs, abdominal exam, gynecological exam), complete blood count (leukocytosis), elevated C-reactive protein, serological tests, blood cultures, molecular syndromic tests, placental swabs, amniotic fluid cultures, imaging tests
Fetal and neonatal clinical findings	Respiratory distress, neonatal sepsis, neonatal meningitis, placental and fetal abscesses, black meconium, stillbirth, preterm birth, low birth weight, lethargy or poor feeding
Fetal and neonatal investigations	Ultrasound for fetal well-being assessment, examination of the newborn at birth, histopathological examination of the placenta and membranes, microscopic examination (e.g., detection of gram-positive rods), cord blood cultures, rapid molecular tests, imaging tests for detecting meningitis or abscesses, complete blood count in the newborn (leukocytosis), lumbar puncture for cerebrospinal fluid analysis

purpura, papules, and petechiae, are infrequent symptoms [17], as demonstrated by the present case. Neonatal listeriosis commonly presents with symptoms like septicemia, respiratory distress, or meningitis [10,11]. The "early onset" form refers to symptoms in a neonate at birth or within 48 h of birth, resulting from in-utero infection, and is associated with higher morbidity and mortality. The term "late onset" is used when a neonate develops symptoms more than 48 h after birth, typically caused by infection during passage through the birth canal, and is often associated with meningitis and central nervous system sequelae [4]. *Lm* is commonly susceptible to penicillins, with ampicillin being a suitable and effective choice of medication. In contrast, cephalosporin antibiotics do not exhibit activity against this pathogen. Nevertheless, cephalosporins are frequently administered as an initial treatment for infections not yet identified, often due to non-specific symptoms and the time-consuming nature of blood culture testing [18,19].

Current diagnostic techniques often result in a delayed but specific and accurate diagnosis, taking 3 to 4 days to produce the final report. However, the rapid diagnosis of listeriosis is of utmost importance for the application of the optimal treatment. Laboratory investigations, including a complete blood count, may reveal a high leukocytosis (white blood cell count). A serological test to detect the presence of anti-listerio-lysin-O antibodies in the blood can also be performed. Real-time PCR is highly sensitive for early detection of *Lm*. The gold standard for diagnosing maternal-fetal listeriosis is through placental cultures. There are no standardized management guidelines or recommendations for conducting placental tissue or umbilical cord blood cultures [2]. Table 1 shows the main clinical findings and investigations for both the mother and fetus/newborn.

This case apparently represents the first report of the use of umbilical cord blood and placental swabs for rapid diagnosis of listeriosis. The introduction of novel molecular assays, such as rapid syndromic panels, may also aid in addressing the diagnostic challenges posed by this infection, giving results in a few hours [20,21].

Improved maternal surveillance and targeted health education during pregnancy are necessary to raise awareness of the risk factors associated with *Lm* infection. Pregnant women are advised to always wash fruits and vegetables, store them carefully, and consume mostly cooked foods during pregnancy. It is especially important to avoid the consumption of raw fish and meat [1,2]. Currently, no evidence supports routine blood tests for markers of potential *Lm* infection during regular check-ups. However, in the presence of maternal symptoms or suspicion of infection (such as placental infection or chorioamnionitis), it is advisable to conduct both blood tests for markers indicative of listeriosis and placental swabs on the maternal and fetal sides [22]. In these cases, the rapid diagnosis of *Lm* infection could be a "lifesaver", especially for preterm newborns.

4. Conclusions

Lm infections during pregnancy pose a significant concern, impacting both the mother and the newborn. The present case report underscores the importance of employing innovative molecular biology techniques to achieve an early diagnosis of listeriosis, facilitating the prompt initiation of targeted antibiotic therapy. It highlights the need for updated approaches that include innovative technologies for rapid diagnosis, thereby improving clinical management and maternal-fetal health.

Contributors

Francesco D'Aleo contributed to conception of the case report, acquiring and interpreting the data, and drafting the manuscript.

Attilio Tuscano, Tarcisio Servello, Marcello Tripodi, Carmela Abramo, and Roberta Bonanno contributed to patient care, acquiring and interpreting the data, and revising the article critically for important intellectual content.

Ferdinando Antonio Gulino, Sara Occhipinti, and Giosuè Giordano Incognito contributed to acquiring and interpreting the data, undertaking the literature review, and revising the article critically for important intellectual content.

Luigi Principe contributed to conception of the case report, acquiring and interpreting the data, and drafting the manuscript.

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Conflicts of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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