"Listeria monocytogenes" infection during pregnancy

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ABSTRACT

Listeria monocytogenes is an important pathogenic bacteria found in soil or water being the causative agent of listeriosis, a severe foodborne disease during pregnancy. The outcome can lead up to miscarriage, stillbirth, preterm birth and congenital neonatal infections, under occult or overt illness of the mother. We performed a literature review in the medical database PubMed, searching relevant information regarding listeriosis during pregnancy and neonatal outcome. Higher incidences were observed in ethnic minorities, as a reflection of specific dietary habits and where surveillance is not thoroughly implemented. Also, the infection was most commonly seen during the second or third trimester of pregnancy, with maternal presentation under the form of flu-like or pyelonephritis symptoms, or even asymptomatic. Regarding the neonatal infection, there are two types described according to the way of acquiring the bacteria. The obstetric outcome ranges from premature delivery to miscarriage and stillbirth. Treatment of choice is a combination of ampicillin and aminoglycoside. Despite the advances in the field of infectious diseases, challenges remain to completely understand the mechanism of placental invasion of Listeria monocytogenes and the severe consequences on fetal development.

Keywords: Listeria monocytogenes, listeriosis, pregnancy, early-onset, late-onset, rhombencephalitis

INTRODUCTION

Listeria monocytogenes is an important Gram-positive pathogenic bacterium for newborn, immunosuppressed patients, pregnant women and elderly, being the causative agent of listeriosis. It is the etiological agent of an important foodborne disease with a particular notoriety regarding development during gestational period due the increased incidence of listeriosis, 10 to 100 times higher compared to the non-pregnant population [1-4]. The outcome can lead up to miscarriage, stillbirth, preterm birth, and congenital neonatal infections, with all these complications possibly occurring in the absence of clinical illness of the mother, delaying the medical interventions [5].

There are two forms of neonatal infections: “the early onset” sepsis as a result of maternal chorioamnionitis and “the late onset” meningitis from perivaginal and perianal colonization of the mother with Listeria from the gastrointestinal tract, by transition through the birth canal. For infants with underdeveloped macrophage, the immunity system is impaired and invasive infection is more likely to occur if colonization of the liver, gastrointestinal tract or respiratory system appeared. Treatment of listeriosis involves use of ampicillin together with an aminoglycoside [6].

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Epidemiology

The incidence of maternal-neonatal listeriosis is estimated around 4-10/100,000 pregnant women per year in Europe and North America, with higher incidence rates in countries where surveillance methods are not clearly defined [7-10]. Bearing in mind the foodborne character of this disease, more cases were reported and observed in ethnic minorities, as a reflection of specific dietary habits, for example Hispanic women in the US or African women in France [6,11-13].

Infection is most commonly seen in the first 30 days of life, with the two possibilities of acquiring the infection, as described before or in patients older than 60.

Clinical manifestation is as outbreaks of febrile gastroenteritis syndrome, with an average incubation period of approximately 24 h. As a foodborne pathogen, reported sources included sea food, rice salad, chocolate milk, corn salad, ready-to-eat meats, jellied pork and fresh cheese [6].

Pathophysiology

The mechanism of placental colonization and dissemination to the fetus of Listeria monocytogenes involves the active cross of the epithelial barrier of the intestine after ingestion, translocation via lymph nodes and reach the primary target: organs as the liver and spleen where it can establish infectious foci that can be efficiently cleared by cell-mediated immunity in an immunocompetent human (the subclinical infection). Opposite, in immunocompromised adults, these primary inadequately resolved foci can lead to the dissemination of the bacteria into the bloodstream. It results in febrile bacteraemia and, eventually, invasive infection of the brain [14].

In pregnant women, L. monocytogenes colonizes the uterus in addition to the liver and spleen. While the infection is controlled in the last two organs, the uterine in addition to the liver and spleen. While the infection is controlled in the last two organs, the placenta [17]. Literature suggests that early treatment of the mother who has Listeria sepsis can prevent transplacental infection or treat the fetus in utero, with subsequent delivery of a normal uninfected infant [18]. Unfortunately, this only happens when the medical community is aware of this problem in a particular geographic region through public health reports. Only limited information regarding neurological involvement in pregnant women is mentioned, slight related to immunosuppressed mothers [19].

Diagnosis

Diagnosis of all forms of L. monocytogenes infection depends on germ's isolation from a sterile site, usually blood or cerebrospinal fluid. Particular for pregnant women, stool or vaginal cultures may be positive when selective media for L. monocytogenes are used for culture.

In some forms of central nervous system infection, particularly rhombencephalitis, several samples may need to be obtained to isolate the bacteria. In case of focal neurologic findings, characteristic for rhombencephalitis, prompt computed tomography or magnetic resonance imaging scanning should be performed. The finding of multiple microabscesses in the hindbrain raises suspicion for Listeria rhombencephalitis and empiric treatment should be started.

Fetal and Neonatal Infection

Depending on the mode of acquiring the infection from the mother, current literature describes two types of neonatal infection: “the early-onset” and “the late onset” [20,21].

Due to the impaired cell-mediated immune response to L. monocytogenes in pregnant women along with the decreased gastrointestinal motility seen in pregnancy, it may be a predisposition to invasive listeriosis and subsequent transplacental infection of the infant. Occult or overt bacteraemia can result in chorioamnionitis producing early-onset neonatal listeriosis [22]. This is the mechanism for “early-onset” listeriosis characterized by the delivery of an often premature and severely ill infant. Spontaneous recovery of the mother from Listeria sepsis normally occurs after delivery, but neonates have severe affections. Clinical features include prematurity, sepsis at birth, fever, a diffuse maculopapular cutaneous eruption, and evidence of significant hepatic involvement with jaundice [17]. The mortality rate of early-onset listeriosis, even with treatment, is very high, and stillbirth is also
common in this setting. If recognized before giving birth, appropriate antibiotic therapy can save the infant.

The second type is the “late-onset” listeriosis, when the infant is infected during the transition through a colonized birth canal by maternal gastrointestinal carriage of *L. monocytogenes* without sepsis. In these cases, clinical disease in the infant develops 7 to 14 days later. Direct cutaneous invasion is unlikely, and it is believed that aspiration of the organism into the respiratory tract or swallowing of the organism by the infant may occur during the incubation period. A unique outbreak of neonatal listeriosis in Costa Rica has been described: the vehicle was *L. monocytogenes*-contaminated mineral oil used to clean infants after delivery from healthy mothers, with cross contaminations of shared mineral oil [5].

### OBSTETRICAL OUTCOME

It ranges among the most severe maternal-neonatal infections. In only 5% of cases, the pregnancy course develops well, accomplishing with the delivery of a healthy baby [6]. Information from the MONALISA cohort study indicated several problems: a risk for fetal loss of approximately 25%, an increased risk for preterm birth before 32 weeks of gestation and enhanced changes of affected fetuses with early and late-onset listeriosis [6].

Clinical maternal signs include decreased fetal movements, perception of uterine contractions, or abdominal pain, vaginal bleeding or even premature rupture of membrane, that can lead to chorioamnionitis. Beside the meconium-like amniotic fluid, several abnormalities of the fetal digestive tract can be observed on the ultrasound. They include: fetal ascites, gallbladder enlargement and intestinal echo enhancement [23]. The gestational age correlated with the onset of infection has a fundamental influence on the prognosis of newborns. An infection diagnosed in early pregnancy leads to more than half of the pregnancies ending with abortion, while in infections occurring in the second or third trimester of pregnancy, only a quarter of cases can end up in stillbirths, uterine fetal loss or abortion [24]. Usually, the infection with *Listeria* occurs in the late pregnancy [25].

### REFERENCES

1. Elinav H, Hershko-Klement A, Solt J, Glikman D, Nir-Paz R. Pregnancy-associated listeriosis: many beliefs, few facts. *Lancet Infect Dis.* 2015 Oct;15(10):1128-1130.
2. Elinav H, Hershko-Klement A, Valinsky L, Jaffe J, et al.; Israeli Listeria Study Group. Pregnancy-associated listeriosis: clinical characteristics and geospatial analysis of a 10-year period in Israel. *Clin Infect Dis.* 2014 Oct;59(7):953-61.
3. Pouillot R, Hoelzer K, Jackson KA, Henao OL, Silk BJ. Relative risk of listeriosis in Foodborne Diseases Active Surveillance Network (FoodNet) sites according to age, pregnancy, and ethnicity. *Clin Infect Dis.* 2012 Jun;54 Suppl 5:S405-10.
4. Goulet V, Hebert M, Hedberg C, Laurent E, Vaillant V, De Valk H, Desenclos JC. Incidence of listeriosis and related mortality among groups at risk of acquiring listeriosis. *Clin Infect Dis.* 2012 Mar 1;54(5):652-60.

### TREATMENT

*L. monocytogenes* remains susceptible to most β-lactam antibiotics, except cephalosporins, to which the organism is usually resistant.

When listeriosis is a likely diagnosis, the use of ampicillin or, in penicillin-allergic patients, vancomycin provides empiric coverage for *L. monocytogenes* until the diagnosis is made by culture. A combination of ampicillin and gentamicin is the current therapy of choice for all forms of listeriosis. The duration of treatment for invasive listeriosis has not been studied. Relapses appear to be uncommon, and 2 to 3 weeks of therapy with ampicillin and gentamicin is sufficient for most forms of listeriosis. Rhombencephalitis with abscess formation in the central nervous system may require more prolonged therapy, but there is not available information to support the use of treatment beyond 4 weeks. Still, there is some data suggesting that this combination is not useful and could be harmful. Trimethoprim-sulfamethoxazole is an alternative treatment that has been recommended.

### CONCLUSIONS

Antenatal care and pregnancy plan should inform pregnant women of the potential risks of foodborne diseases including *Listeria monocytogenes*, with particular attention to ethnic minorities, but without any form of discrimination. If suspicion for *Listeria* is high in a pregnant woman with fever, flu-like or gastrointestinal symptoms, blood cultures should be considered rapidly due to the severe consequences on fetal development, even fetal loss. Listeriosis during pregnancy carries a poorer prognosis for fetuses affected during the first trimester compared to second and third one, with more than half of the pregnancies ending with abortion.

Several measures can help reduce the risk of infection: use of fresh food and follow strict rules of storage, cooking food, especially meat thoroughly, washing very good fruits and legumes under running water and keeping good hygiene of the instruments for food preparing.

All in all, despite the advances in science, the mechanism of placental invasion and the severe complications on the fetal development of this pathogenic bacteria cannot be fully explained or understood.
5. Vázquez-Boland JA, Krypтовu E, Scortti M. Listeria Placental Infection. mBio. 2017 Jun 27;8(3):e00949-17.
6. Schlech WF. Epidemiology and Clinical Manifestations of Listeria monocytogenes infection. Microbiol Spectr. 2019 May;7(3).
7. Travier L, Guadagnini S, Gouin E, Dufour A, et al. Acta promotes Listeria monocytogenes aggregation, intestinal colonization and carriage. PLoS Pathog. 2013 Jan;9(1):e1003131.
8. Low JC, Renton CP. Septicaemia, encephalitis and abortions in a housed flock of sheep caused by Listeria monocytogenes type 1/2. Vet Rec. 1985 Feb 9;116(6):147-50.
9. Schlech WF 3rd, Lavigne PM, Bortolussi RA, Allen AC, Haldane EV, et al. Epidemic listeriosis — evidence for transmission by food. N Engl J Med. 1983 Jan 27;308(4):203-6.
10. Büla CJ, Bill J, Glauser MP. An epidemic of food-borne listeriosis in western Switzerland: description of 57 cases involving adults. Clin Infect Dis. 1995 Jan;20(1):66-72.
11. Koch J, Dworak R, Prager R, Becker B, Brockmann S, et al. Large listeriosis outbreak linked to cheese made from pasteurized milk, Germany, 2006-2007. Foodborne Pathog Dis. 2010 Dec;7(12):1581-4.
12. Heiman KE, Garaideh VB, Gronostaj M, Jackson KA, Beam S, Joseph L, et al. Multistate outbreak of listeriosis caused by imported cheese and evidence of cross-contamination of other cheeses, USA, 2012. Epidemiol Infect. 2016 Oct;144(13):2698-708.
13. Law JW, Ab Mutalib NS, Chan KG, Lee LH. An insight into the isolation, enumeration, and molecular detection of Listeria monocytogenes in food. Front Microbiol. 2015 Nov 3;6:1227.
14. Charlier C, Disson O, Lecuit M. Maternal-neonatal listeriosis. Virulence. 2011 Dec;2(11):391-397.
15. Bakardjieva AI, Theriot JA, Portnoy DA. Listeria monocytogenes traffic from maternal organs to the placenta and back. PLoS Pathog. 2006 Jun;2(6):e66.
16. Vázquez-Boland JA, Kuhn M, Berche P, Chakraborty T, Dominguez-Bernal G, Goebel W, González-Zorn B, Wehland J, Kreft J. Listeria pathogenesis and molecular virulence determinants. Clin Microbial Rev. 2001 Jul;14(3):584-640.
17. Mylonakis E, Paliou M, Hohmann EL, Calderwood SB, Wing EJ. Listeriosis during pregnancy: a case series and review of 222 cases. Medicine (Baltimore). 2002 Jul;81(4):260-9.
18. Charlier-Woerther C, Lecuit M. Listeriosis and pregnancy. Presse Med. 2014 Jun;43(6 Pt 1):676-82.
19. Lu B, Yang J, Gao C, Li D, Cui Y, Huang L, Chen X, et al. Listeriosis Cases and Genetic Diversity of Their L. monocytogenes Isolates in China, 2008-2019. Front Cell Infect Microbiol. 2021 Feb 19;11:608352.
20. Srídama V, Pacini F, Yang SL, Moawad A, Reilly M, DeGroot L. Decreased levels of helper T cells: a possible cause of immunodeficiency in pregnancy. N Engl J Med. 1982 Aug 5;307(6):352-6.
21. Wald A, Van Thiel DH, Hoeschtetter L, Gavaler JS, Egler KM, Verm R, Scott L, Lester R. Effect of pregnancy on gastrointestinal transit. Dig Dis Sci. 1982 Nov;27(11):1015-8.
22. Girard D, Leclercq A, Laurent E, Lecuit M, de Valk H, Goulet V. Pregnancy-related listeriosis in France, 1984 to 2011, with a focus on 606 cases from 1999 to 2011. Euro Surveill. 2014 Sep 25;19(38):20909.
23. Hasbún J, Sepúlveda-Martínez A, Haye MT, Astudillo J, Parra-Cordero M. Chorioamnionitis caused by Listeria monocytogenes: a case report of ultrasound features of fetal infection. Fetal Diagn Ther. 2013;33(4):268-71.
24. Centers for Disease Control and Prevention (CDC). Vital signs: Listeria illnesses, deaths, and outbreaks – United States, 2009-2011. MMWR Morb Mortal Wkly Rep. 2013 Jun 7;62(22):448-52.
25. Wang Z, Tao X, Liu S, Zhao Y, Yang X. An Update Review on Listeria Infection in Pregnancy. Infect Drug Resist. 2021 May 26;14:1967-1978.

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