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MEDICAL RESEARCH

Journal of



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Abstract

Objective: To analyze the clinical features, efficacy of antibiotic treatment, and outcome of neonatal listeriosis.

Methods: This was a retrospective study that included all neonates diagnosed with listeriosis between January 2010 and December 2021.

Results: Nine male patients and five female patients were analyzed, including 11 preterm and 3 term infants. The mean gestational age was 34 ± 2.6 weeks (29 + 2-40 + 2 weeks), and the mean birth weight was $2392 \pm 603 \text{ g} (1370-3580 \text{ g})$. The maternal clinical manifestations included fever (13/14 [92.9%]), meconium-stained amniotic fluid (12/14 [85.7%]), and intrauterine fetal distress (11/14 [78.6%]). The neonates presented with fever (14/14 [100%]), generalized maculopapular rash (7/14 [50%]), and convulsions (8/14 [57.1%]). Laboratory tests showed leukocytosis (11/14 [78.6%]), monocytosis (9/14 [64.3%]), elevated C-reactive protein levels (13/14 [92.9%]), and thrombocytopenia (6/14 [42.9%]). Eight patients had central nervous system involvement, and *Listeria monocytogenes* was isolated from the blood in all cases. Empiric antibiotic therapy consisted of a combination of third-generation cephalosporins and penicillin or vancomycin. Four patients died, and 10 patients were cured.

Conclusions: Preterm infants were more susceptible to listeria infection than term infants, with most having multiple organ injuries. Combined antibiotic application improved the effectiveness of treatment.

Keywords

Antibiotic treatment, listeriosis, meningitis, neonate, septicemia, preterm infant

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Introduction

Neonatal listeriosis is the most common form of human listeriosis and is associated with a high case fatality rate of up to 50%.¹⁻³ It is the third leading cause of neonatal meningitis worldwide.^{3,4} Neonatal listeriosis is characterized by early presentation and manifests as bacteremia, pneumonia, and, rarely, meningitis. The late-onset form is mostly observed in term infants born to asymptomatic mothers and presents as meningitis rather than sepsis.⁵⁻⁸

Ampicillin combined with an aminoglycoside is recommended for the treatment of listeriosis. Listeria monocytogenes (L. monocytogenes) is not susceptible to cephalosporins commonly used for empiric treatment of bacterial infections.⁹ Consequently, penicillin or ampicillin is generally included in the empiric antibiotic therapy for infants with bacterial sepsis or meningitis to combat pathogens of most concern, including *L. monocytogenes.*^{1,10} Despite appropriate antibiotic treatment, mortality caused by listeriosis remains high among neonates. Here, we retrospectively analyzed the treatment process and prognosis of neonatal listeriosis to describe the clinical characteristics and relevant treatment experience of this disease.

Methods

This retrospective study was conducted at the First Affiliated Hospital of Xi'an Jiaotong University, Shaanxi, China. Cases of neonatal listeriosis treated between January 2010 and December 2021 were extracted from computerized medical records in the hospital information system using a standardized data collection form. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.¹¹ All patients were diagnosed in accordance with the diagnostic

criteria for neonatal early-onset sepsis established by the Neonatal Group of the Pediatrics Society of the Chinese Medical Association in 2003 for clinical manifestations of infection and L. monocytogenes in blood culture or a sterile body cavity.¹² The study was approved by the ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University (2021-G-86). The information obtained for each patient included the maternal history, patient demographics, clinical presentation, microbiological and laboratory results, imaging results, treatment, and outcomes. Because this was a retrospective observational study, patient informed consent was not required.

After the neonates were admitted to the neonatal intensive care unit (NICU), blood blood culture, gas, routine blood, C-reactive protein, and biochemical examinations were carried out, and any changes were closely monitored. Lumbar puncture was performed in nine patients for cerebrospinal fluid (CSF) examination. Bacterial culture and drug sensitivity tests were performed according to the standard procedures described by the National Clinical Laboratory Operations Guideline.¹³ No formal statistical analysis was applied.

Results

Fourteen neonates, including nine (64%) males and five (36%) females, were identified. Eleven (79%) were preterm and three (21%) were full term, with a mean gestational age of 34 ± 2.6 weeks (range 29 + 2 - 40 + 2 weeks). All infants had a birth weight appropriate for gestational age (range 1370–3580 g). The mothers' ages ranged between 22 and 40 years. Two mothers had a clear history of consumption of uncooked meat, and one mother had a long-term history of exposure to cattle during pregnancy. Thirteen (93%) mothers presented with maternal pyrexia prior to delivery, and three (21%) had flu-like

symptoms. Eight (57%) infants were born via caesarean section, and six (43%) were born via vaginal delivery. In 12 cases (86%), meconium-stained amniotic fluid was observed, and 11 (79%) patients had intrauterine fetal distress. The age of onset was within 3 days in all 14 (100%) infants. All infants developed fever of varying degrees; seven infants (50%) developed a maculopapular rash, and eight infants (57%) presented with intermittent convulsions. Ten (71%) patients presented with asphyxia or respiratory distress requiring endotracheal intubation in the delivery room. An overview of prenatal data and neonatal characteristics is shown in Table 1.

Initial laboratory examinations revealed leukocytosis $(16.5-48.1 \times 10^{9}/L)$ in 11 (79%) and elevated C-reactive protein levels (10.6–183 mg/L) in 13 (93%) infants. elevated mononuclear cell An count (8.2%-44.7%) and thrombocytopenia (26– $92 \times 10^9/L$) were observed in six infants each (64%). Aspartate transaminase and creatine kinase-muscle/brain levels were significantly elevated in 10 (71%) infants, with peak values of 970 U/L and 2279 U/L, respectively. These values gradually normalized after appropriate treatment. CSF examination confirmed purulent meningitis in eight (57%) infants with pleocytosis and hypoglycorrhachia. Furthermore, placental pathology examinations revealed acute chorioamnionitis in three (21%) patients. All infants underwent chest X-ray examination on the day of admission, and the results were consistent with neonatal pneumonia. Cranial magnetic resonance imaging revealed ventriculomegaly of the lateral ventricles, intracranial hemorrhage, or cystic periventricular leukomalacia (Table 2).

On admission to the NICU, 10 (71%) patients required ventilator support, and five (35%) patients were treated with pulmonary surfactant because of respiratory distress. Eight (57%) patients were treated with phenobarbital (loading dose 20 mg/kg,

maintenance dose 5 mg/kg because of intermittent convulsions. However, in Case 4 and 8, convulsion control was not satisfactory, and these patients were successfully treated with midazolam given as an intravenous bolus dose (0.15 mg/kg/ hour) followed by continuous intravenous infusion for 26 hours and 37 hours, respectively. Empiric antibiotic treatment consisted of a third-generation cephalosporin plus penicillin/vancomycin in all cases. After obtaining a positive blood culture for gram-positive bacilli, subsequently identified as L. monocytogenes, meropenem was substituted for the third-generation cephalosporin. L. monocytogenes was isolated from this case series and was susceptible in vitro to penicillin, meropenem, vancomycin, and linezolid. The average duration of antibiotic therapy for the nine (64%) patients treated in our hospital was 27.2 ± 4.7 days (Table 3).

Ten (71%) infants were cured; of whom, nine were treated and discharged from our hospital, and one was transferred to another hospital where they had a full recovery. At follow-up, the surviving infants had good psychomotor development. Among the four patients who died, two patients died in the hospital, and two died after stopping treatment. Case 1 was admitted to the NICU 1 hour after birth with an intrauterine abscess and stench at birth and purulent effusion from the airway, which was managed with tracheal intubation in the delivery room. The patient was treated with cefoperazone sulbactam combined with vancomycin and died of septic shock 35 hours after birth. Cases 2 and 3 were admitted to our hospital at 4 days and 36 hours after birth, respectively. They presented with respiratory and circulatory failure and frequent convulsions on admission and had no response to emergency treatments. Case 14 was admitted to our hospital at 2 hours after birth. She presented a poor response because of severe asphyxia at

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Table

Case No.	: DOB (day/ month/year) Sex	Sex	GA (weeks)	BW MSL (g) grade	Apgar score PROM e (1/5 minutes) (hours) MOD POD	PROM (hours)	MOD	POD	Maternal antenatal symptoms	Age of onset/ admission	Main clinical symptoms
_	26/12/10	Male	33 + 5	2170 III°	2/4	0	S	Our hospital	Fever I day before deliv- ery, intrauterine fetal distress, foul smelling purulent discharge at	0/1 hour	Endotracheal intubation in the delivery room, fever (37.8°C) 3 hours after birth, respiratory distress,
7	20/10/11	Male	39+3	3300 Clear 10/10	r 10/10	2	S	Other hospital	the time of delivery Fever 10 days before delivery, flu-like	72 hours/ 4 days	coaguation disorder, rasin Fever (39.5°C) 72 hours after birth, diarrhea, apnea, convuleion como
m	31/11/13	Female	Female 38+4	2590 III°	01/2	0	S	Other hospital	other hospital Fever 2 days before delivery, flu-like symp- toms, intrauterine fetal distress	0/36 hours	Conversion, Coma Endoctracheal intubation in the delivery room, fever (38.1°C) 24 hours after birth, respiratory failure, shock rash
4	21/02/14	Male	34+2	2700 III°	5/7	0	0	Other hospital	Other hospital Fever 2 weeks before delivery	0/80 minutes	Endotracted intubation in the delivery room, fever (37.9°C) 3 hours after birth, respiratory distress, convulsions, rash, schernderma
ъ	24/07/15	Female	Female 36+5	2650 I°	8/10	0	Д Д	Other hospital	Other hospital Fever 9 hours before delivery, intrauterine feral distract	24 hours/ 48 hours	Fever (37.9°C) 24 hours after birth, severe jaundice,
9	20/06/17	Male	29+2	III°	6/9	20	D	Our hospital	Ford day before deliv- ery, intrauterine fetal distress	15 minutes/ 20 minutes	Endotracted intubation in Endotracteal intubation in the delivery room, fever (38°C) 3 hours after birth, irritability, respiratory dis- tress, convulsion
~	28/07/17	Male	3I + 3	1800 III∘	8/10	0	D	Our hospital	No fever in the antenatal 24 hours/ period 20 min	24 hours/ 20 minutes	Endotracheal intubation in the delivery room, fever (38.5°C) 24 hours after birth, respiratory distress
											(continued)

Case No.DOB (day/ month/year)GABWMSLApgar score and (1/5 minutes)PODPOD817/07/17Male322100III°1/16CSOther hospit930/01/18Female $36+3$ 2920I°9/60CSOther hospit1005/06/18Female $31+5$ 1920II°7/1019CSOur hospital1110/01/19Male $31+5$ 1920II°7/1019CSOur hospital1218/02/19Male $40+2$ 3580II° $5/7$ 0CSOur hospital1315/07/20Male $30-1$ $5/7$ 0CSOur hospital1412/05/21Female $34+2$ 2350II° $4/7$ 0CSOther hospital				
17/07/17 Male 32 2100 III° 1/1 6 CS 30/01/18 Female 36+3 2920 I° 9/6 0 CS 30/01/18 Female 31+5 1920 III° 7/10 19 CS 05/06/18 Female 31+5 1920 III° 7/10 19 CS 10/01/19 Male 40+2 3580 III° 5/7 0 CS 10/01/19 Male 30 1600 Clear 8/10 2 VD 18/02/19 Male 35+1 2450 I° 7/9 0 VD 15/07/20 Male 35+1 2450 I° 7/9 0 VD 12/05/21 Female 34+2 2350 III° 4/7 0 CS		Maternal antenatal D symptoms	Age of onset/ admission	Main clinical symptoms
30/01/18 Female 36+3 2920 ° 9/6 0 CS 05/06/18 Female 31+5 1920 III° 7/10 19 CS 05/06/18 Female 31+5 3580 II° 7/10 19 CS 10/01/19 Male 40+2 3580 II° 5/7 0 CS 18/02/19 Male 30 1600 Clear 8/10 2 VD 18/02/19 Male 35+1 2450 ° 7/9 0 VD 15/07/20 Male 35+1 2450 ° 7/9 0 VD 12/05/21 Female 34+2 2350 II° 4/7 0 CS	C	Other hospital Fever 19 hours before delivery, intrauterine fetal distress	0/3 hours	Endotracheal intubation in the delivery room, fever (39.3°C) 24 hours after birth, respiratory distress, convulsion, hypoelycemia
05/06/18 Female 31+5 1920 11° 7/10 19 CS 10/01/19 Male 40+2 3580 11° 5/7 0 CS 18/02/19 Male 30 1600 Clear 8/10 2 VD 18/02/19 Male 35+1 2450 ° 7/9 0 VD 15/07/20 Male 35+1 2450 ° 7/9 0 VD 15/07/20 Male 35+1 2450 ° 7/9 0 VD 12/05/21 Female 34+2 2350 11° 4/7 0 CS	S	Other hospital Fever I day before deliv- ery, intrauterine fetal distress	15 minutes/ 3.5 hours	Endotracted in the performance of the delivery room, fever (37.8°C) 5 hours after birth, respiratory distress, convulsion, rash, liver and solven edema
10/01/19 Male 40+2 3580 III° 5/7 0 CS 18/02/19 Male 30 1600 Clear 8/10 2 VD 18/02/19 Male 30 1600 Clear 8/10 2 VD 18/02/120 Male 35+1 2450 ° 7/9 0 VD 15/07/20 Male 35+1 2450 ° 7/9 0 VD 12/05/21 Female 34+2 2350 II° 4/7 0 CS	S	r hospital Fever 12 hours before delivery, intrauterine fetal distress	0/25 minutes	Endotracted intrubation in the delivery room, fever (38.5°C) 5 hours after birth, respiratory distress
18/02/19 Male 30 1600 Clear 8/10 2 VD 15/07/20 Male 35+1 2450 1° 7/9 0 VD 15/07/21 Female 34+2 2350 11° 4/7 0 CS	S	r hospital Fever 2 hours before delivery, flu-like symp- toms, intrauterine fetal distress	0/20 minutes	Fever (37.9°C) 7 hours after birth, respiratory distress, convulsion
I5/07/20 Male 35+1 2450 l° 7/9 0 VD I2/05/21 Female 34+2 2350 III° 4/7 0 CS	2 VD	Fe	0/10 minutes	Endotracheal intubation in the delivery room, fever (37.7°C) 3 hours after birth, respiratory distress, rash
12/05/21 Female 34+2 2350 III° 4/7 0 CS	D	Other hospital Fever 21 hours before delivery, intrauterine fetal distress	7 hours/ 8 hours	Fever (38.2°C) 22 hours after birth, convulsion, rash
	S	Other hospital Fever I day before deliv- ery, intrauterine fetal distress	0/2 hours	Endotracheal intubation in the delivery room, fever (37.8°C) I hour after birth, respiratory distress, convulsion, coagulation disorder

Case WBC No. (×10 ⁹ /L) MO (%) 1 7.44 1.6 2 22.9 18 3 3.9 10.3 4 16.6 21 5 23.32 14.4 6 40.04 10.2	Platelet count (×10 ⁹ /L) 171 175 175 136 26 78 78 50	CRP (mg/L) 45.3 58.3	AST peak value (U/L) 181 29	CKMB peak value (U/L)						
	171 175 136 26 78 50	45.3 58.3	181 29		WBC (×10 ⁶ /L)	Protein (g/L)	Glucose (mmol/L)	Blood	CSF	Cranial MRI
	175 136 26 50	58.3	29	2 4 4	d Z	d N	d N	(+)	٩N	NP
	136 26 78 50			51	5050	3.55	3.57	(+)	(+)	NP
	26 78 50	20.1	8	20.6	ЧN	ЧN	ЧN	(+)	NP	NP
	78 50	9.6	60.4	346	665	I.42	0.1	(+)	(-)	Ventriculomegaly
	50	44.8	158	22.5	1413	5.34	 	(+)	(+)	NP
		15.6	78	267	330	e	I.5	(+)	(-)	Hemorrhage of right
										lenticular nucleus and
										lateral ventricle
7 33.47 5.2	144	63.9	39	82	٩N	٩N	ЧN	(+)	٩N	NP
8 16.52 8.2	83	42.9	202	2279	8	0.92	2.34	(+)	(-)	Cystic periventricular
										leukomalacia
9 48.15 44.7	35	183	970	1246	61	4.56	9.1	(+)	(+)	Punctate white matter
										lesion
	92	20.5	25	115	15	3.5	l.6	(+)	(+)	Ventriculomegaly
11 16.3 10.5	225	16.3	35	20	٩N	٩N	ЧN	(+)	٩N	NP
12 20.25 2.2	180	22.5	113	62	30	3.9	1.2	(+)	(-)	NP
13 19.8 12.5	210	36.7	92	15.5	٩N	٩N	ЧN	(+)	ЧN	Ventriculomegaly
14 24.55 11.1	165	79.5	66	011	150	8 [.]		(+)	(+)	NP

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Tabl€	e 3. Treatm	ent and o	Table 3. Treatment and outcome of the 14 cases of neonatal listeriosis.	natal listerios	is.			
Case No.		CGAD (weeks)	Length of hospital CGAD Antibiotics and duration of stay (days) (weeks) use (days)	Pulmonary surfactant	Mechanical ventila- Pulmonary tion and oxygen surfactant intake time (days)	Vasoactive drugs	Anticonvulsant therapy Outcome	Outcome
_	2	34	Cefoperazone, sulbactam 2+, vancomvcin 2	Yes	Invasive 2	Yes	No	Death within 34 hours after admission
2	7	4 0 + 3	Latamoxef 3, vancomycin 5+, ceftriaxone sodium 5	٩	Non-invasive 2,	Yes	Phenobarbital I day	Stopped treatment (death)
m	_	38+5	Ceftriaxone 1+, penicillin 1	No	Invasive I	Yes	No	Death within 23 hours after admission
4	26	38	Mezlocillin I, cefoperazone sulbactam 22+, penicillin 22, meropenem 5+,	Yes	Invasive 7, non-invasive 2, oxygen 11	Yes	Phenobarbital 3 days + midazolam 26 hours	Cured
5	_	36+6	vancomycın 5 Mezlocillin 1+, meropenem 1	٥N	Oxygen I	No	No	Transferred to another hosnital (cured)
9	29	3 3 + 3	Penicillin 26+, meropenem 26	Yes	Invasive I, non- invasive 9, oxvaen 20	Yes	Phenobarbital I day	Cured
Ч	28	35+3	Mezlocillin 2+, latamoxef 2, penicillin 1+, latamoxef 1, penicillin 17+,	Yes	oxygen 3 oxygen 3	° Z	°Z	Cured
ω	23	35 + 2	Latamoxef 1+, penicillin 1, meropenem 2, meropenem 21+ vancomvcin 21	Yes	Invasive 3, non- invasive 7, ovven 3	Yes	Phenobarbital 3 days + midazolam 37 hours	Cured
6	38	4 +6	Ceftazidime 1, penicillin 3+, meropenem 3, vancomycin 13+, meropenem 13, meropenem 21+, linezolid 21	°Z	Invasive 6, non- invasive 1, oxygen 12	Yes	Phenobarbital I day	Cured
9	30	36	Mezlocillin 1+, meropenem 1, penicillin 28+, meropenem 28	°Z	Invasive 5, non- invasive 5, oxygen 3	°Z	Ŷ	Cured

(continued)

Table	Table 3. Continued.	ued.						
Case No.	Length of Case hospital CGAD Antibiotics No. stay (days) (weeks) use (days)	CGAD (weeks)	Length of Case hospital CGAD Antibiotics and duration of No. stay (days) (weeks) use (days)	Pulmonary surfactant	Mechanical ventila- Pulmonary tion and oxygen surfactant intake time (days)	Vasoactive drugs	Anticonvulsant therapy Outcome	Outcome
=	29	44 +3	Penicillin 28+,	No	Non-invasive 2,	No	Phenobarbital 2 days Cured	Cured
12	32	34 + 4	meropenem 28 Mezlocillin I, penicillin 27+, meropenem 27	° Z	oxygen I Invasive 3, non- invasive 8,	Yes	o Z	Cured
13	25	38 +5	Mezlocillin 2+, latamoxef 2, penicillin 22+,	° Z	oxygen 6 Non-invasive 3, oxygen 2	Yes	Phenobarbital I day	Cured
4	_	34 + 3	meropenem 22 Penicillin I+, meropenem I No	No	Invasive I	No	Phenobarbital I day	Stopped treatment (death)
CGAL	D, corrected g	sestational	CGAD, corrected gestational age at discharge; Oxygen, nasal catheter oxygen inhalation.	heter oxygen i	inhalation.			

the time of birth. Although treatment was prompt, frequent convulsions still occurred, and the patient died of coagulation disorder.

Discussion

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L. monocytogenes is a gram-positive, rodshaped bacterium that causes listeriosis. It is usually acquired through the consumption of contaminated food and generally affects those at age extremes, including newborn infants and the elderly, immunocompromised hosts. and pregnant women.^{1,6,14–18} Listeriosis is 20 times more common in pregnant women than in the non-pregnant population and may result in severe outcomes including miscarriage, preterm delivery, sepsis, and fetal and neoinfection.^{8,15–20} The natal correlation between the incidence of pregnancyassociated listeriosis and dietary habits has been documented. Furthermore, a high prevalence of L. monocytogenes has been reported on farms, and ruminant farms are considered a potential reservoir for this foodborne pathogen.^{5,21}

Infection is commonly observed in the third trimester of pregnancy, and the incidence was reported to be two times higher after 28 weeks of gestation.^{1,17,18} The incidence during the first month of pregnancy could be underestimated because of undiagnosed spontaneous or premature abortions.15,20 Fetal infection can occur through transplacental dissemination.⁵ Less frequently, contamination may occur from the lower genital tract of the mother, and infection may occur in the birth canal during labour.^{2,20,22} Cross contamination in the same nursery or outbreaks because of contact with contaminated clinical equipment are rare but have been reported.⁵

Maternal infection may be asymptomatic or may present as a non-specific, flu-like syndrome.^{1,5,17,22} Maternal infection precedes delivery by 2 to 14 days and in

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approximately 70% of cases. Newborns delivered at less than 35 weeks of gestation exhibit a high prevalence of early-onset neonatal listeriosis, 5,20,22 which is consistent with our findings. The most common antepartum presentations were fever (93%), meconium staining of the amniotic fluid (86%), and intrauterine fetal distress (79%). Three mothers presented with flulike symptoms during their pregnancy, and the three women who gave birth in our hospital showed acute chorioamnionitis in placental pathology examinations. This finding emphasizes the importance of placental pathology evaluation in suspected cases.^{19,23} Clinicians should pay full attention to women with high risk factors such as fever, influenza-like symptoms, a history of intrauterine distress, and amniotic fluid contamination during delivery. Placental tissue and vaginal secretions should be collected in a timely manner during delivery for clinical diagnosis and treatment.

Neonatal listeriosis is described to have two distinct infection forms, early-onset and late-onset infection.⁷ The signs of early sepsis are apparent from birth, with a mean symptom onset at 1.5 days of life.^{4,5,19,24} The onset time was within 3 days after birth for all patients in our study. The most common symptoms included septicemia and respiratory symptoms.^{6,15,20} The high frequency of respiratory tract involvement may result from inhalation of contaminated amniotic fluid.⁴ In our study, most patients developed asphyxia or respiratory distress shortly after birth, requiring endotracheal intubation in the delivery room. These patients also had septic shock, and blood gas analysis suggested various levels of respiratory/metabolic acidosis. The severity of acidosis was correlated with the severity of infection, respiratory distress, and insufficiency of tissue perfusion.

Blood culture confirmed the diagnosis in all cases. Incorrect determination of culture

results because of the resemblance of the organism to diphtheroids, cocci, or diplococci and the ability to decolorize during the gram staining procedure contributes to the paucity of confirmed diagnoses of neonatal listeriosis.^{2,,3,19,25} Therefore, isolation of diphtheroids from the blood or CSF should alert clinicians to the possibility of L. monocytogenes infection.²⁶ Even in the absence of positive culture results, this infection should be highly suspected in patients presenting signs of early sepsis, respiratory distress, pneumonia, and meconium-stained amniotic fluid at delivery.¹⁰ Serological studies are not helpful in the diagnosis of listeriosis. However, they are important to assess the severity of infection. The hemogram results in our study showed that leukocytosis and thrombocytopenia were common in patients. Neonatal listeriosis mainly occurs in premature infants, who are more susceptible to brain injury because of immature cerebrovascular development. coagulation disturbances. hypoxia, and inflammatory reactions. Therefore, in the diagnosis and treatment of listeriosis, it is important to check for signs and symptoms of central nervous system involvement, such as assessments of the state of consciousness, muscle tension, primitive reflexes, head circumference. and size of the anterior fontanelle. Neuroimaging evaluation, including bedside cranial ultrasound and cranial magnetic resonance imaging, is recommended to monitor the occurrence and evolution of brain damage.

The first-line drugs used for the treatment of listeriosis are penicillin, ampicillin, or amoxicillin, which are often used in combination with an aminoglycoside, classically gentamicin, because of their synergistic bactericidal effects *in vitro*.^{1,5,7,9,14,15,20} Although this combination therapy has failed to show any significant advantage in animal models, some studies have reported a decreased risk of death with this combination. In the case of penicillin allergy or unresponsiveness, vancomycin or trimethoprim/sulfamethoxazole can be used as an alternative therapy.^{18,25} Vancomycin is ineffective for neurolisteriosis because of its inability to cross the blood-brain barrier.¹⁴ In contrast, trimethoprim/sulfamethoxazole has extracellular and intracellular bactericidal activity and penetrates well central nervous system.²⁶ into the However, it is contraindicated in neonates because of the potential risk of bilirubin displacement and kernicterus. Linezolid is also considered adequate for the treatment of neurolisteriosis because of its elevated CSF and intracellular concentrations. Even though the data are currently limited to support routine administration of this drug for neurolisteriosis, several case reports with favorable outcomes following linezolid therapy have been documented.^{14,27} Meropenem has a lower minimum inhibitory concentration against L. monocytogenes than that of ampicillin. However, one study reported a higher mortality rate in patients receiving meropenem than in those receiving amino penicillin and benzyl penicillin, but the limited number of neonates and children enrolled in the study does not qualify its conclusion for this age group.^{9,14} In our study, despite *in vitro* susceptibility results, Case 9 failed to respond to penicillin/vancomycin combined with meropenem and was successfully treated with linezolid combined with meropenem. The recommended duration of treatment is 2 weeks for bacteremia patients with normal CSF, and for severe cases of infection or meningitis, the treatment period should be no less than 3 weeks because relapses have been documented with shorter durations of therapy.^{2,19,22,25} The treatment should be extended to at least 6 weeks for patients with brain abscess.³

In conclusion, neonatal listeriosis is a serious infection associated with a high mortality rate. Early diagnosis and prompt treatment with appropriate antibiotics are essential for a good neonatal outcome. Careful interpretation of culture results and a high index of suspicion are essential for an early and accurate diagnosis. Treatment with a combination of antibiotics improves the bactericidal effect and helps reduce mortality. Finally, educating pregnant women on dietary habits and establishing other preventive strategies are crucial to reduce the frequency of neonatal listeriosis.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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