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【 CASE REPORT 】

Systemic Lupus Erythematosus Complicated with Listeria Monocytogenes Infection in a Pregnant Woman

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Abstract:

A 41-year-old woman with systemic lupus erythematosus (SLE) was admitted to our hospital due to a fever at 35 weeks of pregnancy. Laboratory testing revealed a low platelet count and elevated liver enzymes. Emergency Caesarean section was performed due to the risk of SLE exacerbation or hemolytic anemia, elevated liver enzyme, and low platelet count syndrome. Based on the blood culture results, the patient was diagnosed with Listeria monocytogenes bacteremia. She was treated with ampicillin and eventually recovered, and the neonate did not have any complications. Pregnant women with SLE are at risk of complications. Listeriosis should be monitored for and, if found, managed appropriately.

Key words: Listeria monocytogenes, listeriosis, pregnancy, SLE

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Introduction

Listeriosis is a rare foodborne infection that can be severe in pregnant women, fetuses, immunocompromized hosts, and elderly individuals (1). Furthermore, this infection is not common among individuals with systemic lupus erythematosus (SLE) and is often mistaken for an SLE flare due to its nonspecific clinical manifestations (2).

We herein report a case of SLE complicated with Listeria monocytogenes (LM) infection in a pregnant woman wherein the infection was difficult to distinguish from SLE-related complications, such as disease flare and hemolytic anemia, elevated liver enzyme, and low platelet count (HELLP) syndrome.

Case Report

A 41-year-old woman with SLE was admitted to our hospital. The patient had given birth to her second child via Caesarian section at 33 years old. There was no history of abortion or miscarriage. At 38 years old, the patient had been diagnosed with SLE due to malar rash, photosensitivity, thrombocytopenia, and positivity to antinuclear antibody and anti-ds-DNA antibody. She had been treated with oral prednisolone (PSL) 30 mg/day for thrombocytopenia and oral hydroxychloroquine (HCQ) 300 mg/day. Her disease activity was stable with HCQ treatment, and visceral organ damage had not been observed within the past few years. She became pregnant again at 40 years old, and her pregnancy had been progressing well. However, at 35 weeks and 5 days of pregnancy, the patient was hospitalized due to a fever and general malaise that had lasted for the past 2 days.

Upon admission, the patient's vital signs were as follows: blood pressure, 122/79 mmHg; pulse rate, 117 beats/min; respiratory rate, 17 breaths/min; and temperature, 38.3℃. The patient's quick Sequential Organ Failure Assessment (qSOFA) score was 0, and her SOFA score at baseline was 3, subsequently increasing to 4. A laboratory examination was performed on the day after admission, and results

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Table. Patient Laboratory Data on the Next Day after Admission (Reference Range, Adults).

<Hematology>			<Coagulation>		
White blood cells	6,110 /μL	(3,860-8,600)	PT	89.4 %	(70.0-130.0)
Neutrophil	74.6 %	(48-61)	APTT	38.3 sec	(23.7-37.2)
Lymphocyte	18.3 %	(25-45)	Fiblinogen	359.1 mg/dL	(160-300)
Monocyte	6.7 %	(4-7)	D-dimer	2.4 μg/mL	(0-1)
Eosinophil	0.2 %	(1-5)			
Basophil	0.2 %	(0-1)	<Immunology>		
Red blood cells	3.55×10^4 /μL	($3.86\text{-}4.92\times10^4$)	Anti-nuclear Ab	80×	(<40)
Hemoglobin	10.6 g/dL	(11.6-14.8)	Anti-ds DNA Ab	3.8 IU/mL	(<10)
Hematocrit	30.8 %	(35.1-44.4)	Anti-U1 RNP Ab	<0.5 U/mL	(<3.5)
Platelet	3.9×10^4 /μL	(15.8-34.8)	Anti-Sm Ab	25.7 U/mL	(<7.0)
Schistocyte	0.3 %		Anti-SS-A/Ro Ab	<0.5 U/mL	(<7.0)
			Anti-SS-B/La Ab	<0.5 U/mL	(<7.0)
<Biochemistry>			Anti-cardiolipin IgG Ab	<8.0 U/mL	(0-10)
Total bilirubin	0.4 mg/dL	(0.4-1.5)	Anti-CL-β2GP1 Ab	<0.7 U/mL	(0.0-3.5)
AST	50 IU/L	(13-30)	Lupus anticoagulant	1.2 Ratio	(<1.2)
ALT	38 IU/L	(7-23)	C3	109.9 mg/dL	(73-138)
LDH	192 IU/L	(124-222)	C4	14.1 mg/dL	(11-31)
ALP	655 IU/L	(106-322)	PA-IgG	54.4 $ng/10^7$	(<30.2)
Urinary acid	3.7 mg/dL	(2.6-5.5)	Direct Coombs test	Positive	
Blood urea nitrogen	6 mg/dL	(8-20)			
Creatinine	0.46 mg/dL	(0.46-0.79)	<Urinary>		
C-reactive protein	3.55 mg/dL	(0.00-0.14)	Protein	(±)	
Procalcitonin	0.28 ng/mL	(<0.05)	Occult blood	(-)	
Haptoglobin	<3.0 mg/dL	(19-170)	Cast	(-)	
Ferritin	47.5 ng/mL	(12-60)			
ADAMTS-13 activity	59 %	(>10)			
ADAMTS-13 inhibitor	<0.5 BU/mL	(<0.5)			
HBs Ag	0 IU/mL	(<0.05)			
HCV Ab	0.1 C.O.I	(<1.0)			

AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, Ag: antigen, Ab: antibody, PT: prothrombin time , APTT: activated partial thromboplastin time , CL: cardiolipin, PA: platelet-associated, HBs Ag: hepatitis B antigen, HCV Ab: hepatitis C antibody

showed a progressive decrease in the platelet count level (39,000/μL), low haptoglobin level (<3.0 mg/dL), mildly elevated liver enzyme levels (aspartate aminotransferase level, 50 IU/L; alanine aminotransferase level, 38 IU/L), and normal proportion of schistocytes (0.3%) (Table). Exacerbation of SLE or HELLP syndrome was suspected due to rapidly progressing thrombocytopenia and hemolytic anemia.

Emergency Caesarean section was performed at 35 weeks and 6 days of pregnancy due to the risk of difficulty in maintaining the pregnancy. There were no findings suggestive of chorioamnionitis. The patient started taking oral PSL 50 mg/day for 7 days due to the risk of SLE flare-up and ceftriaxone 1 g twice a day empirically after surgery. Gram-positive bacilli were detected in the two sets of blood culture collected on admission (Figure A). Thus, treatment with intravenous ampicillin (ABPC) 2 g three times a day was started, and oral PSL was tapered. We then found that the bacillus in the culture on blood agar was LM (Figure B).

A cerebrospinal fluid examination revealed no cell proliferation or bacteria. The patient was treated with ABPC for 14 days, and her general condition improved. Thrombocytopenia, elevated liver enzyme, hemoglobin, and haptoglobin normalized 10 days after the treatment. Furthermore, the neonate showed no signs of infection after birth. The patient was discharged on day 19 of hospitalization. Six months after giving birth, her SLE activity had subsided after treatment with HCQ but without PSL.

Discussion

Listeriosis is a rare infection, with an incidence of 0.65/1,000,000 individuals in Japan (1), and it has a high mortality rate at 16% among foodborne infections (3). LM is widely found in the environment and is transmitted orally on a daily basis. In foods, it is particularly frequently found in raw food (vegetables, milk, and meat) and processed food (meat, cheese, sausage, ham, and smoked salmon) (4). LM grows under normal storage conditions in refrigerators because it can survive in a wide range of temperatures (−0.4-45℃) (3). High-risk individuals must therefore take preventive measures, such as washing fresh vegetables and fruits, not storing raw and processed food in the refrigerator for a long time, heating foods before eating them, and storing foods in the freezer. In the present case, the patient had con-

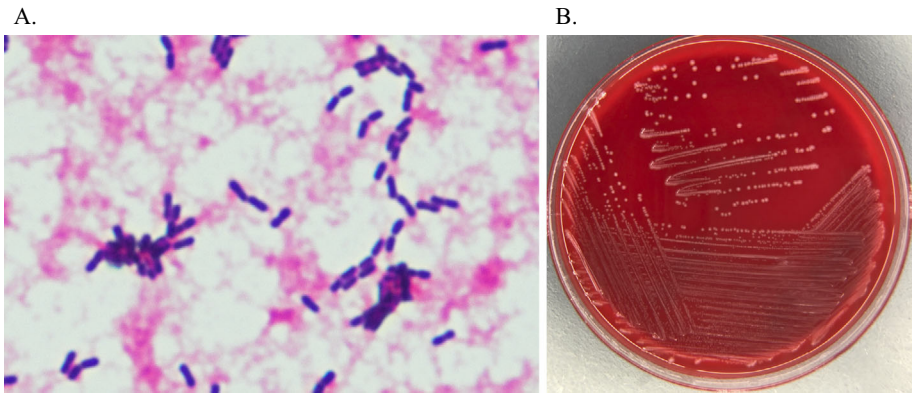

Figure. Gram staining of the blood culture revealed the presence of Gram-positive rod bacilli (A). Colony on the blood agar plate cultured at 30 °C for 3 days (B).

sumed cheese that had been stored in the refrigerator at one week prior to the onset. Whether or not the cheese had been contaminated with LM could not be validated because no sample was available. However, no other possible sources of infection other than the cheese were identified. The patient might therefore have been infected by consuming contaminated cheese.

Through oral transmission, LM infiltrates the small intestine, proliferates in the intestinal mucosa, and spreads to the whole body via the lymph and blood flow. Because this bacterium is an intracellular parasite, biological defense is mainly dependent on cellular immunity (5, 6). Immunocompromised hosts (e.g. those with hematological malignancies and human immunodeficiency virus infection, those who received organ transplantation, and those on corticosteroid treatment), neonates <1 month old, pregnant woman, and elderly individuals over 60 years old are at a higher risk than others of developing listeriosis, which can be particularly severe (7). LM has an affinity for the central nervous system, where it causes encephalitis and meningitis (8). Listeriosis is most likely to occur in the third trimester of pregnancy (9) due to the fact that the levels of progesterone, which suppresses cell-mediated immunity, are highest at 26-30 weeks of pregnancy (10). In addition, the fetus can be infected via the placenta, which leads to sepsis, or via the birth canal, which leads to postnatal meningitis (8). Notably, ABPC is the primary choice for the treatment of LM because these bacteria are generally resistant to cephalosporin antibiotics (11).

LM infection is a rare complication in patients with SLE. In most case reports, the bacteria were detected in blood cultures and cerebrospinal fluid (2). Disease-related immunological dysfunction itself and immunosuppressive treatment are associated with a high risk of infection among patients with SLE (12). In the current case, the patient was not taking any immunosuppressants. However, in addition to the predisposing conditions of SLE, an impaired immune function during late pregnancy may be a risk factor for LM infection.

Pregnant women with SLE are at a higher risk of conditions, such as disease flare, pre-eclampsia, fetal loss, premature birth, intrauterine growth restriction, and HELLP syndrome, than others (13). HELLP syndrome is generally diagnosed when lactate dehydrogenase (LDH) >600 IU/L, aspartate transaminase (AST) >70 IU/L, and platelet count < 100,000/μL are observed (Saibai's criteria) (14). However, not all of the criteria are always met. In such cases, in addition to pre-eclampsia, there is also a concept called partial HELLP syndrome, which is diagnosed when elevated liver enzymes [AST or alanine aminotransferase (ALT) >40 IU/L] and thrombocytopenia (<150,000/μL) are noted. Partial HELLP syndrome can progress to HELLP syndrome over time. In the present case, emergency Caesarean section was performed due to the risk of SLE flare or HELLP syndrome based on progressive thrombocytopenia and elevated liver enzyme levels. LM infection is often difficult to differentiate from SLE-related complications due to the lack of specific findings. In the current case, the administration of ABPC was started immediately after the detection of Gram-positive bacilli in the blood culture. The symptoms then improved, and severe organ damage and fetal infection were not observed.

Conclusion

We encountered a case of SLE complicated with LM bacteremia during late pregnancy. Not only complications associated with SLE but also listeriosis during pregnancy must be considered. Pregnant women and immunocompromised hosts are at a higher risk of listeriosis than others. Thus, such infection, which can be transmitted from raw and processed foods, should be monitored for and, if found, managed appropriately.

Written informed consent was obtained from the patient prior to the publication of this article.

The authors state that they have no Conflict of Interest (COI).

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