Two Cases of Neonatal Lupus and Literature Review

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Neonatal lupus is a rare rheumatic disease. Clinical manifestations include characteristic annular or macular rashes, congenital heart block, cytopenias, and hepatitis. Neonatal lupus is caused by transmission of maternal immunoglobulin G autoantibodies such as anti-SSA/Ro antibody or anti-SSB/La antibody to the fetus through the placenta. We report two cases of neonatal lupus. The first case refers to a 18-day-old male with annular rashes on both cheeks, neutropenia, positive tests for antinuclear antibody, anti-SSA/Ro antibody, and anti-SSB/La antibody. His mother was diagnosed with systemic lupus erythematosus characterized by positive tests for antinuclear antibody, anti-SSA/Ro antibody, and anti-SSB/La antibody. The second case represents a 32-day-old female with annular rash on both hands, soles, and the genital area, neutropenia, hepatitis, positive tests for antinuclear antibody, and anti-SSA/Ro antibody. Skin punch biopsy was conducted. Her mother did not have history of connective tissue diseases. We referred her mother to the division of rheumatology of the department of internal medicine. The mother was suspected with primary Sjögren’s syndrome because of arthralgia and dry eye symptoms with positive tests for antinuclear antibody, anti-SSA/Ro antibody, anti-SSB/La antibody, and rheumatoid factor. It is necessary to suspect neonatal lupus in neonates or infants with characteristic annular rash with or without maternal history of connective tissue disorders.

Keywords: Neonatal lupus; Autoantibodies; Exanthema

INTRODUCTION

Neonatal lupus (NL) is a rare disease with a prevalence of 1 out of 20,000 live births. The disease occurs when autoantibodies such as anti-SSA/Ro antibodies (Ab) or anti-SSB/La Ab are transmitted from the mother to the fetus through the placenta [1-3]. NL appears in babies born to mothers with systemic lupus erythematosus (SLE), Sjögren’s syndrome, and other collagen vascular diseases [2].

Symptoms of NL include annular skin rash, anemia, neutropenia, hepatitis, and congenital heart block. Diagnosis is based on clinical symptoms and the blood tests including autoantibodies of mother and baby. Treatment depends on the symptoms, and cardiac function should be monitored periodically to confirm cardiac complications. NL usually has a favorable prognosis, and in most cases, it improves naturally. However, a congenital heart block often requires a pacemaker. About 60% of patients with congenital heart block require a pacemaker and deaths may result following the failure of the pacemaker [1].

We experienced two cases of NL and report it with a review of literature (Table 1).

CASE REPORT

1. Case 1
A 23-day-old male neonate visited the pediatric outpatient clinic in Soonchunhyang University Cheonan Hospital because of a red, round ring-shaped rash on both cheeks. There was no specific family history. This pediatric patient was born healthy without any problems with a weight of 2,860 g on the third day of the 40th
Week, but several red papuloid rashes appeared on both cheeks on the 18th day after birth. On the 25th day after birth, the diameter of the rashes ranged from approximately 5 to 15 mm, the central part of the round rash turned purple. The outer rim of the rash slightly bulged, changed to the shape of a target or round ring, and some rashes fused together (Fig. 1).

The absolute neutrophil count (ANC) was decreased to 710/mm³ in complete blood count. The blood chemistry test showed that aspartate aminotransferase (AST)/alanine aminotransferase (ALT) was within the normal range of 46/25 IU/L (normal range, 22–63/12–45 IU/L), and antinuclear antibody (ANA) was positive (qualitative test, speckled type). At that time, the patient was diagnosed with erythema multiforme and was administered antihistamine. The color of the rash became faint and slightly improved.

On the 38th day after birth, the color of rashes on both cheeks became prominent and darker, and the rashes worsened again. In the blood test conducted at that time, anti-SSA/Ro Ab was 191.96 U/mL (<7, negative; 7–10, equivocal; >10, positive) and anti-SSB/La Ab was 167.26 U/mL (<7, negative; 7–10, equivocal; >10, positive), and the results were positive. We also found that the mother of the boy had been diagnosed with SLE at the other hospital’s division of rheumatology, and the mother’s blood test showed anti-SSA/Ro Ab positive (274.50 U/mL [<7, negative; 7–10, equivocal; >10, positive]), and anti-SSB/La Ab positive (179.06 U/mL [<7, negative; 7–10, equivocal; >10, positive]). Based on these findings, we diagnosed the boy as NL. Echocardiography and electrocardiography (ECG) findings were normal.

Skin rash disappeared without scarring on the 122nd day after birth, and ANA was normal at age 3 months, and neutropenia was normal at age 6 months. Anti-SSA/Ro Ab and anti-SSB/La Ab were positive at age 6 months and changed to negative with 5.4 U/mL and 5.2 U/mL at age 12 months, respectively. The boy is currently undergoing follow-up observations.

2. Case 2

A 56-day-old female infant visited the pediatric outpatient clinic because of a round-shaped rash around the hands, soles and the genital area. The mother of the girl had no history of connective tissue disease. The patient was born healthy at second day of 38th week, and weighed 3,380 g. The skin rash started around the hands, soles and the genital area on the 32nd day after birth. In the blood test conducted at that time, anti-SSA/Ro Ab was 191.96 U/mL (<7, negative; 7–10, equivocal; >10, positive) and anti-SSB/La Ab was 167.26 U/mL (<7, negative; 7–10, equivocal; >10, positive), and the results were positive. We also found that the mother of the girl had been diagnosed with SLE at the other hospital’s division of rheumatology, and the mother’s blood test showed anti-SSA/Ro Ab positive (274.50 U/mL [<7, negative; 7–10, equivocal; >10, positive]), and anti-SSB/La Ab positive (179.06 U/mL [<7, negative; 7–10, equivocal; >10, positive]). Based on these findings, we diagnosed the boy as NL. Echocardiography and electrocardiography (ECG) findings were normal.

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## Table 1. Two cases of neonatal lupus: a clinical profile

| Variable                        | Case 1                                      | Case 2                                      |
|---------------------------------|---------------------------------------------|---------------------------------------------|
| Sex                             | Male                                        | Female                                      |
| Age                             | 25 days old                                 | 32 days old                                 |
| Skin rash                       | Annular rash on both cheeks                 | Annular rash on both hands, sole and genital area |
| Hematologic problem             | Neutropenia                                 | Neutropenia, anemia                         |
| Aspartate aminotransferase/alanine aminotransferase (IU/L) | Not elevated                               | Not elevated                               |
| Congenital heart block          | None                                        | None                                        |
| Antinuclear antibody            | Positive                                    | Positive                                    |
| Patient's autoantibodies        | Anti-SSA/Ro (+), anti-SSB/La (+)             | Anti-SSA/Ro (+), anti-SSB/La (-)             |
| Maternal autoantibodies         | Anti-SSA/Ro (+), anti-SSB/La (-)             | Anti-SSA/Ro (+), anti-SSB/La (+)             |
| Maternal rheumatic disease      | Systemic lupus erythematosus                | Sjögren’s syndrome                          |

![Image](Fig. 1. A 4-week-old male baby showed annular rash on both cheeks on the 18th day after birth. His mother had systemic lupus erythematosus history. The skin lesion improved on the 88th day after birth. (A) 25th day after birth. (B) 28th day after birth. (C) 68th day after birth. (D) 122nd day after birth.)
pneumonia in addition to skin rash on the 33rd day after birth.

At the time of admission, anemia (hemoglobin, 9.5 g/dL [normal lower limit, 10.0 g/dL]; hematocrit, 27.1% [normal lower limit, 31%]; neutropenia [ANC, 780/mm³]; and increased ALT [AST/ALT, 61/54 IU/L; normal value, 22–63/12–45 IU/L]) were detected. Respiratory syncytial virus was detected via polymerase chain reaction. The girl was discharged after improvement in the respiratory symptoms whereas the skin rash persisted.

On the 56th day after birth, round-shaped skin rashes appeared on the forehead, neck, palms, and soles (Fig. 2). At this time, hemoglobin was 9.5 g/dL (normal lower limit, 10.0 g/dL) and hematocrit was 27.6% (normal lower limit, 31%), and ANC was reduced to 900/mm³, AST/ALT increased to 68/71 IU/L, and ANA was positive (qualitative test, speckled type).

The blood test results on the 66th day after birth showed positive for anti-SSA/Ro Ab (> 600 U/mL), and negative for anti-SSB/La Ab and U1-ribonucleoprotein Ab. We suspected NL and transferred the baby’s mother to the division of rheumatology for evaluation of connective tissue disease. She had not visited a rheumatologist until then.

We performed a skin punch biopsy on the patient on the 75th day after birth. It revealed the hyperkeratosis, basal cell layer hydropic degeneration, and increase in dermal mucin, consistent with NL findings (Fig. 3). The mother presented dry eye symptoms and arthralgia, with results indicating positive for ANA (1:80), rheumatoid factor (228.8 IU/mL; reference range, 0–15 IU/mL), anti-SSA/Ro Ab (> 600 U/mL; reference range, < 7 U/mL), and anti-SSB/La Ab (26 U/mL; reference range, < 7 U/mL), respectively. Therefore, she was diagnosed as the primary Sjögren’s syndrome and prescribed anti-malarial drugs.

The skin symptoms were disappeared on the 120th day after birth. AST/ALT, ANC, and ANA levels were normalized at 7 months of age. The patient tested positive for anti-SSA/Ro Ab up to 10 months of age and turned negative (< 1 U/mL) at age 18 months. ECG conducted till the age of 6 months revealed no congenital heart block. The patient is currently under follow-up in the outpatient clinic.

**DISCUSSION**

NL is a rare disease in infants caused by autoantibodies trans-
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Immediate treatment of NL includes blood tests such as complete blood count and liver function tests. The mother was diagnosed with primary Sjögren syndrome, which necessitated referral of the mother to the division of rheumatology. In case 2, NL diagnosis of the baby was confirmed by specific question. In case 2, NL diagnosis of the baby was confirmed by specific question. In case 1, we didn’t know mother’s SLE history at first, but we came to know that through specific question. In case 2, NL diagnosis of the baby was followed by referral of the mother to the division of rheumatology. The mother was diagnosed with primary Sjögren’s syndrome, because of arthralgia and dry eye symptoms with positive ANA, anti-SSA/Ro Ab, anti-SSB/La Ab, and rheumatoid factor.

We should suspect NL when neonates or infants manifest typical skin rash, with or without a maternal history of connective tissue disorders.

Liquefactive degeneration, follicular plugging, and dermal perivascular infiltrates with lymphocyte predominance, although skin biopsy is not always needed [10,11]. If maternal anti-SSA/Ro Ab or anti-SSB/La Ab are positive, fetal echocardiograms should be routinely monitored on a weekly or bi-weekly basis starting from 16–18 weeks of gestation [12].

Fluorinated corticosteroids such as dexamethasone and betamethasone may be used in prenatal mothers to prevent congenital heart block in fetal period. However, risks such as maternal infection, hypertension, avascular osteonecrosis, insulin resistance, gestational diabetes, oligoamnios, and fetal growth retardation are increased. In addition, intravenous immunoglobulin injections, exchange transfusions, and hydroxychloroquine may be used [13,14]. After birth, echocardiography and electrocardiogram should be conducted at 1 month and 1 year after birth [15] despite normal fetal echocardiogram. In case of complete heart block, a pacemaker insertion may be warranted [1].

Conservative treatments are indicated depending on the symptoms. Most skin symptoms improve without scarring, without the need for special treatment. Topical steroid ointment, anti-malarials, and laser treatments are available. In addition, sunscreens and protective clothing are beneficial because exposure to sunlight can worsen the lesion [1].

In the cases reported here, the authors administered systemic steroids considering the possibility of heart block or invasion of internal organs. In the future, guidelines for the use of steroids are needed. It is difficult to find literature about when anti-SSA/Ro Ab and anti-SSB/La Ab turn negative. In case 1, anti-SSA/Ro Ab and anti-SSB/La Ab were negative at age 12 months. In case 2, anti-SSA/Ro Ab was positive until age 10 months and turned negative at age 18 months.

Medical history of the mother is crucial for the diagnosis, but caution is needed because approximately half of the mothers have no symptoms at the time of their diagnosis [2]. In case 1, we didn’t know mother’s SLE history at first, but we came to know that through specific question. In case 2, NL diagnosis of the baby was followed by referral of the mother to the division of rheumatology. The mother was diagnosed with primary Sjögren’s syndrome, because of arthralgia and dry eye symptoms with positive ANA, anti-SSA/Ro Ab, anti-SSB/La Ab, and rheumatoid factor.

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Worsening of the lesions and appearance of new skin lesions in the cases reported here were controlled by systemic therapy of prednisolone. In case 1, the dosage of prednisolone was increased from 0.5 mg/kg/day to 1 mg/kg/day followed by tapering. In case 2, prednisolone was increased from 0.5 mg/kg/day to 2 mg/kg/day. In both cases, prednisolone was stopped after 6 months because of increased side effects. In case 2, prednisolone was stopped at age 12 months and methasone was started because of severe rash. In case 1, methasone was started at age 10 months and stopped at age 18 months. In case 2, methasone was started at age 12 months and stopped at age 18 months.

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