Siblings with neonatal lupus erythematosus

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Siblings with neonatal lupus erythematosus

Abstract

Neonatal lupus erythematosus (NLE) is a rare disease that is caused by an abnormal immune response. While reported cases of NLE among siblings have demonstrated similar manifestations, we present 2 cases of cutaneous NLE occurring in siblings with significantly different cutaneous manifestations, an uncommon occurrence. The two-child policy led to more families having a second child, so the incidence rate of NLE in siblings may increase too.

KEYWORDS

neonatal lupus erythematosus, cutaneous manifestations, siblings

1 | INTRODUCTION

Rarely seen, Neonatal Lupus erythematosus (NLE) is characterized by cutaneous lesions and/or congenital heart block in infants at birth or shortly afterwards. This syndrome is linked to the mother's transplantation of maternal auto antibodies (usually anti Ro/SS-A, La/SS-B or rarely anti-U(1)RNP). Mothers of affected children may have signs of Sjögren's Syndrome or other Connective Tissue Diseases, or they may be asymptomatic.[1]

In light of decreasing global fertility rates, numerous nations are implementing measures to encourage higher fertility rates and encourage more families to have a second child.[2] Therefore, it is estimated that the incidence rate of NLE in siblings will increase too, so we should raise the awareness of NLE in siblings, which is very important for the monitoring, evaluation, diagnosis and management of NLE.

2 | METHODS We collect clinical data of two siblings with NLE, including their medical history, clinical images, and results from laboratory and pathological examinations. We aim to compare and analyze the differences in clinical manifestations between the siblings, as well as track their prognosis.

3 | CASE REPORTS

3.1 | Case 1

In October 2015, a 15-day-old girl (patient 1) was presented at the dermatology clinic with erythema on her body. She was born full term to a 29-year-old Chinese woman via normal spontaneous vaginal delivery.

Physical examination revealed that targetoid erythematous plaques with central atrophy and raised margins were present on her face (Fig. 1a), trunk, arms, legs, palms, and soles of her feet (Fig. 1b). Laboratory studies showed the liver and kidney functions, blood routine tests were normal. Serologic autoantibody tests revealed strongly positive SSA (Ro) and SSB (La) antibodies, and a reactive ANA of 1:1000 with multiple nuclear dots. Syphilis serological test was negative. Normal results were obtained from the newborn's echocardiogram and

electrocardiogram (ECG). Finally, cutaneous manifestations of the neonatal lupus erythematosus (NLE) were confirmed by clinical features and serology tests.

Further questioning, the infant's mother described having dry mouth for more than 2 years, and was subsequently diagnosed with Sjogren's syndrome. She was treated with prednisone 20mg/d, reduced to 10mg/d after 3 years, and hydroxychloroquine 400mg/d. The patient 1 was protected from the sun, and the rash resolved after 6 months without specific therapy due to the absence of symptoms.

3.2 | Case 2

6 years later, the mother became pregnant again. At 4 weeks of pregnancy, serologic tests found strongly positive SSA (Ro) and SSB (La) antibodies, a reactive ANA of >1:1000 with multiple nuclear dots, and an elevated ESR of 90mm/h (normal < 10mm/h). Due to the mother's active condition, she was treated with prednisone 10mg/d, hydroxychloroquine 400mg/d, and calcium carbonate 600mg/d. and her doctor suggested that close monitoring was necessary throughout the perinatal period. However she didn' t strictly implement.

A male infant (patient 2) was born at 39 weeks' gestation by performing a caesarean section because of fetal macrosomia, with a birthweight of 4500g. One week after birth, the child gradually developed a rash dominated by erythema and papules (Fig. 2a), with different sizes and partially fused into patches. The skin lesions were limited, mainly on the head and face. This was quite different from the rash of his sister, which were mainly characterized by scaly red patches, with a wide range of skin lesions, including the head, face, trunk, and limbs. The test found both the SSA (Ro) and SSB (La) were positive, ANA was reactive 1:100 with multiple nuclear dots. Skin biopsy showed vacuolar change of epidermal basal cells, perivascular and periadnexal mononuclear infiltrate in the dermis (Fig. 2b). A diagnosis of NLE was made as his sister. The rash start to partially subside from 2.5 months, and the rash resolved after 5.5 months without specific therapy, which was very similar to his sister. At present, both siblings are still in follow-up.

The typical cutaneous manifestations of NLE include erythematous annular plaques. Lesions in the periorbital region often result in the characteristic appearance of an "eye mask" or a "raccoon-like". In our cases, the skin lesions of patient 1 showed typical annular plaques and patient 2 showed untypical rare red papules, which is very interesting.

Consent for publication of this case report and accompanying images was obtained from the patient's parents after they were fully informed and had provided written authorization.

4 | RESULTS

We present 2 cases of NLE in siblings with significantly different cutaneous manifestations, which is very helpful for clinical doctors to understand and comprehend NLE.

5 | DISCUSSION

An acquired immune-mediated disorder, NLE is an extraordinary occurrence, caused by maternal IgG antibodies against Ro/SSA, La/SSB, or U-RNP in the newborn. It occurs in approximately 1 per 20,000 newborns,[1]and 2% in offspring of mothers with Sjogren's syndrome with an 18 to 20 percent recurrence rate in subsequent pregnancies.[3]

Clinical signs of NLE may include annular skin rash, cytopenia, hepatitis, and congenital heart block. It is essential to keep track of these patients over time, as they are more prone to autoimmune disorders in later childhood or adulthood.[4]

Confirmation of the diagnosis of NLE can be achieved by considering the patient's medical history, conducting a physical examination, and detecting the presence of specific antibodies in both the fetus and the mother. While a skin biopsy is helpful, it is not necessary in order to establish the diagnosis. Other conditions that may need to be considered when making a differential diagnosis include congenital syphilis, tinea corporis, sarcoidosis, granuloma annulare, Langerhans histiocytosis, Sweet syndrome, and urticaria.

While cases of NLE among siblings have been reported,[5]they typically present with the same or similar manifestations, making it a rare occurrence due to the increased risk of pregnancy in affected women. In our cases, it is very interesting that cutaneous NLE occurs in two siblings with significantly different cutaneous manifestations. The various clinical expressions may be attributed to a different specificity of Anti-Ro autoantibodies among siblings.[6] Additionally, other foeto-maternal factors including environmental, intrauterine, or genetic influences may affect the pathogenesis and expression of NLE.[7]

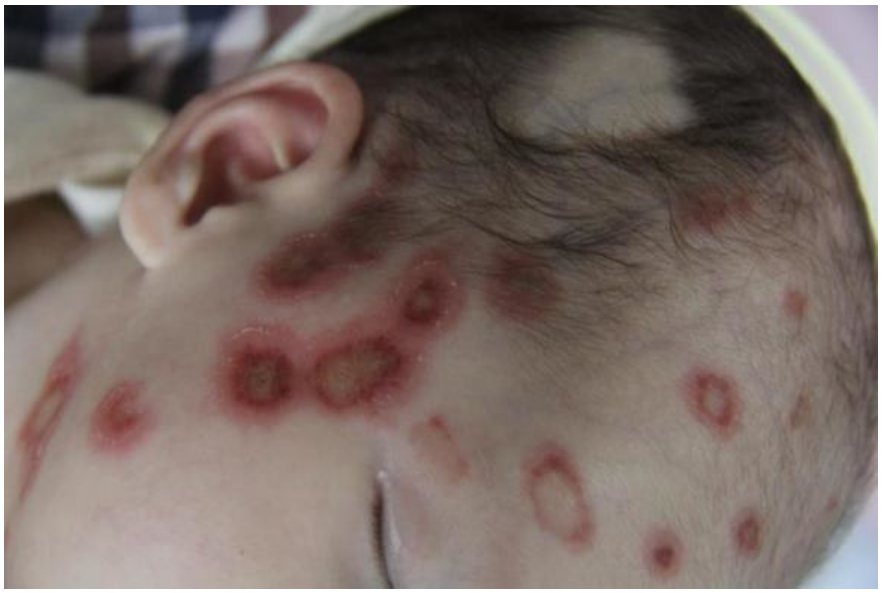
It is believed that pregnant women who test positive for autoantibodies to Sjogren's syndrome autoantigens types A or B are considered to have a high-risk pregnancy, particularly those with a prior history of NLE,[8] due to the increased danger of NLE in offspring of future pregnancies.[3]

It was deemed highly hazardous for the mother and her unborn child not to keep track of the fetal PR interval through echocardiogram during gestation, thus necessitating the implementation of counseling advice, fetal screening, maternal screening, and prevention or management of heart disease.[8] Current recommendations are to conduct an echocardiogram weekly between 16-26 weeks' gestation and biweekly between 26-32 weeks.

The mainstay of management for infants with cutaneous manifestations is to actively prevent sun exposure by utilizing methods such as sunscreen and protective clothing,[9] just like in our cases, both children only presented with rashes, the key of the management is photoprotection.

The sister followed up for 7 years and the younger brother followed up for 1 year. So far, neither of the siblings has experienced any recurrence of skin lesions, and developed any autoimmune diseases. At present, both siblings are still following up at the outpatient clinic to monitor biochemical tests、echocardiogram and ECG.

As global fertility declines, many countries are implementing policies to stimulate fertility growth. The Chinese government, for instance, liberalized the two-child policy in 2016,[10] and further liberalized the "three-child" policy in 2021. This has not caused a baby boom, but rather a moderate rise in fertility,[11] resulting in more families having a second child.[2]Therefore, it is estimated that the incidence rate of NLE in siblings will increase too, so we should raise the awareness of NLE in siblings, which is very important for the monitoring, evaluation, diagnosis and management of NLE.



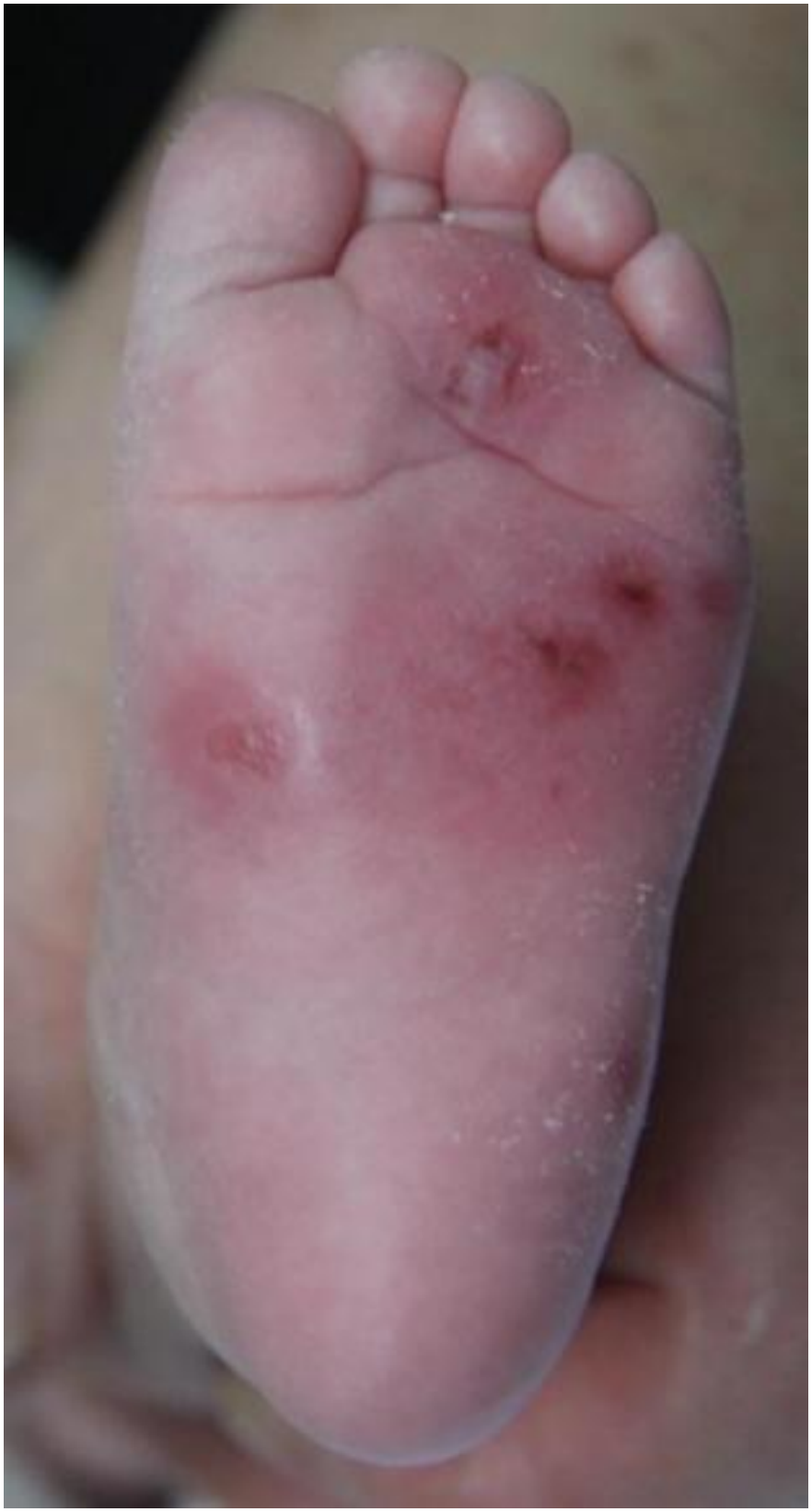
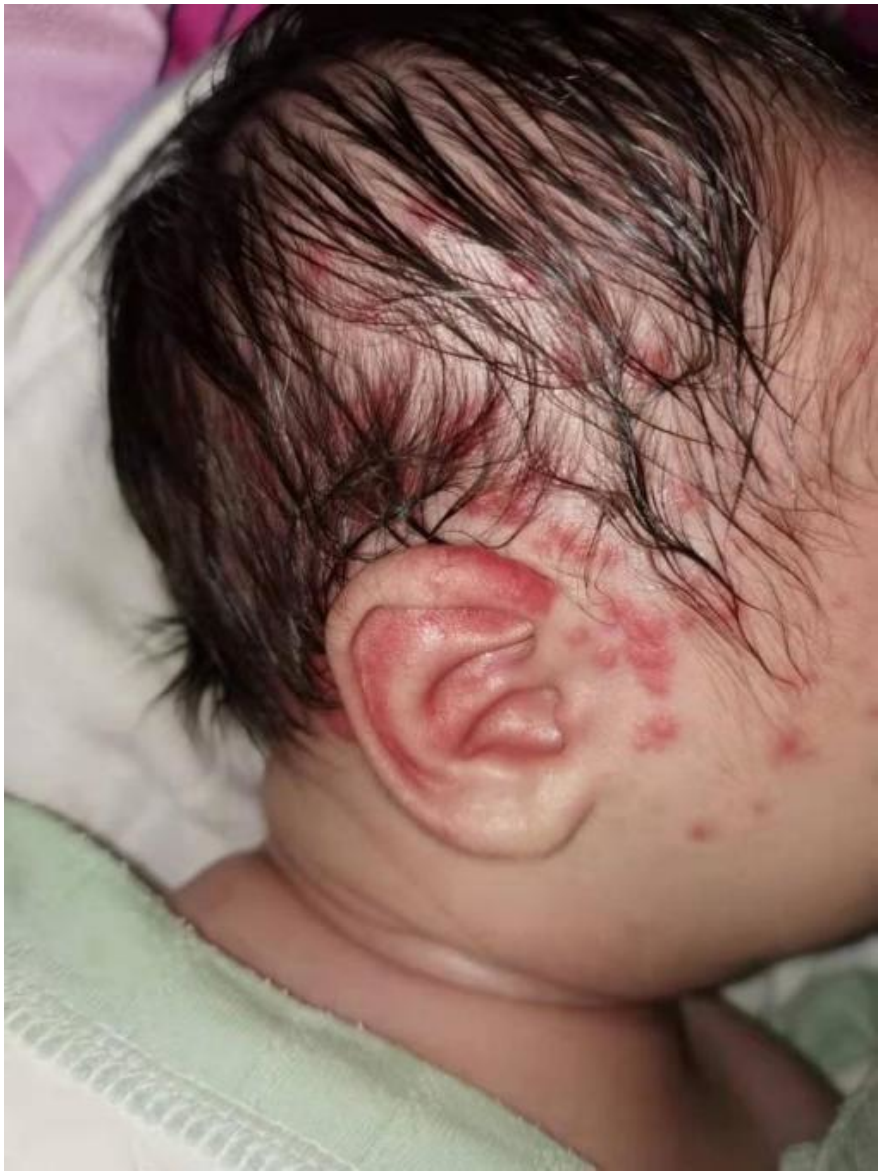


Fig 1.(a) Case 1: Clinical appearance of head lesions: inflammatory annular plaques, with hyperkeratotic borders and atrophic centres. **(b)** Case 1: Multiple discoid skin lesions on the left sole.



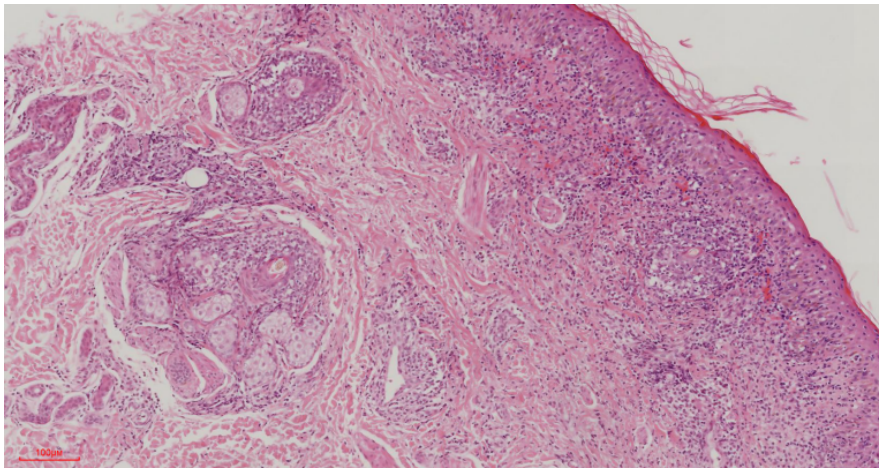


Fig 2. (a) Case 2: Multiple erythema and papules on the face.**(b)**Case 2: Histology of lesional skin: slight epidermal atrophy and hyperkeratosis, vacuolar degeneration at the dermal-epidermal junction, perivascular and periadnexal mononuclear infiltrate in the dermis. (Hematoxylin–eosin stain, original magnifification, $\times$100).

6 | CONCLUSIONS

We present 2 cases of cutaneous NLE occurring in siblings with significantly different cutaneous manifestations, an uncommon occurrence, which is very important for the monitoring, evaluation, diagnosis and management of NLE.

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