Siblings with Systemic Erythema and Papules

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Abstract

Neonatal lupus erythematosus (NLE) is an unusual and acquired immune-mediated disease. Although cases of NLE among siblings have been reported, they all have the same or similar manifestations. We first report 2 cases of presentation of cutaneous NLE to occur in two siblings with significantly different cutaneous manifestations.

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Abstract

Neonatal lupus erythematosus (NLE) is an unusual and acquired immune-mediated disease. Although cases of NLE among siblings have been reported, they all have the same or similar manifestations. We first report 2 cases of presentation of cutaneous NLE to occur in two siblings with significantly different cutaneous manifestations. 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

Neonatal lupus erythematosus (NLE) is a rare syndrome characterized essentially by cutaneous lesions and/or congenital heart block occurring in infants at birth, or shortly after. It is related to transplacental crossing of maternal auto antibodies (usually anti Ro/SS-A, La/SS-B or rarely anti-U(1) RNP) from the mother to the infant. Mothers of affected children have signs of Sjögren's syndrome or other collagenosis or are asymptomatic.

2 | CASE REPORTS

2.1 | Case 1

A 15-day-old girl (patient 1) presented to the dermatology clinic with erythema on her body in October 2015. The patient 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), her trunk, and her arms and legs, involving her palms and the soles of her feet (Fig. 1b). Laboratory studies showed the liver and kidney functions, blood routine tests were normal. Serologic autoantibody test found both the SSA (Ro) and SSB (La) were strongly positive, ANA was reactive 1:1000 with multiple nuclear dots. Syphilis serological test was negative. The newborn's echocardiogram and electrocardiogram (ECG) were normal. Cutaneous manifestations of the neonatal lupus erythematosus (NLE) were confirmed by clinical features and serology tests. Further questioning, the mother described having dry mouth for more than 2 years, and she was referred to a rheumatologist and received a diagnosis of Sjogren's syndrome, treated it with prednisone 20mg/d, reduced to 10mg/d after 3 years, and hydroxychloroquine 400mg/d. The patient was protected from the sun, and the rash resolved after 6 months without specific therapy because there were no symptoms.

2.2 | Case 2

6 years later, the mother became pregnant a second time, at 4 weeks of pregnancy, the test found both the SSA (Ro) and SSB (La) were strongly positive, ANA was reactive >1:1000 with multiple nuclear dots, ESR was 90mm/h (normal < 10mm/h). Considering that the mother's condition was active, the doctor recommended termination of pregnancy, but the mother did not accept it and was aware of the risk of malformation

and abortion if continuing pregnancy. During pregnancy, the mother was treated with prednisone 10mg/d, hydroxychloroquine 400mg/d and calcium carbonate 600mg/d.

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), which was quite different from the rash of his sister. 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 two and a half months. At present, he is still in follow-up. Written informed consent was obtained from the parents of the patient for publication of this case report and accompanying images.

3 | DISCUSSION

NLE is an unusual and acquired immune-mediated disease, attributed to the presence of maternal IgG antibodies against Ro/SSA, La/SSB, or U-RNP in the neonate. 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.[2]

The clinical manifestations of NLE include annular skin rash, cytopenia, hepatitis, and congenital heart block. Long-term follow-up is vital in these patients, since they are at an increased risk of developing autoimmune diseases in late childhood or adulthood.[3] Typical cutaneous manifestations include erythematous annular plaques. In the periorbital area, lesions frequently give rise to the typical "eye mask" or "raccoon-like" appearance. In our case, the skin lesions of patient 1 showed typical annular plaques and patient 2 showed untypical rare red papules, which has not been reported so far.

The diagnosis of NLE can be confirmed through history, physical examination and the presence of specific antibodies in fetal and maternal circulation. Skin biopsy is useful, although not essential to establish diagnosis. Differential diagnosis includes congenital syphilis, tinea corporis, sarcoidosis, granuloma annulare, Langerhans histiocytosis, Sweet syndrome and urticaria.

Although cases of NLE among siblings have been reported,[4] they all have the same or similar manifestations, and it is very rare, because of the high risk of pregnancy in affected women. In our case, it is the first description of cutaneous NLE to occur in two siblings with significantly different cutaneous manifestations. Various clinical expressions may be explained by a different specificity of Anti-Ro autoantibodies among siblings.[5] Some authors have suggested that apart from maternal immunoglobulin G antibodies, other foeto-maternal factors including environmental, intrauterine or genetic influences may affect the pathogenesis and expression of NLE.[6]

Pregnant women who test positive for autoantibodies to Sjogren's syndrome autoantigens types A or B are thought to have a risk pregnancy, above all those with a previous history of NLE,[7] because the risk of NLE in children of future pregnancies is increased.[2] In our case, although the mother's Sjogren's syndrome was not well controlled, she still insisted on having a second child. Therefore, we should strengthen the management of the mother, and it is recommended to get pregnant after the condition is controlled, so as to reduce the recurrence rate of NLE.

The management includes counseling advice, fetal screening, maternal screening, and prevention or management of the heart disease.[7]Current recommendations are to monitor the fetal PR interval by echocardiogram weekly between 16 and 26 weeks' gestation, and biweekly between 26 and 32 weeks. In our case, it was very dangerous for the mother and her fetus not to monitor the fetal PR interval by echocardiogram during pregnancy.

Avoidance of sun exposure including sunscreen and protective clothing is the mainstay of management for infants with cutaneous manifestations,[8] just like in our case, both children only presented with rashes, the key of the management is photoprotection. The rash of patient 1 progressively disappeared over a period of 6 months, and did not recur or developing autoimmune diseases during the 7-year follow-up. The rash of

patient 2 start to partially subside from two and a half months. At present, he is still in follow-up, and is ordered to return to the hospital every month to monitor biochemical tests、echocardiogram and ECG.

Global fertility declines have become an inevitable trend. As a result, many countries are adopting policies to drive fertility increases. For example, Chinese government began to fully liberalize the two-child policy in 2016,[9] and it further fully liberalized the "three-child" policy in 2021. The two-child policy won't result in a baby boom, but rather a moderate increase in fertility,[10] and it has led to more families having a second child.[11] 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) Clinical appearance of head lesions: inflammatory annular plaques, with hyperkeratotic borders and atrophic centres.(b) Multiple discoid skin lesions on the left sole.

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

Author Contributions:

Pengyue Tang: Have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. Drafted the manuscript.

Ping Li: Revised the manuscript critically for important intellectual content. Given final approval of the version to be published.

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