

Cutaneous Neonatal Lupus Erythematosus

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CASE SUMMARY

History

A one-month-old baby girl developed skin eruption over her face and limbs five days after birth. The rash spread symmetrically over her cheek, arms and lower legs. There was no constitutional upset and her six-year-old elder sister enjoyed good health. She was a full-term baby born after a normal spontaneous delivery with birth weight of 3.24 kg. The whole pregnancy was uneventful and her mother had a normal antenatal checkup including serum VDRL. Her parents are non-consanguineous and healthy. They have no similar skin eruption or any history of rheumatism.

Physical examination

No dysmorphic facial feature was noted. She was afebrile with normal developmental milestone. Her body weight and length span were in 50th to 75th percentile.



Figure 1: Targetoid lesions at left side of face

The eruption distributed symmetrically over her cheek (Figure 1), forearms (Figure 2) and thighs (Figure 3). Skin eruption started with erythematous macule which slowly developed to oval and annular patches. Targetoid lesion was formed where the center showed dusty color macule with some epidermal atrophic change. No scaling, follicular plugging, scarring or blister was noted. The periorbital area and trunk were spared. Mucosal membrane, hair and nails were not affected.

Differential diagnosis

The differential diagnoses included neonatal lupus erythematosus and erythema multiforme. However, the neonatal infection such as congenital syphilis should be excluded as well.



Figure 2: Lesions were also noted at her right arm



Figure 3: Targetoid lesions at right leg

Investigations

The baby girl had normal complete blood picture, renal and liver tests with ESR of 25. VDRL, FTA and viral study were all negative. Anti-nuclear factor was found to be 1:1280 with positive anti-Ro and anti-La, while immunoglobulin pattern, C3, C4 and C-reactive protein were within normal range. Her mother was found to be anti-nuclear factor positive with titre of 1 in 2560. Her anti-Ro and anti-La were also positive. With the provisional diagnosis of neonatal lupus erythematosus, electrocardiogram and echocardiogram were performed for the baby girl and both results were normal.

An incisional skin biopsy was performed on her right thigh for histology and direct immunofluorescence study. Microscopically, it showed interface dermatitis with prominent vacuolar degeneration and lymphocytic infiltrate. The lymphocytic infiltrate extended deep down and around blood vessel and skin appendages. The direct immunofluorescence study was negative.

Diagnosis

She suffered from cutaneous neonatal lupus erythematosus without cardiac involvement.

Treatment

The diagnosis and its benign and self-subsiding nature were fully explained to her mother. At the same time, sun protection was advised and liberal aqueous cream as emollient was prescribed. She was followed up by neonatologist and dermatologist in skin clinic. Her mother was also referred to rheumatologist for assessment.

Progress

She was re-assessed one month later in dermatology clinic with no new skin lesion was noted. The targetoid erythematous lesions over the face and limbs were subsiding.

REVIEW ON NEONATAL LUPUS ERYTHEMATOSUS

The first reported case of neonatal lupus erythematosus (NLE) was probably from Aylward in 1928.¹ He described two siblings with congenital heart

block born from a mother who had Sjogren's syndrome. It was McCuiston and Schoch² in 1954, and Hogg³ in 1957 who pointed out the possible relationship between maternal autoimmune disease and congenital heart block.

Neonatal lupus erythematosus is a disease of newborn infants, which is related to transplacental passage of maternal autoantibodies. The majority of maternal autoantibodies are anti-Ro (SS-A) and anti-La (SS-B), though cases of maternal anti-nRNP (U1RNP) with negative anti-Ro (SS-A) had been reported in the literature.⁴ Tissue injury is presumed to be dependent on the transplacental passage of maternal IgG autoantibodies via Fc receptor-bearing trophoblasts. The target antigens of the antibodies have been cloned and identified as Ro protein, 52 and 60 kDa, which have disparate locations and share no sequence homology, and La 48 kDa.⁵

Although the exact prevalence of NLE is not known, it is probably at least 1 in 20,000 live births and has been estimated that only 1% of all babies born to mothers who have anti-Ro have clinical NLE.⁶

Neonatal lupus erythematosus is characterized by the development of cutaneous lupus lesions and cardiac involvement. Other rare manifestations include cholestatic hepatitis and thrombocytopenia. Both liver impairment and thrombocytopenia are transient and normalization of liver and platelet function is the rule. Approximately half of the cases of NLE have cardiac involvement. The characteristic finding of cardiac NLE is complete heart block with female to male ratio of 2:1. Heart block usually develops in the second or third trimester. Once the congenital heart block develops, it is permanent and does not respond to corticosteroid or other treatment. In a retrospective case report analysis from Japan,⁷ prenatal maternal corticosteroid given before 16 weeks' gestation might reduce the risk of antibody-mediated congenital heart block but not the cutaneous manifestations.

Histology usually showed fibrosis and calcification of atrioventricular node area. Mortality of cardiac NLE is around 20% and is associated with severe cardiac anomalies, cardiomyopathy or myocarditis. Other associated congenital cardiac abnormalities have been detected in 30% of affected infants. These defects include patent ductus arteriosus, ventricular septal defect, transposition of the great vessels, atrial septal

defects, patent foramen ovale, coarctation of the aorta and tetralogy of Fallot.

Skin manifestation occurs in half of the cases, with female to male ratio of 2 to 3: 1. The typical cutaneous lesions occur within the first few weeks of life with predilection at face and scalp. Periorbital area involvement will give a characteristic "raccoon eye" appearance. Every part of the body can be involved by cutaneous NLE. The individual skin lesion consists of annular, sharply demarcated erythematous non-scaling patches and rarely, crusted lesion may be noted.⁸ Scarring, follicular plugging and dermal atrophy are not characteristic, although dermal atrophy has, on rare occasions, been observed. These lesions may expand peripherally leaving a central ecchymotic area. Cutaneous NLE may be exacerbated by sun exposure. It resembles adult subacute cutaneous lupus erythematosus. The cutaneous NLE must be differentiated from infantile seborrheic dermatitis, tinea facie, psoriasis and atopic eczema, but the age of onset, lack of epidermal involvement and a negative KOH test usually differentiate these. Positive maternal anti-Ro, anti-La or anti-U1RNP will differentiate cutaneous NLE from erythema multiforme, congenital syphilis, and other photosensitive genodermatoses like Rothmund-Thomson, Cockayne and Boom syndromes.

Histological findings of cutaneous NLE are identical to those of adult subacute cutaneous lupus erythematosus. Vacuolar interface dermatitis with basal cell damage and relatively sparse mononuclear cell infiltrate in the superficial dermis are typical. Direct immunofluorescence typically shows a lupus band of granular IgG, IgM and C3 at dermoepidermal junction.

The expected outcome of cutaneous NLE is spontaneous resolution with a median of 17 weeks⁹ or by the age of six months. Cutaneous lesions generally heal without any evidence of scar formation. A transient post-inflammatory hypopigmentation or hyperpigmentation may occur and residual telangiectasia may occur at the site of previous involvement.^{8,9} In the largest retrospective cohort of cutaneous NLE without heart block, 47 mothers whose sera contain anti-Ro, anti-La and anti-U1RNP were recruited.⁹ About 30% of the mothers were totally asymptomatic, one quarter was diagnosed to have autoimmune disease and the remaining was classified as undifferentiated autoimmune syndrome (UAS). After five years, seven out of 13 asymptomatic mother experienced disease

progression to either autoimmune disease or UAS. Therefore mother of NLE should have long-term follow up by rheumatologist.

In the same cohort of cutaneous NLE without heart block, 20 subsequent pregnancies were identified. 1/3 of babies were unaffected, 1/3 had cutaneous involvement only and one third had either cardiac or dual involvement.

The long-term prognosis of cutaneous NLE without cardiac involvement with a mean follow up for 77 months was evaluated in the same cohort. Four out of 57 developed signs or symptoms of autoimmune disease namely Hashimoto's disease, juvenile rheumatoid arthritis and Raynaud's phenomenon.

The management of cutaneous NLE can be divided into two parts: directed to cutaneous NLE and directed to parents. As cutaneous NLE is self-limiting, there is no specific treatment for the baby. But a good rapport with parent and in-depth counseling and reassurance is important to lessen parent's anxiety in the initial presentations. Sun-avoidance or sun-protection is advised to avoid exacerbation of cutaneous lesions. Liberal emollient and low potent topical steroid can be used when required. Pulse dye laser may be tried in residual telangiectasia if it does not subside as expected when the disease becomes quiescent. Long-term follow up is advised as 7% of cutaneous NLE without heart block may develop some kind of autoimmune disease years later.⁹ Mother of NLE must be referred to a rheumatologist for further investigations and management, as one half of asymptomatic mother may develop rheumatism five years later.⁹ Family counseling on subsequent pregnancies should stress the lack of reliable predictor on the outcome of future pregnancies. The general comment on future pregnancies is that 1/3 will not be affected, 1/3 may result in cutaneous NLE without heart block and 1/3 may crossover to more serious cardiac involvement with or without cutaneous manifestation.⁹ Serial fetal echocardiographic surveillance of subsequent pregnancy from the mother is warranted.

Learning points:

Complications of neonatal lupus erythematosus include heart block, cholestatic hepatitis and thrombocytopenia. Maternal connective tissue disease should be excluded.

References

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