

Neonatal Lupus Erythematosus: Our Local Experience

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Abstract

Introduction: Neonatal lupus erythematosus (NLE) presents clinically with either cutaneous lesions or cardiac involvement and is related to the transplacental passage of anti-Ro antibodies from mother to foetus. We report a series of 10 cases seen at the National Skin Centre between 1990 and 1998 including a pair of siblings. **Clinical Picture:** The female to male ratio was 2.3:1 and most presented with rash between 3 to 5 weeks of life while 4 had lesions at birth. Four of the 9 mothers had SLE, one was diagnosed to have a lupus-like illness, 2 had Sjogren's syndrome and the remaining two had very high ANA titres but the final diagnosis was uncertain. **Outcome:** The rash resolved spontaneously by 3 to 6 months of age.

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Introduction

Neonatal lupus erythematosus (NLE) is related to the transplacental passage of anti-Ro antibodies from mother to foetus. The commonest manifestations involve the skin and the heart. We report a series of 10 cases of NLE seen at the National Skin Centre between 1990 and 1998 (Table I). This is an update of the 3 cases which were reported.¹

Case Series

There were 7 female and 3 male infants, giving a female to male ratio of 2.3:1. Of the 10 cases, 4 had cutaneous lesions at birth. The onset of rash in the remaining infants was between 3 and 5 weeks of life. Affected infants presented with classical annular erythematous lesions with or without scaling (Fig. 1) of which 1 had "raccoon eyes" while a few had distinctive vasculitic-looking lesions (Fig. 2). The commonest site of involvement was the face, which was involved in all 10 cases, followed by the trunk in 7 cases. Three patients had upper limb involvement and 4 patients had lower limb involvement including 2 patients with lesions on the soles (Figs. 3 & 4).

One interesting feature, rarely reported, is the presence of atrophy and scarring of the skin of the face in 2 neonates. One also had aplasia cutis of hands and feet.

Majority of the cases (7/10) had either anti-Ro antibodies in the infant or in the mother or in both. Anti-La antibodies were present in 5/10, including 3 patients (a pair of siblings

and another infant) who did not have concomitant anti-Ro antibodies. Two patients had mild transaminitis with levels less than two times the upper limit of normal. None had evidence of congenital heart block. The rash resolved by 3 to 6 months of age in all cases.

Four of the 9 mothers had systemic lupus erythematosus (SLE). One mother had 2 affected children and was diagnosed only after the delivery of the first affected child. Two mothers had Sjogren's syndrome (1 diagnosed after delivery) while 1 was diagnosed to have a lupus-like illness without sufficient criteria for SLE. The remaining 2 mothers both had high ANA titres of 1/640 and were referred to the rheumatologist.

Discussion

The first report linking autoimmune disease in the mother and cutaneous lupus in the newborn was by McCuiston and Schoch.² In 1957, Hogg noted a possible relationship between autoimmune disease in the mother and congenital heart block in her child.³ In the early eighties, Weston et al⁴ reported the association between NLE and maternal anti-Ro autoantibodies. The non-cardiac manifestations of NLE are transient, resolving at 6 months of life, with the disappearance of maternal autoantibodies from the neonatal circulation. The incidence of NLE is about 1 in 20,000 live births.

The skin^{5,6} is affected in approximately half the cases,

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TABLE I: NEONATAL LUPUS ERYTHEMATOSUS CASES SEEN AT THE NATIONAL SKIN CENTRE BETWEEN 1990 AND 1998

No.	Age of onset	Sex	Clinical features	Sites	Autoantibodies	Others	Clearance	Mother	
1	3 weeks	M	Oedematous red scaly annular lesions	Face, scalp, back	Anti-Ro +	Hepatitis; Referred to cardiology; ? outcome	Defaulted follow-up	SLE x 10 years	1st child
2	3 weeks	M	Annular erythematous scaly lesions (initially diagnosed as bullous impetigo, insect bite reaction, EM)	Face, shoulder, LL including soles	Anti-Ro + Anti-La + ANA + 1/360 homogenous Anti-dsDNA borderline	Heart normal	Resolved at 3 months	Anti-Ro + Thrombocytopenia Anti-La + Leukopenia ANA + 1/640 speckled & homogenous Anti-dsDNA, anti-sm & anti-RNP -ve → diagnosed to have lupus-like illness by rheumatologist, not fulfilling criteria for SLE	1st child
3	4 weeks	F	Annular erythematous scaly lesions	Face, trunk, UL, LL	Anti-Ro + Anti-La - ANA - Anti-dsDNA +	Heart normal	Resolved at 5 months	Sjogren's syndrome x 3 years Anti-Ro + Anti-La - Anti-dsDNA -	1st child
4	5 weeks	F	Annular erythematous lesions (initial diagnosis: EM)	Face, trunk, UL, LL	Anti-Ro - Anti-La + ANA + 1/640 speckled	Mild transaminitis Heart normal	Resolved at 5 months	Diagnosed SLE after delivery Anti-Ro - Anti-La + ANA + 1/640 speckled	1st child
5	3 weeks	F	Annular lesions, target-like	Face, scalp, trunk	Anti-Ro - Anti-La + ANA + 1/640 speckled Anti-dsDNA + Anti-RNP -	Heart normal	Resolved at 5 months	Same mother as Case 4	2nd child
6	3 weeks	F	Small annular vasculitic lesions	Face, trunk, UL, soles	Anti-Ro - Anti-La - ANA + 1/160 speckled	Heart normal	Resolved at 4 months	Sjogren's syndrome diagnosed after delivery Anti-Ro + Anti-La + ANA + 1/640 Anti-dsDNA & anti-sm -	1st child
7	At birth	F	Vasculitic rash with patchy hyper- and hypopigmentation and areas of mild atrophy	Face	Anti-Ro + Anti-La - ANA + 1/200 speckled Anti-dsDNA -	Heart normal	Resolved at 6 months leaving hypopigmentation	SLE x 3 years Anti-Ro + ANA + 1/160 speckled Anti-dsDNA - Anti-sm + Anti-RNP -	4th child (1st 3 children not affected)
8	At birth	F	Dusky, atrophic lesions	Face	Anti-Ro + Anti-La - ANA + 1/160	Heart normal Also had aplasia cutis of hands & feet	Healed after ? months with mild atrophy	Known SLE Anti-Ro + Anti-La - ANA + 1/160	2nd child (1st child not affected)
9	At birth	F	Dusky, erythematous annular lesions with petechiae & telangiectasia	Face, scalp	Anti-Ro - Anti-La + ANA + 1/40 speckled	Heart normal	Resolved at 5 months	Anti-Ro - Anti-La + ANA + 1/640 speckled Referred to rheumatologist: outcome unknown	2nd child (1st child not affected)
10	At birth	M	Erythematous scaly annular lesions with areas of atrophy	Face, scalp, trunk	Anti-Ro + Anti-La + ANA + 1/640 speckled	Heart normal	Resolved after 4 months with hyperpigmentation	Anti-Ro + Anti-La + ANA + 1/640 speckled Referred to rheumatologist: outcome unknown	5th child (4th child affected but records not found)

EM: erythema multiforme; LL: lower limb; UL: upper limb

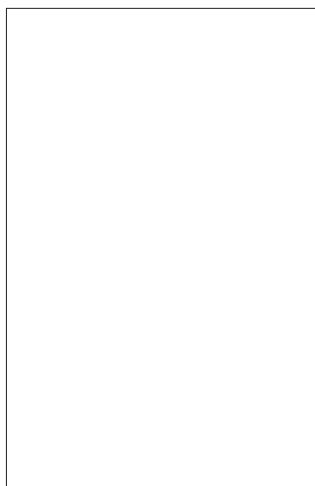


Fig. 1.

Fig. 1. Annular erythematous plaques on the face and scalp.

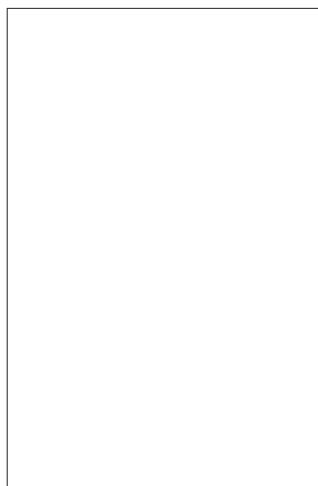


Fig. 2.

Fig. 2. Vasculitic-looking rash on the face of an affected infant with prominent periorbital involvement.

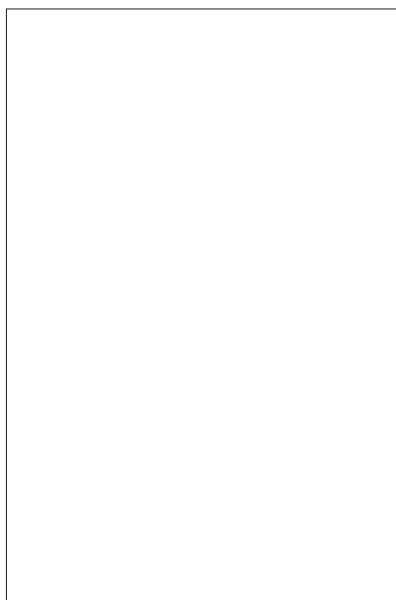


Fig. 4. Erythematous discoid patches on the soles with scaling.

and females are more often affected than males (F:M = 2:1). We had a similar experience with more females affected (2.3:1). Lesions are annular, erythematous patches, sometimes with fine scales or wrinkling which appear during the first few weeks of life, although a few cases have been reported to be present at birth as in Case 7 to Case 10 in our series. Hypopigmentation may be prominent, particularly in babies with dark skin, and telangiectasia occasionally occur. Case 7 in our series, a Malay infant, had hypopigmentation which persisted after the erythematous rash had resolved. More characteristic lesions of discoid lupus erythematosus (DLE) such as scarring, follicular plugging and dermal atrophy are not characteristic of the neonatal skin rash. Cutaneous NLE lesions are histologically

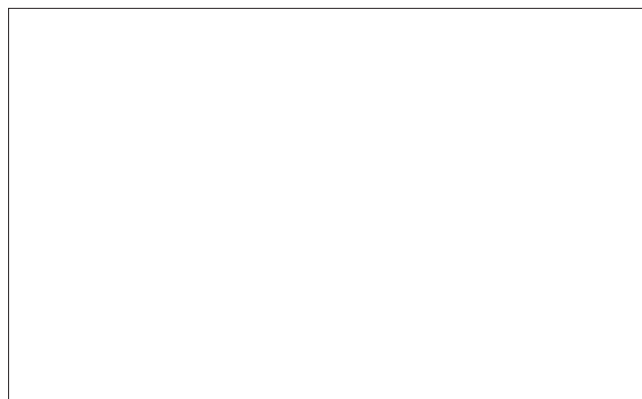


Fig. 3. Annular erythematous plaques on the legs of an infant with NLE.

and clinically more similar to subacute cutaneous lupus erythematosus (SCLE) than DLE. Differential diagnoses of NLE include atopic dermatitis, seborrhoeic dermatitis, discoid eczema, insect bites, acute urticaria, erythema multiforme, annular erythema and cutaneous vasculitis. In our series, they were often misdiagnosed as atopic eczema by the general practitioners as the rashes were on the face and cheeks.

The face and scalp are the commonest sites of involvement, although any part of the skin may be involved. The periorbital skin may be strikingly involved, presenting as “racoon eyes”. The cutaneous lesions may be brought on or exacerbated by sun exposure and may also appear on sun-protected skin. In our series, besides the face being invariably involved, 7 of the 10 patients also had lesions on covered sites.

Most children have spontaneous resolution of skin lesions by age 6 months and the autoantibodies become undetectable. Pigmentary abnormalities may take many more months to resolve while telangiectasias may persist indefinitely. Two of our patients had post-inflammatory hyperpigmentation. Two neonates, Case 8 and Case 10, had an unusual shallow atrophy and scarring of the face especially on the cheeks which has rarely been reported. Although one had aplasia cutis of the fingers and toes, the scarring of the face was not caused by epidemolysis bullosa but was related to NLE. Generally, cutaneous NLE leave no permanent scars.

The most serious complication, cardiac involvement,^{5,7} occurs in 50% of cases. The characteristic cardiac finding is complete heart block, although lesser degrees of block especially second degree A-V block have been reported. It usually develops in the second trimester (bradycardia can be picked up by ultrasound or auscultation) and is permanent. Fibrosis is seen in the atrio-ventricular node on histopathological examination. There is a mortality rate of 15% to 22% with the greatest risk occurring in the first few weeks of life. Significant cardiac impairment may

accompany heart block in 10% of cases and the prognosis is much worse as pacemaker insertion does not completely restore cardiac function. In our series, none of the infants had cardiac involvement, the most likely reason being that only cases with cutaneous involvement are referred to our centre while those with isolated congenital heart block may be seen by the paediatric cardiologists. Only a small proportion of NLE cases (about 10%) have both cardiac and cutaneous manifestations.⁵

Hepatic involvement takes the form of neonatal cholestasis with abnormal bilirubin levels and normal or minimally elevated transaminases.^{8,9} In babies that survive the cardiac manifestations, hepatic disease usually resolves. In our series, 2 cases had mild transaminitis but none had evidence of cholestasis and both resolved spontaneously within 3 months. Hepatomegaly is seen in 30% and splenomegaly in 40%.⁶

Haematologic abnormalities have been described, particularly thrombocytopenia.¹⁰

Anti-Ro (SSA) autoantibodies in maternal sera have been demonstrated in almost all cases of NLE.^{4,11} These antibodies are found in high frequency in sera of persons with Sjogren's syndrome or SLE, in some of their clinically normal relatives and sporadically in healthy people.¹² Anti-La (SSB) autoantibodies are found almost invariably in association with anti-Ro antibodies. However, anti-Ro antibodies were absent in 3 cases in our series, including a pair of siblings, despite the presence of anti-La antibodies. The most plausible explanation is that immunodiffusion, the technique used then for detecting the anti-Ro antibodies, was not sensitive enough giving rise to false negative results. It is also possible that these patients may have had anti-La antibodies in isolation, although this is rare. A few cases of NLE have been reported with antibodies to U1RNP in the absence of antibody to either Ro or La.¹³

Ro autoantibodies bind to both the 52kD Ro antigen and the 60kD Ro antigen which are distinct. The 48kD La (SSB) protein does not share antigenic determinants with the Ro polypeptides, although Ro and La have been shown to be components of the same ribonucleoprotein complex. A study of 20 NLE maternal sera showed the following frequency of antibodies: anti-60kD Ro, 100%; anti-52kD Ro, 90%; and anti-La, 45%.¹⁴ No relationship was found between autoantibody specificity and clinical findings in the baby. Anti-p57 has also been reported in association with NLE (40%).¹⁵ Antibody to calreticulin, a high affinity, calcium-binding protein has also recently been described.¹⁶

Serological HLA typing has shown an association with B8, DR3 and DQ2 in the mother but no HLA association in babies. These genetic associations are probably most strongly associated with predilection for producing anti-Ro antibodies.⁵

Many women do not have symptoms suggestive of autoimmune disease at the time of diagnosis of the baby's disease. Follow-up studies have shown that a significant number (up to 50%) of those previously asymptomatic women develop symptoms of Sjogren's syndrome, SLE or undifferentiated disease with time.¹⁷ Of the 9 mothers in our series, 4 had SLE, of whom 1 was diagnosed just after the delivery of the affected infant. One was diagnosed to have a lupus-like illness and 2 had very high ANA titres but the final diagnosis was not known. Two mothers had Sjogren's syndrome.

Work-up for an infant suspected to have NLE should include the following: full blood count, anti-Ro and anti-La antibodies, anti-nuclear antibody (ANA), anti-double stranded DNA antibody (dsDNA) and anti-U1RNP antibody for both mother and baby. In addition, an electrocardiogram (ECG) and liver function tests should be performed on the baby. The diagnosis should be suspected in any infant with typical cutaneous lesions or complete congenital heart block especially those born to mothers with SLE, rheumatoid arthritis, Sjogren's syndrome or other connective tissue diseases.

Skin lesions, when biopsied, demonstrate basal cell damage and a relatively sparse mononuclear infiltrate in the superficial dermis. Direct immunofluorescence may show particulate IgG deposits throughout the epidermis rather than the dermo-epidermal junction (similar to what has been described previously in SCLE). There may be granular IgM deposits at the dermo-epidermal junction.

The prognosis for subsequent pregnancies is generally good. In about 15% to 25% of subsequent pregnancies, the baby will develop NLE (either cutaneous or cardiac)^{6,17}; in most cases, the baby will be affected in the same manner as his sibling.¹⁸

Infants with NLE should be protected from sun exposure until about 8 months of age. Topical steroids are recommended for cutaneous lesions but systemic steroids are usually not required except for serious manifestations such as severe thrombocytopenia and cholestasis. Antimalarial therapy is not advisable because of its potential toxicity and the transient and benign nature of the skin lesions. Telangiectasias, if they occur, may be treated with a modality such as pulsed dye laser⁴ when the child is older.

Many (60%) with cardiac involvement require permanent pacemaker implantation. Although initially congenital heart block was thought to be benign, death has occurred in about 15% to 20% of affected cases, often from intractable heart failure in the newborn period.

The long-term prognosis for individuals who had neonatal lupus is unknown. At least 2 children have been reported to develop SLE in adulthood.^{19,20}

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