

CASE REPORT

Neonatal Lupus Erythematosus

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SUMMARY. This is a case of an infant with neonatal lupus erythematosus who presented the characteristic cutaneous lesions without evidence of systemic involvement. NLE is a rare condition which affects newborn infants from mothers who may be asymptomatic or have a connective tissue disease, with or without autoantibodies to extractable nuclear antigens Ro (SS-A), LA (SS-B) or ribonucleoproteins.

The skin lesions are usually annular in configuration and resemble those of subacute cutaneous lupus erythematosus. Congenital complete heart block (CHB) may be present in addition to the cutaneous lesions. This is a review of NLE focusing on its clinical manifestations, serologic markers, pathogenesis and treatment.

Neonatal lupus erythematosus (NLE) is an uncommon autoimmune disease with skin lesions that seem to be analogous to those seen in subacute cutaneous lupus erythematosus of adults. Infants with the disease may present themselves either with non scarring lesions, congenital complete heart block (CHB) or both. IgG Ro (SS-A) autoantibodies may be detected in the sera of the mothers of such patients. These autoantibodies cross the placenta and are important in the pathogenesis of the disease.

This is a case report of an infant with NLE who was recently evaluated in our institution. We review of the literature of this condition focusing on its clinical manifestations, serologic markers, pathogenesis and treatment.

Case Report

A two month old female infant came for evaluation to the Pediatric Dermatology Clinic because of a six week history of asymptomatic skin lesions on the face and the extremities. They began on the temple area and enlarged to involve the forehead and the scalp. Similar lesions appeared on the exposed areas of the upper and lower extremities. The skin lesions were unresponsive to topical steroids and antifungal creams.

She was born after of a full-term pregnancy from a healthy 27 year-old G3, P3, A0 in an uncomplicated

vaginal delivery. The mother did not have any history of systemic disease, was asymptomatic and the family history was negative for connective tissue disease. On physical examination the infant appeared healthy. Skin examination showed erythematous scaly patches with annular configuration and slight hyperpigmentation on the scalp, forehead, temples and periorbital areas (Fig. 1,2). Similar lesions with scattered telangiectasias were

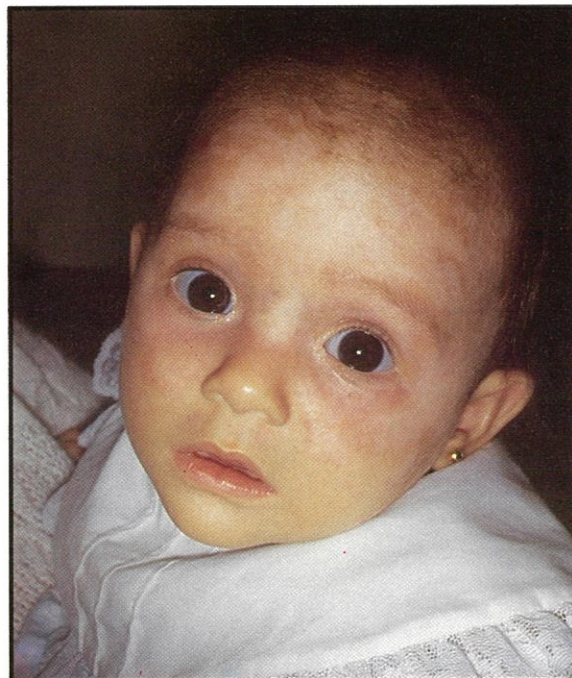


Figure 1. Annular erythematous lesions on the periorbital region, the forehead and scalp.



Figure 2. Lateral view of the skin lesions on the scalp and face.

present in the upper and lower extremities. No other physical abnormalities were noted. Hepatomegaly or splenomegaly were not present.

Laboratory investigations demonstrated normal complete blood count and urinalysis; GGT-27; AST-40; ALT-35; LDH-268, alkaline phosphate-227, total bilirubin-1; VDRL non reactive. EKG-normal sinus rhythm with no evidence of A-V block. The serologic data for the mother and patient is shown in Table I.

Histopathologic examination from a skin biopsy on right side of the forehead showed vacuolar alteration of the basal layer, a thin epidermis and a sparse perivascular lymphocytic infiltrate with telangiectasias. These changes were interpreted to be those of cutaneous lupus erythematosus (Fig. 3).

After the initial evaluation, the skin lesions slowly resolved while on strict sun avoidance and use of low

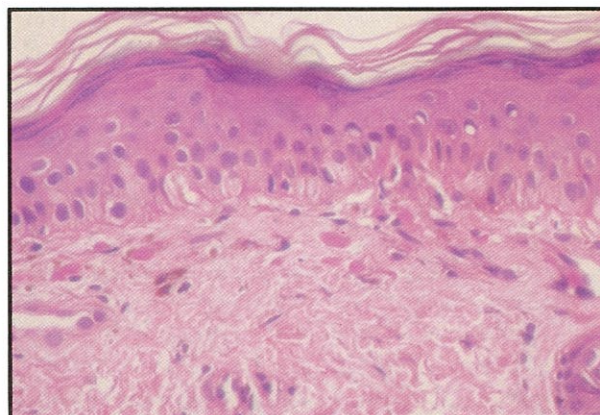


Figure 3. Focal vacuolar alteration of the basal cell layer of the epidermis with a scant mononuclear cell infiltrate and vascular dilatation of the upper dermal plexus. (Hematoxylin and eosin stain, original magnification X100).

potency topical steroids. She has remained in good health with no evidence of systemic involvement. Her mother remains asymptomatic.

Discussion

In 1954, McCuistion and Schoch postulated that a woman with systemic lupus erythematosus (SLE) may convey the disease to her neonate via the transplacental passage of unknown factors. (1) This hypothesis gained further support in 1981 when several groups of investigators observed that Ro (SS-A) autoantibodies are frequently found in the sera of mothers who bear infants with NLE skin disease and in the sera of the affected neonates.(2-4) The incidence of NLE is not known although information concerning the incidence of congenital heart block estimates that it occurs in 1 of 20,000 live births. (5) Since congenital heart block accounts for perhaps half of the cases of NLE, it is reasonable to assume that the incidence of NLE is likely to be around 1 in 20,000 live births. Most of the cases develop either skin lesions or CHB (6) approximately 10% of cases will develop both. Liver disease, (7) aplastic anemia,(8) and thrombocytopenia (9) have also been observed. Lee in 1993, (10) in a series of more than 30 infants with NLE, observed various combinations of systemic involvement. Thus, in a given infant, any combination of findings is possible, but the most common clinical features are cutaneous lesions and isolated CHB (4, 11-13).

Nearly half of these infants develops characteristic LE skin lesions (6). They may be present at birth but usually appear days or weeks later, and sometimes months after birth. They are commonly found on the head, particularly on the periorbital, malar, and scalp areas, and express as

Table 1. Serologic Data

	Patient	Mother
ANA	1:80 (speckled)	1:160 (speckled)
anti ds DNA	negative	negative
Ro (SS-A)	positive*	positive*
La (SS-B)	positive**	positive**
Anti-Sm	negative	negative
Anti U ₁ RNP	negative	negative
RF	negative	negative
C ₃ , C ₄ levels	normal	normal

*TIA method

**EIA method

erythematous macules or patches that enlarge into round, elliptical, or annular plaques with fine overlying scale. They resolve spontaneously within weeks to months, sometimes with transient dyspigmentation, telangiectasias, and mild atrophy. They may be precipitated or exacerbated by ultraviolet light exposure. It has been stated that clinically and histopathologically they are similar to those of subacute cutaneous lupus erythematosus (SCLE). Histopathological examination of lesional skin shows characteristic vacuolar degeneration of the basal keratinocytes and a sparse lymphocytic perivascular infiltrate in the upper dermis. (14) Direct immunofluorescence studies show immune deposits in and about the basal keratinocytes and along the basement membrane region. This pattern of immune deposition is a distinctive feature of the skin lesions of NLE and SCLE. (15-16).

The cardiac lesion is characteristically an isolated complete heart block that begins during gestation. It has been detected as early as the sixteenth week of gestation but may appear later. (10) The major histologic findings in the conduction system are fibrosis and calcification replacing the atrioventricular node. (17-18) In some cases the sinoatrial node has also been involved. (19-20) Because of the fibrosis in the conduction system, heart block is almost always permanent and the patients need pacemaker implantation. About 10% of babies with heart block do not respond to pacemaker implantation, probably because of coexistent myocardial disease and die of intractable heart failure. Infants who survive the perinatal period do well. (22) The diagnosis of complete heart block may be suspected during routine obstetric examination because of a slow fetal heart rate. It can be confirmed by fetal ultrasound that will show atria and ventricles beating at different rates. The diagnosis of NLE can be confirmed by testing the child and mother for autoantibodies.

Thrombocytopenia has been estimated to occur in 10% to 20% of NLE infants. (23) It is transient and generally does not require treatment. It has been associated with skin purpura and rarely with gastrointestinal hemorrhage. (7,23) Transient leukopenia and hemolytic anemia have also been reported. (9)

Liver enlargement has been reported in 20% to 40%. (7) of the cases. It may be secondary to extramedullary hematopoiesis or passive congestive changes from congestive heart failure. Liver biopsies from infants with NLE may show a variety of pathological changes including hepatitis, cholestasis, fibrosis, ductal hyperplasia and extramedullary hematopoiesis.(7)

Splenomegaly, pneumonitis, hypocalcemia, and myelopathy occurring in association with NLE have also been reported. Whether these were related or incidental

findings is not yet clear.

Ro (SS-A) autoantibodies are present in roughly 82% of NLE patients and 92% of their mothers. (6) These antibodies are not specific for NLE. They may be found in the majority of patients with primary Sjogren's syndrome, subacute cutaneous LE and homozygous C₂ and C₄ complement deficiency with SLE-like disease.(24) Approximately 40% of SLE patients and less than 1% of normal pregnant women have these autoantibodies.(25,26) La (SS-B) autoantibodies are present in roughly 47% of NLE patients, and 60% of their mothers.(6) Approximately 13% of SLE patients and less than 1% of normal pregnant women have these autoantibodies. There are only several reports of La (SS-B) autoantibodies in NLE infant and maternal sera in the absence of Ro (SS-A) autoantibodies.(27)

It is infrequent to find U₁ ribonucleoprotein (RNP) autoantibodies in NLE. However, at least seven case reports have described infants with NLE who had RNP autoantibodies in the absence of Ro (SS-A) or La (SS-B) autoantibodies.(28-32) These patients had skin disease but no evidence of heart disease.

Mothers of patients with NLE almost always have antibodies to Ro (SS-A). These IgG autoantibodies cross the placenta. The hypothesis that maternally-derived autoantibodies play a direct role in the pathogenesis of the NLE skin disease is supported by the fact that as maternally-acquired antibodies are cleared from the infant's circulation, the skin lesions resolve.(33)

Lee et al(10) injected purified human Ro autoantibodies into mice engrafted with human skin. The antibodies bound preferentially in and about the human basal keratinocytes. This binding was markedly augmented by ultraviolet light-B exposure. The pattern of immunoglobulin deposition in the grafted skin was characteristic of the pattern found in biopsies from NLE and SCLE skin lesions(15,16) and paralleled the location of keratinocyte injury that is found histopathologically in these two diseases.

The hypothesis that Ro (SS-A) and La (SS-B) autoantibodies play pathogenic roles in NLE cardiac disease is further supported by data that shows that these antibodies bind to human fetal heart conduction tissue.(34,35) Alexander et al(36) have shown that Ro autoantibodies bind selectively to neonatal rather than adult cardiac tissue inhibiting repolarization. The fact that many fetuses exposed to Ro, La, and/or RNP autoantibodies never develop disease is evidence that other factors are required to induce the disease.

Women who have had an infant with NLE are at greatest risk for having another affected child. Affected children are most likely to have the same manifestations as the previous sibling. There have been families in which one

sibling manifested only cutaneous disease, whereas other siblings had CHB.(37,38)

Women with Ro autoantibodies and a history of an autoimmune disorder constitute the next highest risk group. In a study of mothers with SLE who had Ro autoantibodies, 6 of 79 (7.6%) live births resulted in infants who developed NLE.(39) Women who are normal or have ill-defined symptoms that are producing Ro and/or La autoantibodies, may be at lower risk of having a child with NLE. Unfortunately, women in this later group are unlikely to be identified beforehand, yet bear approximately half of all infants affected by NLE.(6)

Mothers with La autoantibodies may have a higher risk of having a child affected by congenital heart block. Buyon et al(40) have determined that the presence of La autoantibodies are more predictive of the development of CHB than are Ro autoantibodies. The frequency of monitoring a pregnancy for the development of heart block in the fetus and what should be done to prevent its development or to treat it in utero once it has developed are difficult issues that have been previously addressed.(40)

Treatment for the skin lesions is not necessary, however, twice-daily applications of low potency steroid creams may be of benefit. Sun avoidance for the first six to eight months of life is advisable. Treatment of cardiac disease is more problematic and is generally conducted under the guidance of the obstetrician, pediatrician and a cardiologist. Resuscitative measures and/or pacemaker implantation are required for a minority of patients in the neonatal period. Pacemaker insertion can often be delayed but needs to be considered, particularly if signs and symptoms of inadequate cardiac output develop.

The mother of an affected infant should be informed that NLE may develop in future pregnancies and that she is at high risk of developing a rheumatic disease later in life. (23) Future pregnancies must have early prenatal care and be treated as high risk by an informed obstetrician. Few patients with NLE may develop a collagen disease later in life, but a long-term follow-up is not considered to be necessary.

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