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# Neonatal Lupus Erythematosus

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*Neonatal lupus erythematosus (NLE) is a rare syndrome of newborns and infants defined by the presence of maternal autoantibodies and the characteristic clinical features of the infant. The clinical findings most often reported are congenital heart block and cutaneous lesions; however, many children have cardiomyopathy, hepatobiliary disease, and/or hematologic diatheses. We present the case of a 1-day-old African American boy who presented with an annular, ulcerated facial eruption at birth and went on to develop subacute cutaneous LE (SCLE) and heart block.*

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## Case Report

The patient was a 1-day-old African American boy born full term by vaginal delivery to a subway worker with no significant medical history. The boy was born with an ulcerating facial eruption for which pediatric dermatology was consulted.

Results of a physical examination revealed indurated violaceous plaques in a periocular distribution on the nose and periorally, with extension above the eyebrows and down to the angle of the mandible. Ulcerations and hypopigmentation were noted in each of the plaques (Figure 1).

Based on the "raccoon eyes" appearance of the lesion, two 2-mm punch biopsies were performed: one for hematoxylin-eosin staining and one for direct immunofluorescence microscopy. The result of the first biopsy revealed a lymphocytic infiltrate with neutrophils, eosinophils, and significant pigmentary incontinence as demonstrated by melanophages in the dermis. Mild hyperkeratosis

was noted. The result of the direct immunofluorescence microscopic examination was negative.

Results of bacterial and viral cultures of the wound were negative. Results of a Tzanck test and a direct fluorescence antigen test for herpes simplex viruses 1 and 2 were negative, as were tissue cultures for bacteria, viruses, and fungi. Cardiac examination and echocardiogram results were within reference range. Results of an ophthalmologic examination with fundoscopic evaluation demonstrated a small retinal hemorrhage believed to be secondary to birth trauma.

Results of complete blood counts and liver function tests were within reference range; rapid plasma reagin and HBsAb test results were negative. At birth, the boy had a positive antinuclear antibody (ANA) with a titer of 1:640 (speckled pattern) and high anti-Ro and anti-La antibody titers. The patient also had negative extractable nuclear antigen, anti-double stranded DNA, and anti-Smith antibodies. The mother had no cutaneous lesions but was ANA positive with a titer of 1:1280, homogeneous pattern. The mother also was anti-Ro and anti-La antibody positive with negative extractable nuclear antigen, anti-Smith, anti-centromere, and anti-Scl-70 antibodies. She denied any arthralgias, headaches, or photosensitivity. The results of the mother's liver function tests showed elevations of alanine aminotransferase and aspartate aminotransferase levels; however, her gastroenterologist may have erroneously attributed this to chemical exposure during pregnancy while cleaning the subway system.

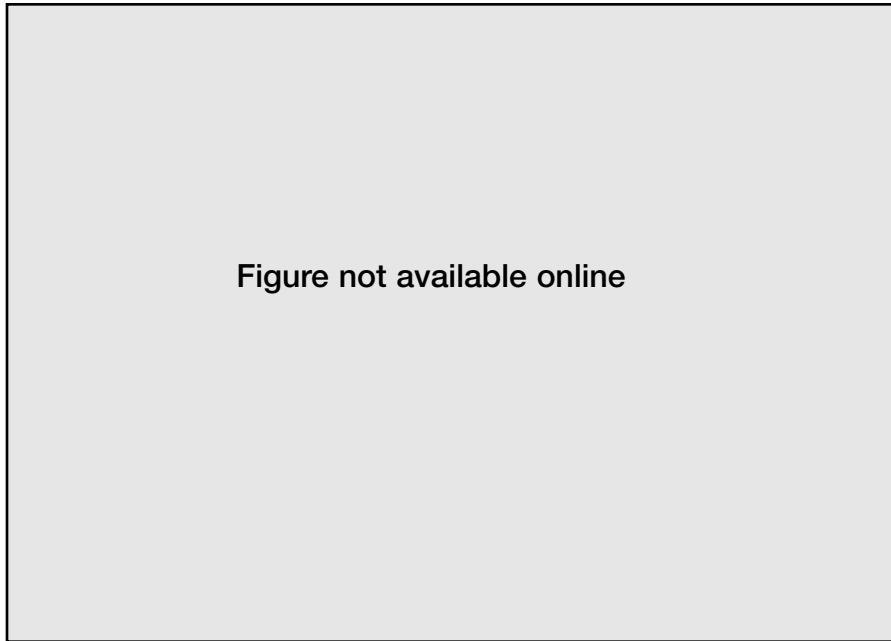
A clinical diagnosis of neonatal lupus erythematosus (NLE) was made. It was determined that the mother had silent ANA positivity. Annular erythematous plaques consistent with subacute cutaneous LE (SCLE) were noted on the patient's forearms (Figure 2) and legs in his first 3 months of life. At age 1 month, the baby was placed on a therapeutic regimen of twice-daily topical tacrolimus 0.03% ointment to the face. At the time of the initial diagnosis of NLE, the patient was begun on a therapeutic regimen of a titanium dioxide sunscreen with a sun protection factor of 45 in the

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**Figure 1.** Face of the patient a few days after birth.

morning. When the acral lesions were noted, his parents were instructed to apply the tacrolimus 0.03% ointment twice daily to the affected areas of the face, forearms, and legs. The acral lesions responded well and flattened within a few days without postinflammatory changes. New acral lesions continued to arise for another 2 months but continued to respond to topical tacrolimus ointment almost immediately. During the first 3 months of the boy's life, the ulcerations on the face healed with extensive hypopigmentation and atrophy



**Figure 2.** Annular subacute cutaneous lupus erythematosus lesions on the arm of the patient at 3 months of age.

(Figure 3). Consequently, Mederma<sup>®</sup> Skin Care for Scars<sup>™</sup> was added to the regimen in an attempt to improve healing. Steady improvements in the texture, thickness, and pigmentation of the facial skin were noted during the next 6 to 9 months. At 1 year of age, the areas were almost fully repigmented, with only mild mottling and some localized dyspigmentation (Figures 4 and 5).

The infant's ANA, anti-Ro, and anti-La antibodies were negative on repeat testing at age 3 months; however, despite the initially negative cardiac examination, the results of an electrocardiogram noted skipped heart beats. The child is now being followed for a first-degree atrioventricular node heart block, which was not complete (ie, not third degree).

### Comment

NLE, sometimes referred to as neonatal lupus syndrome, is an uncommon disease of the newborn characterized by a wide variety of manifestations including cutaneous, cardiac, hepatobiliary, and hematologic abnormalities. NLE is associated with transplacental passage of maternal immunoglobulin G antibodies (anti-Ro/SSA, anti-La/SSB, and/or anti-U<sub>1</sub>RNP) into the fetal circulation. The incidence with subsequent pregnancies has been estimated to be 16% to 25%.<sup>1,2</sup>

NLE was first reported by McCuistion and Schoch<sup>3</sup> in 1954 in a newborn with an eruption consistent with LE. The infant was born to a healthy mother who developed systemic LE 11 months later. It was not until 1981 that the strong association between NLE and the presence of maternal anti-Ro

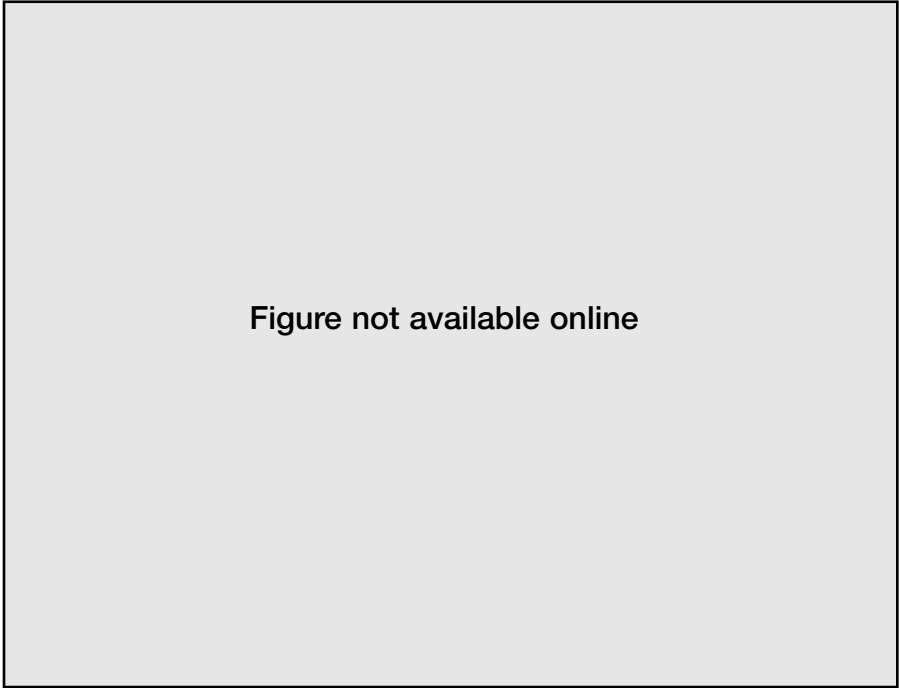


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**Figure 3.** Mottled pigmentation of the face after 3 months of healing.

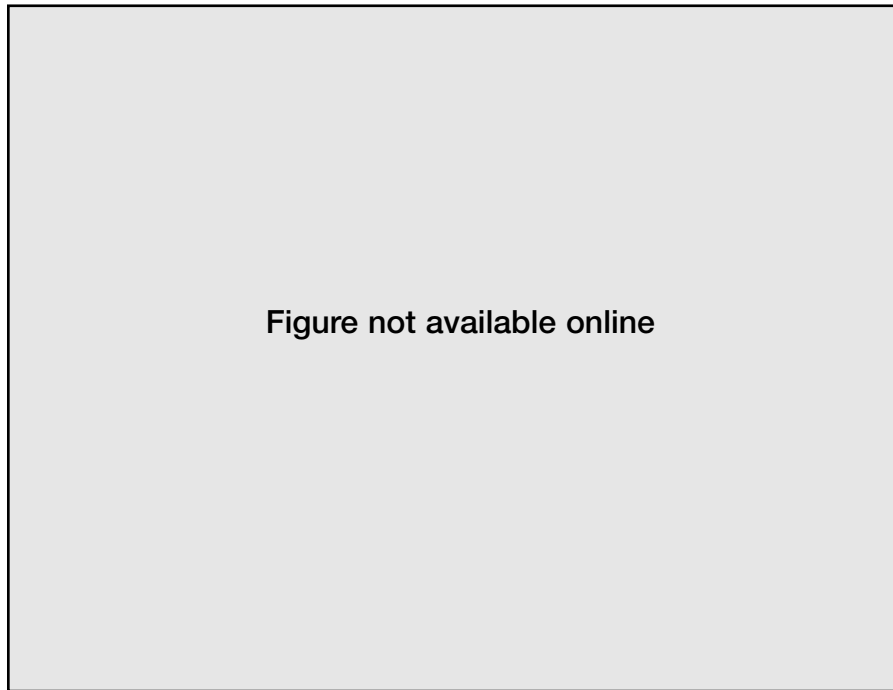
antibodies was recognized.<sup>4</sup> Approximately one quarter to one half of infants with NLE have skin lesions. The female-male ratio in large studies has been 1:1, but some studies have suggested a 3:1 ratio.<sup>1,4</sup>

It has been suggested that UV radiation promotes the appearance of Ro antigen on the surface of keratinocytes, which may make it more accessible to anti-Ro antibodies.<sup>5</sup> Estrogen has been shown to increase Ro expression on keratinocytes, which may explain the overexpression of NLE skin lesions in newborn and infant girls.<sup>6</sup> There are 3 classifications of NLE: (1) skin lesions only, (2) skin lesions associated with systemic manifestations, and (3) heart involvement with or without skin manifestations.<sup>7</sup>

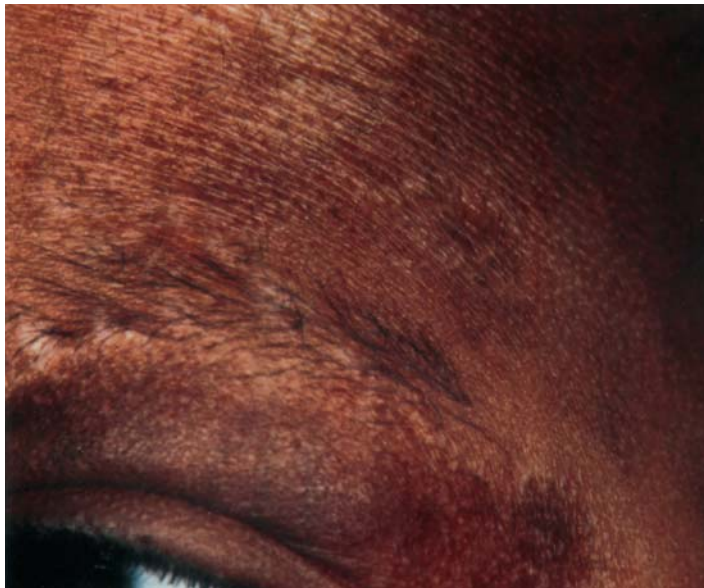
The skin lesions are usually circumscribed or confluent erythematous macules, papules, and/or plaques.<sup>8</sup> The plaques tend to be discrete and round or elliptical, with fine hyperkeratosis and mild atrophy. The lesions have a propensity to involve the face and scalp; however, the rash may occur in sites not exposed to the sun, such as the palms and soles or the diaper area. Lesions also can develop in utero, demonstrating that UV light is not a prerequisite.<sup>9</sup> The lesions are present at birth in two thirds of patients and develop in the rest of patients by the second or third month of life. Lesions are often induced or exacerbated by sun exposure. Resolution of the lesions can begin as early as 6 months of age and is usually complete by 12 months of age.<sup>7</sup> Residual telangiectasias and mild atrophic scarring occasionally can be seen.<sup>8</sup>

The residual scarring, atrophy, and dyspigmentation of NLE lesions can persist. The oldest child reported to have persistent scars was a 12-year-old white girl.<sup>2</sup> The cardiac manifestations of NLE are irreversible. The anti-Ro antibody is believed to bind to and cause fibrosis of the atrioventricular bundle of the developing cardiac conduction system. Structural congenital cardiac lesions found in patients with NLE are partial congenital heart block or, more commonly, complete congenital heart block (CCHB); transposition of the great vessels; ventricular and atrial septal defects; patent ductus arteriosus; and anomalous pulmonary venous return. CCHB is by far the most common finding.<sup>7</sup> Isolated CCHB occurs in approximately 1 in 20,000 births, and NLE accounts for more than 90% of all cases.<sup>9</sup> Many patients with CCHB present after the neonatal period. Infants may present at any time within the first year of life with heart block symptoms that can include congestive heart failure. It has been reported that 40% to 67% of patients with CCHB require pacemaker insertion during or after the neonatal period.<sup>1</sup> A large registry cohort demonstrated a 19% mortality rate in children with NLE involving the conduction system.<sup>1</sup>

NLE should be suspected in newborns with characteristic skin lesions or CCHB. The diagnosis can be confirmed by a positive anti-Ro, anti-La, or anti-U<sub>1</sub>RNP antibody test result of the newborn and mother, the latter being associated with skin lesions in the absence of cardiac disease.<sup>10</sup> The higher the ANA and anti-Ro antibody titers, the greater the



**Figure 4.** Face of the patient at 1 year of age.



**Figure 5.** Close-up of the forehead revealing improved color and reduced atrophy.

risk of transmitting NLE to offspring. Interestingly, some mothers positive for the anti-Ro antibody have infants with NLE, whereas others do not. This observation may indicate another factor predisposing to the disease. Most asymptomatic mothers eventually go on to develop photosensitivity and signs of systemic LE. Thus, treatment is prudent, particularly if further childbearing is desired by the mother. A registry of mothers of babies with NLE

revealed that 73% of those who had more children had healthy offspring.<sup>1</sup> If the mother of a baby with NLE remains untreated, she may have more children with NLE. Factors that may reduce titers of anti-Ro in mothers, such as oral terbutaline, systemic corticosteroids, or plasmapheresis, may reduce the risk of NLE in future offspring or the severity of disease in fetuses who had fetal echocardiograms with abnormal results. Broad spectrum sunscreens are especially prudent in mothers of babies with NLE, because UV light exposure is associated with worsening of systemic LE. Serial fetal echocardiograms may be indicated at 16, 18, 20, 22, and 24 weeks in fetuses of mothers with high anti-Ro titers.<sup>1</sup>

Skin lesions of NLE usually resolve spontaneously without scarring by 12 months of age. The transient nature of skin lesions can be well explained by the disappearance of maternal antibodies from the infants' sera by ages 6 to 12 months.

Thornton et al<sup>8</sup> reported the occurrence of telangiectasias in areas unaffected by the NLE lesions in infants of mothers positive for anti-Ro antibody, which suggests that telangiectasias may be a manifestation of NLE. Mothers of infants with isolated telangiectasia should be screened for the presence of anti-Ro and anti-La antibodies.<sup>8</sup> Results of biopsies of lesions usually show epidermal basal cell damage, vacuolar degeneration of the basement

membrane, and a mild mononuclear cell infiltrate in the dermis with particulate deposits of immunoglobulin G seen on direct immunofluorescence microscopic examination.<sup>11</sup>

Treatment is usually symptomatic, often consisting of mild therapies such as hydrocortisone cream or avoidance of UV light. Pulsed dye laser treatment has been shown to be effective for the treatment of cutaneous telangiectasia.<sup>7</sup> There has been a single case report of a 12-year-old child with persistent scars that responded to tretinoin, hydroquinone, and photoprotection.<sup>1</sup> As a prophylactic measure to prevent CCHB in newborns, plasmapheresis and prednisone can be administered to pregnant women who have high titers of anti-Ro or anti-La antibodies. Our patient's active NLE lesions did well with sun block and topical tacrolimus 0.03% ointment. His scarring responded well to Mederma. These treatments should be considered as alternative therapies for NLE.

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