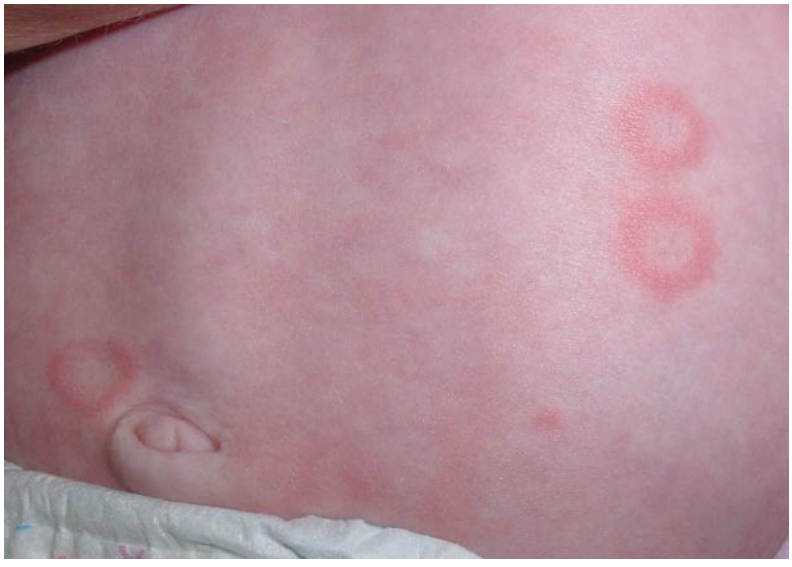
What Is Your Diagnosis?



A 1-month-old well-appearing infant presented with numerous erythematous annular plaques on her abdomen, scalp, and extremities.

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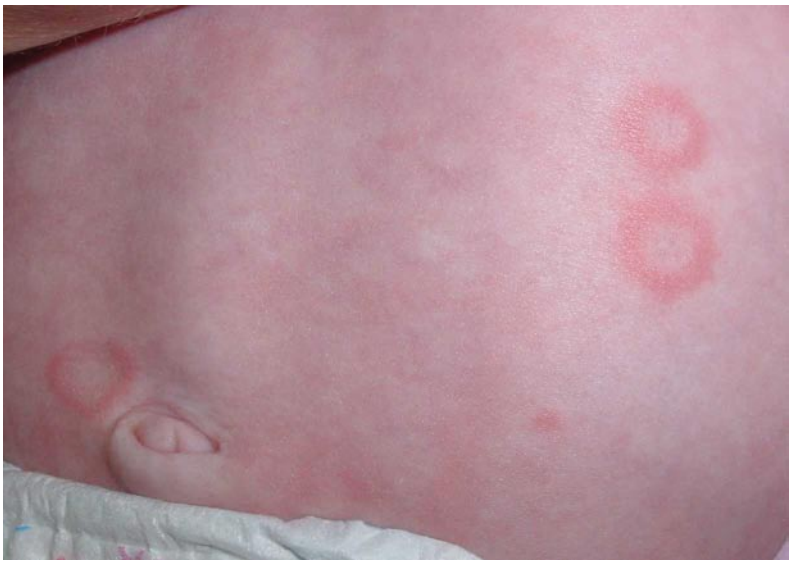
The authors report no conflict of interest.

The Diagnosis: Neonatal Lupus Erythematosus



This infant presented with a 3-week history of a rash, which started as red papules and evolved into annular erythematous plaques. Other than sleep apnea, this full-term newborn was healthy. The pregnancy was uneventful with the exception of maternal group B streptococcal infection that was treated successfully during labor. On examination, numerous erythematous, annular, nonscaly plaques with central hypopigmentation were noted on the infant's abdomen, scalp, and lower extremities.

A biopsy specimen of the rash revealed superficial and deep perivascular and interstitial lymphocytic infiltrate admixed with mast cells, eosinophilic leukocytes, and neutrophils. Serologic studies of the infant were positive for anti-Ro(SS-A) (Sjögren syndrome antigen A), and antinuclear antibodies (titer >1:640, speckled pattern), and results of an echocardiogram (2-dimensional echocardiography) were normal. Subsequently, laboratory tests of the infant's 27-year-old asymptomatic mother were positive for rheumatoid factors, antinuclear antibodies (titer >1:640, speckled pattern), anti-Ro(SS-A), anti-La(SS-B) (Sjögren syndrome antigen B), and double-stranded DNA antibodies. Test results for antiribonucleoprotein (anti-RNP), histone immunoglobulin G (IgG), and Smith antigen antibodies were negative. The mother's C-reactive protein levels also were elevated. The findings were consistent with the diagnosis of neonatal lupus erythematosus (NLE). NLE is a rare disorder caused by the transplacental transfer of maternal anti-Ro(SS-A), anti-La(SS-B), or anti-U1RNP autoantibodies.[1] Although the exact prevalence is unknown, data extrapolated from congenital heart block (CHB) statistics suggest a prevalence of NLE in at least 1 per 12,500 live births.[1-3] In some studies, results showed that female infants are more commonly affected by NLE than males.[2,4] This female preponderance may be caused by the increased expression of Ro(SS-A) by keratinocytes exposed to estrogen.[4,5] The most common manifestations of NLE are cutaneous, cardiac, hepatic, and hematologic abnormalities.

Cutaneous lesions occur in approximately 50% of infants with NLE[1,2] and generally consist of small erythematous macules that progress to annular plaques, sometimes with scaling, resembling subacute cutaneous lupus erythematosus.[1,2,6-8] Lesions frequently occur on the face with a periorbital "owl eye" or "eye mask" facial rash and also may involve the neck, scalp, extremities, and trunk. Crusted lesions also have been reported but mostly in the male neonate population.[7] The rash may mimic tinea faciei, eczema, and Langerhans cell histiocytosis.[8] There may be a history of sun-induced lesions; however, the rash may be apparent at birth and also may involve the groin and other sun-protected areas.[4,7] Cutaneous manifestations develop within the first few weeks of life[4] and usually disappear within 6 months, leaving minimal or no residual pigmentary

changes. Features of cutis marmorata telangiectatica congenita have been reported.[7] Telangiectasia may remain after the rash resolves and may be treated by flashlamp pulsed dye laser if persistent. Areas of hypopigmentation and hyperpigmentation also have been reported and usually resolve within a few years.[7] Residual atrophy, scarring, and alopecia rarely have been reported.[4]

Microscopic evaluation of the skin lesions reveals findings analogous to those of subacute cutaneous lupus erythematosus with vacuolar degeneration of the basal cell layer and a perivascular lymphocytic infiltrate. Deposition of IgG around keratinocytes and along the basement membrane may be demonstrated by direct immunofluorescence.[2,7]

The dermatopathologic findings in this case showing superficial and deep perivascular and interstitial lymphocytic infiltrate, although not diagnostic for NLE, are consistent with the condition. These changes also may be seen in annular erythema of infancy,[9,10] which generally is considered a self-limiting, erythematous, annular rash (sometimes with atrophy) and does not fit criteria for other diagnoses. The clinical presentation of this infant, positive serologies of both the infant and mother, and pathology are consistent with NLE.

Although the infant's echocardiogram was normal, cardiac abnormalities may occur and carry a substantial risk of morbidity and mortality. Complete CHB is the most severe and life threatening of these abnormalities.[2] CHB appears to be caused by immunodeposition of Ro(SS-A) antibody around the atrioventricular node, resulting in fibrosis and calcification, and is associated with 15% to 30% mortality.[2,11,12] In one study of surviving affected children, 67 of 107 children (63%) required permanent pacemaker placement.[12] Additionally, infants with NLE may suffer from other heart-associated irregularities, including congenital malformations, congestive heart failure, and less severe conduction aberrations that may manifest as prolonged QT intervals or bradycardia on electrocardiogram.[2,6] Therefore, cardiac evaluation is imperative in these infants.

Additional extracutaneous manifestations include hepatic and hematologic abnormalities. Hepatomegaly is seen in approximately 20% to 40% of infants with NLE. Other hepatic irregularities include elevated aminotransferase levels, cholestasia, fibrosis, and hepatitis.[2,6,7] In 10% to 20% of infants with NLE, transient thrombocytopenia is apparent.[2] Other hematologic abnormalities include neutropenia and anemia.[6] Patients with these laboratory abnormalities often are asymptomatic. As with the dermatologic manifestations, these hepatic and hematologic changes generally are transient in nature and normally resolve without sequelae.[2,6] Complete physical examination and laboratory workup is important in these patients given the broad spectrum of the disease.

NLE develops when maternal IgG autoantibodies against Ro(SS-A), La(SS-B), and less frequently U1RNP are passively transported across the placenta. These antibodies can be found alone or in any combination, though anti-Ro(SS-A) antibody is seen in nearly all cases of infants and mothers with NLE.[2] Cell membranes of basal keratinocytes express the Ro(SS-A) antigen. After UV exposure, this antigen may lead to antibody production that may precipitate cell toxicity.[13] Not all infants born to anti-Ro(SS-A)–positive mothers develop NLE. In one study, approximately half (66/128) of the infants of mothers with anti-Ro(SS-A) and autoimmune disease or a history of a prior infant with NLE had any signs of NLE.[6] Because only some of the infants of anti-Ro(SS-A)–positive mothers develop NLE, other intrinsic factors, including genetic predisposition, and extrinsic factors, such as viral infection, may contribute to the pathogenesis.[2,11] Autoantibodies associated with NLE disappear by 6 months of age because they are maternal in origin, and the skin lesions generally fade.[2] Approximately half of mothers are asymptomatic at the time of delivery. With time, however, many asymptomatic mothers develop systemic lupus erythematosus, Sjögren syndrome, or a combined syndrome of both systemic diseases. In one study, over 5 years, 18 of 21 mothers developed symptoms of collagen vascular disease.[2,14]

Sun protection is the most important element in the treatment of skin lesions of NLE.[2] Topical corticosteroids may be used judiciously when needed. Children with NLE who have only skin involvement have a good long-term prognosis, as do those with CHB as long as the heart block is treated. Furthermore, having cutaneous NLE does not seem to substantially increase the child's risk of developing an autoimmune disease later in life.[2] Early recognition of NLE, possibly even during gestation, may prevent risks associated with undetected cardiac abnormalities. As with our case, the frequent asymptomatic status of the mother makes prenatal recognition of NLE difficult.

It is interesting to note that while the mother in this case reported to be in good health, she later noted a remote history of pleurisy as well as blurry vision for which she had lacrimal plugs placed. She also reported a history of dry mouth and periodic arthralgia. She consulted a rheumatologist secondary to her positive serologic results and has since been diagnosed with Sjögren syndrome.

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