Neonatal Lupus Erythematosus

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Neonatal lupus erythematosus (NLE) is a rare disease characterized by the transplacental passage from the mother to the fetus of autoantibodies, in particular anti-Ro(SS-A), anti-La(SS-B), or both. The majority of infants with NLE exhibit isolated congenital heart block, cutaneous lesions analogous to those of adult subacute cutaneous lupus erythematosus, or both. We report a case of NLE in a 3-month-old male infant, born to a clinically asymptomatic mother, presenting small, annular, erythematous plaques with sharp, hyperkeratotic borders and central clearing localized at the eyebrow region. Both the infant and the mother were positive for anti-Ro(SS-A).

Neonatal lupus erythematosus (NLE) syndrome, first described by McCuistion and Schoch[1] in 1954, is a rare condition related to the transplacental passage of autoantibodies to extractable nuclear antigens, anti-Ro(SS-A) and anti-La(SS-B), or ribonucleoproteins, anti-U1RNP. This syndrome is characterized by the presence of 1 or more of the following conditions: cutaneous lupus lesions, congenital heart block (CHB), cholestatic liver disease, and thrombocytopenia. Cutaneous lesions and CHB are the most common. The skin lesions are usually annular, polycyclic, inflammatory lesions resembling those of adult subacute cutaneous lupus erythematosus, and are most prominent in sun-exposed areas.

Neonatal lupus occurs in babies exposed to maternal anti-Ro(SS-A) or anti-La(SS-B) autoantibodies, and, in a few cases, anti-U1RNP antibodies, in absence of Ro, suggesting that these autoantibodies play a role in the pathogenesis of heart and skin damage that occurs in NLE. It is still unclear why the majority of infants exposed to anti-Ro show no sign of disease, while some develop CHB, cutaneous NLE, or both. The hypothesis of an interaction between genetic factors and autoantibodies in the pathogenesis of the disease has been investigated by immunogenetic studies, indicating a high prevalence of human major histocompatibility antigens (HLA)-DR3 in mothers with NLE.[2-4]

Case Report

A 3-month-old male infant, born at the 35th week of gestation by elective cesarean, presented with small, annular, erythematous plaques of several millimeters diameter with sharp, hyperkeratotic borders and central clearing localized at the eyebrow region (Figure 1). No other physical abnormalities were noted. Complete blood count, electrocardiogram, and hepatosplenic ultrasound were normal. Liver function studies revealed a mild increase of AST and gGT. A skin biopsy showed slight hyperkeratosis, a mild perivascular and perifollicular lymphohistiocytic infiltrate, and minimal edema of the dermis (Figure 2). Direct immunofluorescence testing of the lesional skin gave negative results.

Serologic studies were positive for anti-Ro(SS-A) at a titer of 1:158. Ro(SS-B), Sm, U1RNP, nDNA, and antinuclear antibodies (ANA) were negative. C3 and C4 were normal. Over a 5-month period, the le-

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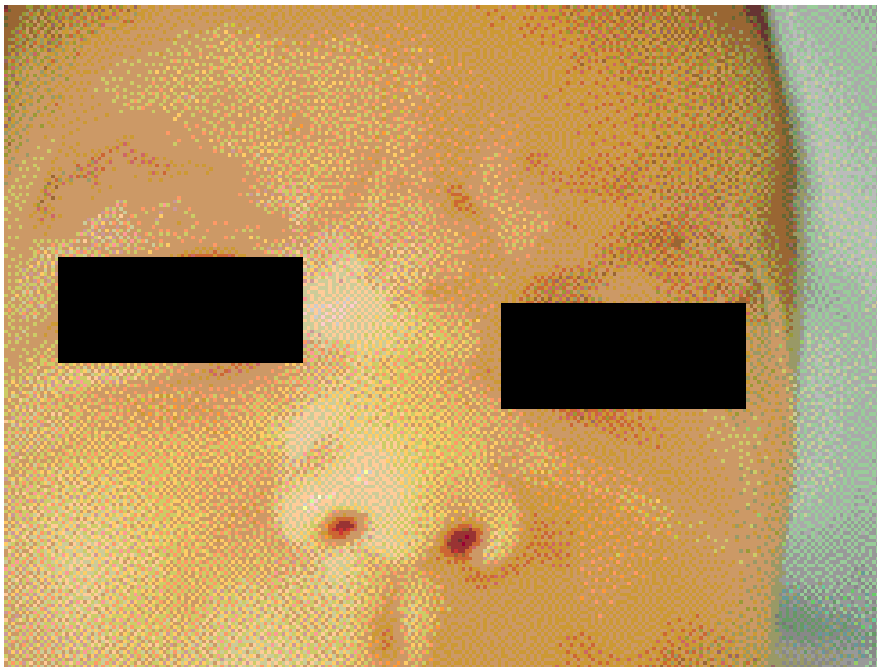

FIGURE 1. Cutaneous lesions of NLE. Erythematous annular plaques with central clearing on the forehead.

sions faded, leaving a mild residual atrophy. Anti-Ro(SS-A) and ANA studies performed at 8 months of age were negative. The HLA phenotype was A2, A23; B58, B49; DR3, DQ6.

The 36-year-old mother was clinically asymptomatic at the time of our observation. This case was her third pregnancy; two previous ones had ended in spontaneous abortion. Laboratory findings showed a hypergammaglobulinemia (IgG 1800 mg/dl), positive ANA (1:80, speckled), and positive anti-Ro(SS-A) antibodies (1:124). La(SS-B), Rm, nDNA, and U1RNP antibodies were all negative. Blood count, liver and renal function tests, and erythrocyte sedimentation rate were normal. Direct immunofluorescence testing of non-photo-exposed skin showed no deposits of immunoglobulins or complement, while in photo-exposed skin a granular deposit of IgM was present in papillary dermis. The HLA phenotype was A2, A29; B58; DR3; DQ6.

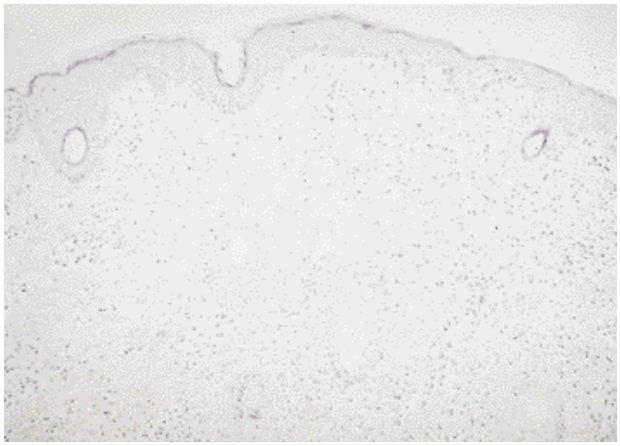

FIGURE 2. Histology of a skin biopsy demonstrating a slight hyperkeratosis and a perivascular and perifollicular mononuclear infiltrate (H&E; original magnification × 10).

Comments

Neonatal lupus syndrome is a rare disease, probably underdiagnosed until 1980, when the association with maternal anti-Ro antibodies was reported.[5,6] Its prevalence is not known, but estimates of 1:12,500 to 1:20,000 live births have been extrapolated from data on CHB incidence.[7,8]

The typical cutaneous lesions, occurring in about 50% of cases, are round or elliptical, scaly, erythematous plaques. They are most frequently localized on the face and scalp, although widespread involvement of body surface may occur. Skin lesions usually disappear in weeks or months, leaving minimal or no residual pigmentation changes. Scarring or atrophy has been rarely reported. Persistent telangiectases are a feature of NLE. They represent a residual of the specific lesions and typically become evident after the initial lesions have resolved. Vascular lesions (telangiectatic macules and angiomatous papules) have been recently reported as the only skin manifestation of several cases of NLE.[9]

Complete, irreversible, isolated heart block occurs in about half of the cases of NLE.[10] A slow fetal heart rate, usually detected in late pregnancy, may lead to the diagnosis of CHB. Heart block may be detected as early as the 18th week of pregnancy.

Liver enlargement and increased transaminase enzymes have been reported in 20 to 40% of NLE in-

fants.[11] Transient thrombocytopenia occurs in 10 to 20% of NLE infants. Aplastic anemia has also been described.[12] Neurologic abnormalities associated with NLE have been recently reported.[13]

Our case presented only typical NLE skin lesions. The course of the disease was benign, as in most cases of cutaneous NLE, with complete clearing of the lesions in a few months. In agreement with data reported in the literature,[2,3] our mother–child couple showed the association of anti-Ro(SS-A) positivity with HLA-DR3 phenotype.

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