

Neonatal lupus erythematosus or Sweet syndrome?



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Key words: lupus erythematosus; neonate; Sweet syndrome.

A 2-month-old baby boy was admitted to our hospital with a diffuse rash. Birth history was uneventful. Prenatal screening serology for HIV and syphilis was negative. The mother was known to have lupus nephritis that had been in remission for 5 years with regular monitoring.

On examination, the baby had indurated, erythematous plaques around both eyes, and the conjunctiva and sclera were normal. He had erosions on the hard palate. On the trunk, back, arms, legs, palms, and soles he had striking annular plaques with a raised erythematous border (Figs 1 and 2). He was afebrile, with a normal blood pressure and pulse rate. Respiratory, cerebrovascular, and central nervous system findings were all normal. His developmental milestones were appropriate for age.

His blood profile revealed a thrombocytopenia of $37 \times 10^9/L$ (normal range, $140\text{--}350 \times 10^9/L$), white cell count of $6.12 \times 10^9/L$ (normal range, $5.50\text{--}18.00 \times 10^9/L$), hemoglobin level of 9.6 g/dL (normal range, 9.1–13.1 g/dL), and mean corpuscular volume of 79.3 fL (normal range, 77.0–105.0 fL). Our laboratory measures antinuclear antibodies using the EliA connective tissue diseases (EliA CTD Screen) fluoro enzyme immunoassay, and results are reported in a ratio as either negative (<0.7), equivocal (0.7–1.0), or positive (>1.0). Our patient had positive antinuclear antibodies of 24.0, a positive anti-SS-A (Ro) greater than 240 U/mL, and a positive anti-SS-B (La) greater than 320 U/mL. Anti-double-stranded DNA antibody was not detected, and complement C3 and C4 were normal. Liver function values were elevated, with an increased alanine transaminase of 210 U/L (normal range, 4–35 U/L), aspartate transaminase of

Abbreviations used:

SLE: systemic lupus erythematosus
SLND: Sweet-like neutrophilic dermatosis

737 U/L (normal range, 0–65 U/L), alkaline phosphatase of 977 U/L (normal range, 82–383 U/L), and gamma-glutamyl transferase of 224 U/L (normal range, 12–122 U/L). The mother's blood profile also revealed a positive anti-(Ro) greater than 240 U/mL and a positive anti-(La) greater than 320 U/mL.

Skin punch biopsy of an annular plaque on the trunk found a spongiotic neutrophilic dermatitis, with a focus of interface inflammation. The dermis showed subepidermal edema with diffuse perivascular and periadnexal dense neutrophilic inflammation (Figs 3 and 4). There was abundant karyorrhectic debris present and scattered eosinophils. No lymphocytes were noted. There was no evidence of vasculitis or blistering. No mucin stains were done. The report concluded that this was a neutrophilic dermatosis, consistent with Sweet syndrome.

The patient's clinical presentation and serology were in keeping with neonatal lupus. An electrocardiogram and cardiac echocardiogram were done, both of which showed normal heart function. On discharge, after 4 days of monitoring in the hospital, his thrombocytopenia had self-corrected, and the liver enzymes showed a decreasing trend without any intervention. The skin lesions were treated with 0.025% fluocinolone acetonide ointment. Over the following 3 months, he attended 2 dermatology and

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Fig 1. Diffuse erythematous annular and discoid plaques on trunk and arms. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: [VM04872](#).



Fig 2. Erythematous annular plaques on back. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: [VM05092](#).

3 rheumatology outpatient clinics, and the lesions resolved with postinflammatory hyperpigmentation (Fig 5). Three months after admission, his liver enzymes had normalized. Heart function remained normal at his 6-month repeat electrocardiogram and cardiac echocardiogram investigations.

DISCUSSION

Neonatal systemic lupus erythematosus (SLE) is a rare acquired autoimmune disease. It affects approximately 10% to 20% of infants born to mothers with anti-Ro and anti-La autoantibodies who either have known or undiagnosed SLE, Sjögren syndrome, or undifferentiated autoimmune syndrome with circulating autoantibodies.¹ Maternal autoantibodies anti-Ro and anti-La are transferred from the maternal circulation across the placenta into the fetal circulation.² Anti-Ro autoantibodies are usually found in Sjögren syndrome, but they can also be found in 30% of patients with SLE with cutaneous involvement.³ Cutaneous clinical presentation of neonatal lupus typically affects sun-exposed areas but may occur on the trunk, palms, and soles.¹ The lesions are erythematous patches or plaques, annular or discoid in shape. There may be atrophic macules or patches with or without telangiectasia.¹

Extracutaneous manifestations of neonatal lupus include heartblock, cardiomyopathy, abnormal liver function tests with or without cholestatic features, hematologic abnormalities including anemia, thrombocytopenia, leukopenia, and central

nervous system findings with hydrocephalus.¹ Congenital heart block develops in 15% to 30% of babies with neonatal lupus with 10% going on to develop cardiomyopathy.¹ An electrocardiogram is recommended at the time of diagnosis of neonatal lupus.⁴ Any abnormality detected warrants referral to a cardiologist for further management. Our patient had cardiac investigations done at diagnosis of neonatal lupus at 7 weeks and at 6 months, which showed normal functioning of his heart. The Research Registry for Neonatal Lupus (United States) reports the mortality rate of cardiac neonatal lupus at approximately 20%.⁵ Treatment of neonatal lupus is organ specific and depends on the severity of the presentation. Infants with neonatal lupus who present with cutaneous, abnormal liver function tests and hematologic abnormalities usually have a resolution of signs and symptoms within 4 to 6 months, with the clearing of maternal autoantibodies.^{1,6} This was true for our patient. Supportive measures such as avoidance of sun exposure and sunscreen application are encouraged. Low- to mid-potency topical steroids and topical calcineurin inhibitors can be prescribed in some patients with cutaneous lesions, although they usually heal with no sequelae.¹ However, there have been reports of atrophy and hyperpigmentation.⁶

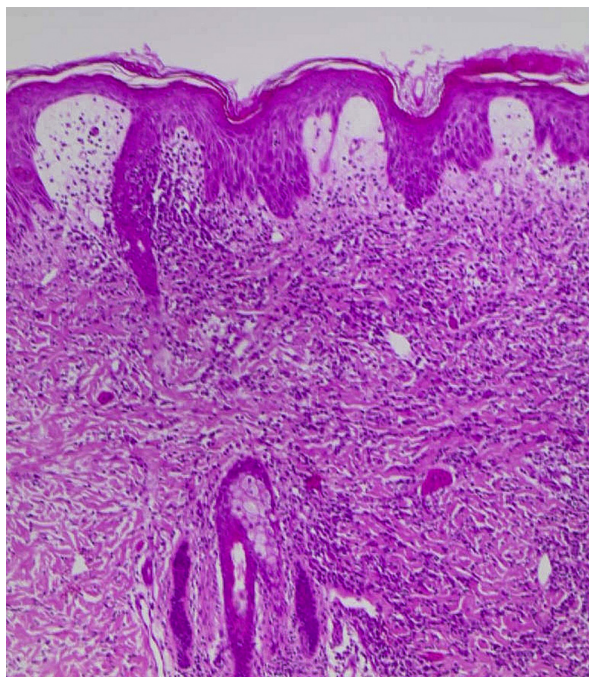


Fig 3. Low-power magnification shows superficial dermal edema and dense perivascular and periadnexal inflammatory infiltrate. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: [VM05093](#).

We are not aware of any children with neonatal lupus who went on to have systemic lupus in childhood or adulthood as a direct result of neonatal lupus. However, there is evidence from familial aggregation studies in SLE that illustrate that 10% to 12% of patients with SLE have first- or second-degree family members with the disease compared with less than 1% of controls.⁷ Thus, the risk of a child of a mother with SLE having systemic lupus is greater than that of the general population.

Histologic findings in neonatal lupus resemble that of subacute cutaneous lupus, with a lymphocytic infiltrate surrounding the superficial vascular plexus and adnexal structures and may extend into the dermis and subcutaneous tissues. An epidermal interface may be present with increased dermal mucin deposition.⁸ The biopsy taken from our patient showed interface inflammation, subepidermal edema, diffuse perivascular and periadnexal neutrophilic inflammation, abundant karyorrhectic debris, and scattered eosinophils, favoring Sweet syndrome. In 2007, Satter and High⁹ reported a similar case to ours of 2 infants with neonatal lupus whose skin biopsies found a dermal neutrophilic infiltrate and neutrophilic debris. Another more recent case report in 2014 described a neonate with neonatal lupus, whose skin biopsy showed a dermal

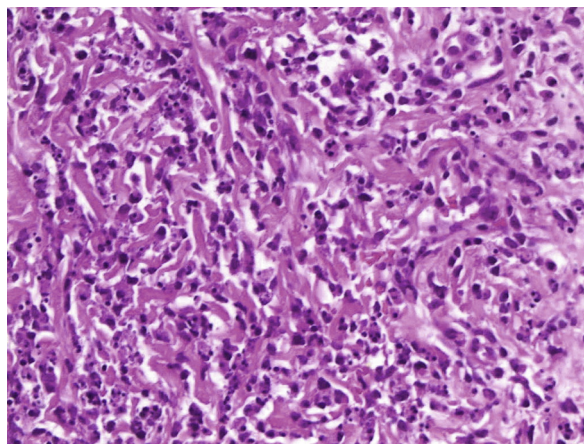


Fig 4. High-power magnification shows neutrophilic inflammation. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: [VM05094](#).

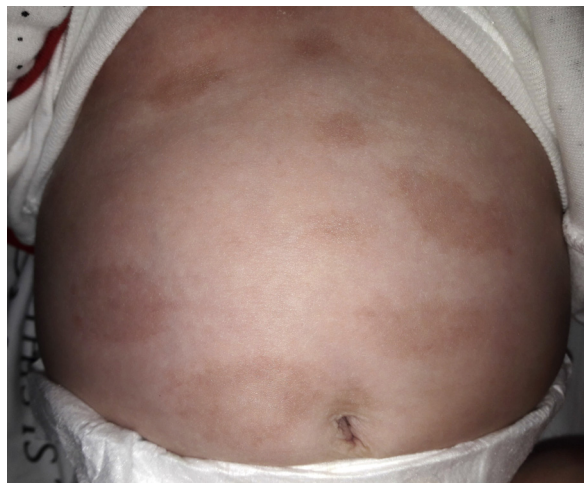


Fig 5. Resolved plaques on the abdomen, healing with post inflammatory hyperpigmentation. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: [VM05095](#).

interstitial lymphocytic and neutrophilic infiltration with nuclear dust.¹⁰ An association between Sweet syndrome and SLE has been described in the literature. The term *nonbullous neutrophilic dermatosis of lupus erythematosus* was first described by Gleason et al¹¹ and later by Satter et al⁹ to illustrate cases of neutrophilic dermatosis associated with SLE.^{9,11,12} It has been suggested that Sweet syndrome can be an initial manifestation of SLE.¹³ Sweet syndrome is a neutrophilic dermatosis. Neutrophilic dermatoses are thought to represent a hypersensitivity immune response in relation to infections, malignancy, medication, or various autoimmune diseases.¹³ In neutrophilic dermatoses, there is

infiltration of the epidermis, dermis, or subcutaneous tissue with polymorphonuclear cells without primary infection.¹⁴ Sweet syndrome can be classified as primary or secondary.¹⁴ Secondary Sweet syndrome can be associated with inflammatory conditions including infections and autoimmune conditions, paraneoplastic or drug related.^{1,14} Histology of Sweet syndrome shows variable epidermal changes and superficial dermal edema sometimes with a subepidermal blister.¹⁵ There is a diffuse neutrophilic dermal infiltrate, which may include lymphocytes, histiocytes, and a few eosinophils.¹⁵ There is no true vasculitis, but leukocytoclasia is common with occasional extravasated erythrocytes.¹⁵ Like Gleason,¹¹ Pavlidakey et al¹³ describe a distinct and unusual eruption consisting of a Sweet-like neutrophilic dermatosis (SLND), in conjunction with previous or concomitant SLE.¹³ This is defined as a neutrophil-predominant infiltrate of the dermis with leukocytoclasia, without the involvement of the epidermis.¹³ Detection of SLND in a patient with SLE suggests the possibility of shared or overlapping pathogenic mechanisms.¹³ It is suggested that SLND is part of a spectrum of SLE and may present as an early manifestation of SLE.¹³

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