

# Skin rash in a 2-week-old infant

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### ABSTRACT

*We presented a case of a male infant with annular patchy rash on his torso since 2 weeks of age. This was initially diagnosed as tinea corporis but did not respond to oral antifungal treatment. Because of the appearance of the rash and a history of a certain disease in a maternal aunt, we suspected the most probable cause of the rash and the diagnosis was confirmed by laboratory testing. Furthermore, laboratory screening of the mother, who was asymptomatic, revealed that she was seropositive for the disease and was counseled on the importance of follow-up. The infant's rash gradually improved and completely disappeared, without any sequelae by 8 months of age.*

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### CHIEF CONCERN

**P**ersistent rash in a young infant.

### HISTORY OF PRESENT ILLNESS

A 3.5-month-old full-term African American boy was referred to the allergy/immunology clinic because of a 1-cm annular patch on his chest, which appeared at 2 weeks of age. The infant was bottle-fed since birth, was afebrile, and had no respiratory or gastrointestinal symptoms. He was initially seen by a pediatrician who prescribed hydrocortisone 2.5% cream application three times a day; however, the lesions multiplied and expanded in diameter. Another physician thought the rash was fungal (tinea corporis) and prescribed oral griseofulvin, without improvement.

### Family History

The infant's 28-year-old mother had asthma, severe atopic dermatitis, and food allergy under good control. A 2-year-old healthy sister had had a similar rash during the neonatal period, which resolved spontaneously. The maternal aunt had systemic lupus erythematosus (SLE).

### PHYSICAL EXAMINATION

At our initial evaluation of the infant at 3.5 months of age, he was well developed and playful, and had normal vital signs. His tonsils were normal in size and appearance. He had small cervical lymph nodes and no palpable liver or spleen. The chest auscultation showed clear lungs and normal heart sounds. The skin showed multiple annular erythematous lesions, with central clearing on the torso, which varied in diameter from 5 to 13 cm (Fig. 1 a).

### QUESTION 1

What Is the Differential Diagnosis?

A variety of conditions can cause a persistent rash in a young infant (Table 1). Given the appearance and course of the cutaneous lesions and the history of SLE in the maternal aunt, neonatal lupus erythematosus (NLE) was at the top of our differential diagnosis list.

### QUESTION 2

What tests need to be done?

Initially, we requested a complete blood cell count with differential, basic metabolic panel, rapid plasma reagin, and antinuclear antibody (ANA). The results were all normal except for a strongly positive ANA.

### QUESTION 3

What further tests are needed?

Because of the positive ANA and the family history of SLE, we requested tests for a variety of autoantibodies; most of the results were positive (Table 2). Results of an electrocardiogram of the infant and of immunologic screening were normal (Table 3). We also evaluated the mother for autoimmune disorders, and

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**Figure 1.** (a) The rash at 3.5 months and at 6.5 months of age.

the result was compatible with subclinical lupus (Table 2).

### DEFINITIVE DIAGNOSIS

The infant was diagnosed with cutaneous NLE secondary to maternal transfer of autoantibodies, without cardiac, hepatic, or hematologic involvement.

### MANAGEMENT

The mother was reassured of the benign nature of the infant's condition and was advised to follow up with a rheumatologist for her own medical care.

### CLINICAL COURSE

When we saw the infant during the follow-up visit at 6.5 months of age, the mother reported an uneventful interval history except for an episode of upper respiratory tract infection. The infant's rash was markedly faded (Fig. 1 b). At 8 months of age, the rash completely resolved, without any depigmentation, and the infant was thriving well and completely asymptomatic.

### DISCUSSION

NLE is estimated to occur in ~1 in 12,500 live births.<sup>1,2</sup> It is probably underdiagnosed, particularly when the mother is asymptomatic, as the case with our patient. It results from transplacental transfer of maternal immunoglobulin G autoantibodies, including anti-Ro/SSA, anti La/SSB, and rarely U1-ribonucleoprotein.<sup>3</sup> NLE is a phenotypically variable disease that can affect one or multiple organs, with the skin being the most common.<sup>4–6</sup> The involvement of only one organ is more frequent than of multiple organs.<sup>1</sup> Cardiac and, less frequently, hepatobiliary and hematologic disorders can occur, with serious sequelae. Other systems are rarely affected. Central nervous system involvement may include vasculitis, macrocephaly,

and hydrocephaly. Musculoskeletal involvement may cause chondrodysplasia, and pulmonary lesions may cause necrotizing capillaritis. Although cutaneous NLE by itself is essentially a benign condition, as in our patient, a subsequent sibling has a 6–10 times higher risk of developing bundle-branch block.<sup>7</sup>

Cutaneous manifestations in NLE are variable. Our patient was initially misdiagnosed as having skin fungal infection and did not respond to antifungal therapy. The most common presentation is annular, erythematous, scaly, and nonscarring patches.<sup>4</sup> Bullous lesions may appear on the soles.<sup>4</sup> Other presentations include subacute cutaneous lesions, petechiae, persistent cutis marmorata, and discoid lesions.<sup>2</sup> Cutaneous lesions in NLE can appear anywhere on the body, including photo-protected areas. However, by far the most common site is the face, particularly around the eyes (giving a raccoon-like or owl-like appearance) in ~60% of all patients with NLE.<sup>8,9</sup> If it affects the scalp, NLE can lead to permanent alopecia.<sup>5</sup> Unlike SLE, malar involvement is uncommon.<sup>1</sup>

In our patient, the rash appeared at 2 weeks of age. The mean age for developing cutaneous lesions is 6 weeks,<sup>9</sup> although, in 10–20% of cases, it can be present at birth.<sup>8</sup> These lesions usually resolve spontaneously with the disappearance of maternal antibodies from the infant's circulation.<sup>1,5</sup> The duration of the cutaneous lesions ranges from 1.5 to 50 weeks, with an average of 17 weeks.<sup>9</sup> Occasionally, skin depigmentation or telangiectatic changes develop. The appearance of cutaneous lesions at birth is associated with a high risk of atrophy and scarring.<sup>10</sup> Our patient's skin lesions markedly improved by age 26 weeks and completely disappeared by 32 weeks of age.

A female preponderance of cutaneous NLE (2:1) was noted in a series from the United States National Research Registry for Neonatal Lupus,<sup>9</sup> whereas isolated cardiac involvement affected both sexes equally. It was hypothesized that the higher incidence in female patients may be due to an estrogen effect on increasing the expression of Ro and La proteins on keratinocytes.<sup>11</sup> However, a later report on a larger series did not confirm a significant female predominance.<sup>12</sup>

Many infants with NLE are born to mothers who are asymptomatic, as in our patient, hence, the importance of obtaining a detailed family history and of evaluating the mother. Only approximately half of mothers of infants with NLE have symptomatic rheumatologic disorders, including SLE, Sjögren syndrome, or undifferentiated connective tissue disease.<sup>13</sup> Jaeggi *et al.*<sup>14</sup> noted that 85% of mothers of infants with cardiac NLE were asymptomatic and had no connective tissue disease, and 98% of them did not have a previous child with cardiac involvement. Only 1–2% of mothers with lupus autoantibodies have offspring with NLE,<sup>13,15</sup> which indicates the involvement of other factors.<sup>5</sup> An

Table 1 Differential diagnosis of rash in the neonate

| Condition                              | Main Features                                                                                                   |
|----------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| Chronic urticaria                      | Annular, linear, or arcuate blanchable raised palpable wheals                                                   |
| Tinea corporis                         | Annular scaly plaque with central clearing                                                                      |
| Congenital syphilis                    | Erythematous maculopapular or bullous lesions, followed by desquamation that involves mainly the hands and feet |
| Cutaneous neonatal lupus erythematosus | Annular erythematous plaques with or without fine scales                                                        |
| Erythema marginatum                    | Annular erythema with elevated edges and flat clear center                                                      |
| Erythema multiforme                    | Annular, sharply demarcated, red and/or pink circular lesions with dark centers (target type)                   |
| Annular erythema of infancy            | Annular, gyrate lesions with red raised borders and central clearing, with or without scaling                   |

Table 2 Autoantibody profile in the infant and the mother

| Test                    | Results  |          |          | Normal Range |
|-------------------------|----------|----------|----------|--------------|
|                         | Infant   |          | Mother   |              |
|                         | At 26 wk | At 32 wk |          |              |
| ANA                     | Positive | Positive | Positive | Negative     |
| Anti-dsDNA level, IU/mL | 7        | 1        | 1        | <5           |
| Anti-SSA/Ro, AI         | >8       | 0.7      | >8       | <0.9         |
| Anti-SSB/La, AI         | >8       | 3.8      | >8       | <0.9         |
| Anti-Scl 70, AI         | <0.2     | <0.2     | <0.2     | <0.9         |
| Anti-Smith, AI          | 3.9      | <0.2     | 0.3      | <0.9         |
| Anti-RNP, AI            | 0.6      | 0.3      | <0.2     | <0.9         |
| RF level, IU/mL         | <7       | <10      | 59.1     | <13.9        |

ANA = Antinuclear antibody; dsDNA = double stranded DNA; SSA/Ro = Sjögren syndrome-related antigen A (also called Ro antigen) AI = antibody index; SSA/La = Sjögren syndrome-related antigen B (also called La antigen); Scl 70 = scleroderma antigen 70; RNP = ribonucleoprotein; RF = rheumatoid factor.

Table 3 Further laboratory evaluation of the infant at 6.5 months of age

| Test                                                | Results | Normal Range |
|-----------------------------------------------------|---------|--------------|
| IgG level, mg/dL                                    | 523     | 215–704      |
| IgA level, mg/dL                                    | 46      | 8–68         |
| IgM level, mg/dL                                    | 64      | 35–102       |
| IgE level, IU/mL                                    | 11.1    | 0.44–16.3    |
| CD3, total no. T cells/mm <sup>3</sup>              | 4182    | 1900–5900    |
| CD4, no. T-helper cells/mm <sup>3</sup>             | 2646    | 1400–4300    |
| CD8, no. T suppressor cells/mm <sup>3</sup>         | 1342    | 500–1700     |
| CD4:CD8 ratio                                       | 1.97    | 1.48–3.77    |
| CD19, no. B cells/mm <sup>3</sup>                   | 2162    | 610–2600     |
| CD16/56 <sup>+</sup> , no. NK cells/mm <sup>3</sup> | 181     | 160–950      |

Ig = Immunglobulin; NK = natural killer.

association was noted between maternal human leukocyte antigen (HLA)-DR3 and increased risk of developing neonatal LE.<sup>6</sup>

The diagnosis of NLE is based on clinical features and the presence of lupus autoantibodies in the

mother's and infant's sera. ANA with a speckled pattern is present in all infants with NLE and their mothers.<sup>2</sup> Autoantibody to Ro/SSA ribonucleoprotein is present in almost all cases; however, autoantibody to La/SSB is less commonly positive.<sup>2</sup> The

level of the autoantibodies is a risk factor in developing cardiac NLE. The latter is very unlikely to occur if the maternal anti-Ro level is <50 U/mL.<sup>14</sup> Therefore, in pregnant women with high levels of anti-Ro, the fetal heart should be monitored by serial prenatal ultrasonography and echocardiography.

Skin biopsy specimen findings in cutaneous NLE are nonspecific.<sup>1,8</sup> They may include keratinocyte damage with vacuolar changes at the dermoepidermal junction and adnexal structures as well as perivascular and periadnexal lymphocytic infiltration. In fewer than half of the cases, there are IgG deposits within the epidermis.<sup>1,8</sup> Cutaneous NLE has a benign course and excellent prognosis. Mild topical corticosteroids and avoidance of sun exposure enhance the resolution and reduce the risk of scarring.<sup>1</sup> Because of the genetic predisposition, children with NLE and their unaffected siblings have a higher risk of developing SLE or other autoimmune disorders later in life.<sup>5</sup> Of interest, our patient's older sister had a similar rash that resolved spontaneously, apparently without being diagnosed as NLE.

## CONCLUSION

NLE should be included in the differential diagnosis of annular rashes in young infants, even when the mother seems healthy. The mother can be asymptomatic despite her being seropositive for lupus. Cutaneous NLE is a benign condition that resolves spontaneously, but associated heart or other organ involvement can have a poor prognosis.

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