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CASE REPORT

Juvenile idiopathic arthritis in a patient with previous diagnosis of severe congenital lupus

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Neonatal lupus (NL) is an acquired autoimmune disease of the newborn, caused by transplacental passage of the maternal autoantibodies anti SS-A/Ro and anti SS-B/La. When the clinical picture starts directly at birth, it is known as congenital lupus (CL). The clinical manifestations are variable. Except for cardiac involvement, the other manifestations tend to be benign, and resolve with the child's clearance of maternal antibodies. We report a patient who presented at birth with very severe involvement of the skin, and subsequent contractures of hands and feet, leading to functional impairment. The patient underwent surgical procedures with excellent result. At the age of 18 months, the patient was diagnosed with oligoarticular juvenile idiopathic arthritis (JIA), and bilateral uveitis at the age of 3 years and a half. Our aim is to alert health professionals about the possibility of a severe course of cutaneous manifestations in CL, as well as the role of CL and NL regarding development of other autoimmune diseases. *Lupus* (2018) **27,** 154–157.

Key words: Neonatal lupus; congenital lupus; cutaneous lupus; cutaneous atrophy; juvenile idiopathic arthritis; childhood autoimmune disease

Introduction

Neonatal lupus (NL) is defined as clinical manifestations in the newborn due to the transplacental passage of maternal autoantibodies, independent of symptoms in the mother.[1,2] Anti SS-A/Ro and anti SS-B/La are the classic NL autoantibodies, and are found in almost all affected newborns. The rare NL cases that were negative for these antibodies had positive anti-U1-ribonucleoprotein (U1-RNP), and were characterized by cutaneous involvement alone.[1,3,4] Despite the role of anti SS-A/Ro and anti SS-B/La autoantibodies in the pathogenesis of NL, only about 2% of mothers who are positive for these antibodies will have a baby with the disease. This finding suggests that genetics and environment may also be involved in NL pathogenesis.[1,2]

Typical cutaneous involvement may be present in up to 25% of newborns with NL.[3,5] Although in some children the rash can be present directly at birth (congenital lupus, CL), most times it appears between four and six weeks of life.[3] The face and scalp are the main locations of the rash, but extremities and trunk may also be affected. After a few months a spontaneous resolution is seen without permanent cutaneous abnormalities.[3,6] Extracutaneous manifestations may be present in up to one-third of newborns with cutaneous NL, and can encompass any organ.[6] Cardiac involvement is not only the most common extracutaneous manifestation of NL but also the most severe one, and carries high mortality and morbidity.[7–9] Hepatobiliary and hematological abnormalities are well recognized in NL, although less common than cutaneous and cardiac involvement.[5,6] Central nervous system (CNS) disease due to NL is extremely rare.[6]

We describe a case report of CL in a girl with extensive skin ulcers at birth, especially on the hands and feet. These ulcers resolved with disabling

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scarring. Mild associated CL manifestations were thrombocytopenia, increased transaminases and cholestasis. At the age of 18 months the girl presented with arthritis of the left ankle, compatible with the diagnosis of oligoarticular juvenile idiopathic arthritis (JIA), and recurrent uveitis during follow-up.

Concise report

A female infant was born at week 35 + 3 of gestational age, with a birth weight of 2520 g. She was the second child from a 29-year-old mother who had a previous diagnosis of Sjögren syndrome, with anti-SSA/Anti-Ro and anti-SSB/Anti-La antibodies, hypothyroidism and heterozygosity for factor V Leiden with previous history of pulmonary embolism. Her first child had developed third-degree heart block as a consequence of maternal autoantibodies, with favorable clinical outcome (no need for pacemaker until nine years old, which is the child's current age). Other than the mother, no one in the family has autoimmune diseases.

Directly at birth, extensive erythema of the face and scalp was present. There were remarkable erythematous erosions and ulcers on the hands and feet, as well as on the trunk (Figure 1). Lab results showed thrombocytopenia, increased transaminases, cholestasis, and positive anti-SSB/Ro. In order to rule out other dermatological and metabolic diseases, a cutaneous biopsy (left flank) was performed on the day of birth. The findings of degradation of basal keratinocytes, as well as massive edema of the dermis cells with a fibrous aspect, were consistent with congenital lupus erythematosus and confirmed the diagnosis. Immunofluorescence did not show any specific deposition of immunoglobulins or complement.

Because of signs of skin infection and elevated C-reactive protein, antibiotics were started on the second day of life. Endovenous methylprednisolone was prescribed as adjuvant therapy during the first two weeks, as well as daily dressing of the wounds with analgesia (paracetamol and opioids). Cardiac evaluation rendered transitory hypertension and minimal ventricular hypertrophy. Electrocardiogram was normal. Amlodipine was started. At the end of the first month, the infant was dismissed from the hospital with home care for regular wound dressing. At this time, ventricular hypertrophy had disappeared and blood pressure was normal. Hence, amlodipine was stopped.

Thrombocytopenia resolved after two weeks of life, and transaminases and cholestasis normalized within four months. Anti-Ro became negative at nine months of age. All wounds healed with conservatory management within the first four months of life. Long-term sequelae included extensive scarring, atrophy, depigmentation, and patchy alopecia. Telangiectasia remained on the scalp. Hands healed with an adduction contracture of both thumbs. Secondary syndactyly and contracture of the second to fifth toes were noticed in both feet, leading to impairment of their function (Figure 2).

At the age of two years old, thumb web space release in the left hand was performed by the plastic surgeon (Figure 3). Three years later the patient underwent bilateral stretching of the skin under her toes, with interdigital release between the third and fourth toes. Both surgeries had satisfactory results, with gain of function of the left hand and both feet.

During the first year of life, the patient developed constitutional eczema. At the age of 18 months, the patient presented with pain and swelling in her ankles, most prominent on the left side. Left ankle MRI showed synovitis and slightly

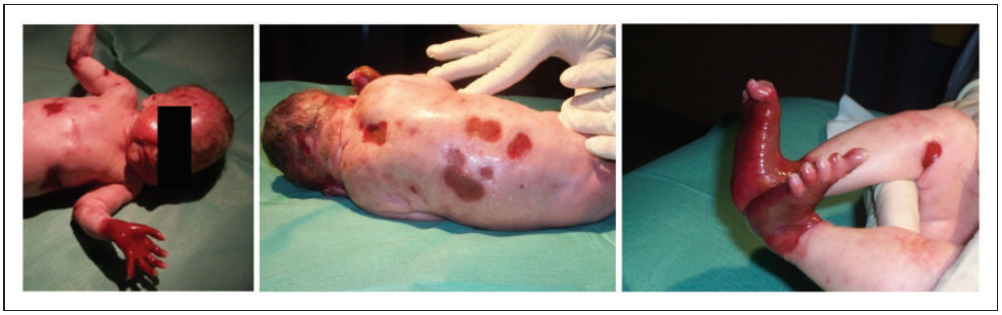

Figure 1 Erythema on the face and plaques adherent to the scalp. There were remarkable erythematous erosions and ulcers on the hands and feet, as well as on the trunk.

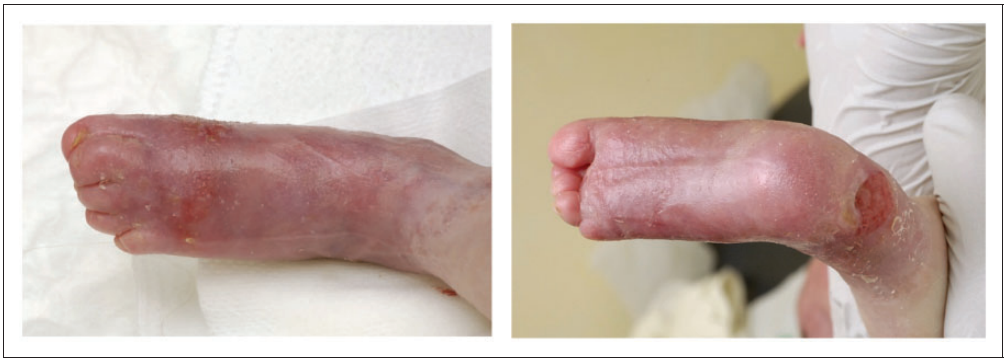

Figure 2 The patient at four months old. Syndactyly of the second to fifth toes was noticed in both feet. (a) Right foot. (b) Left foot.

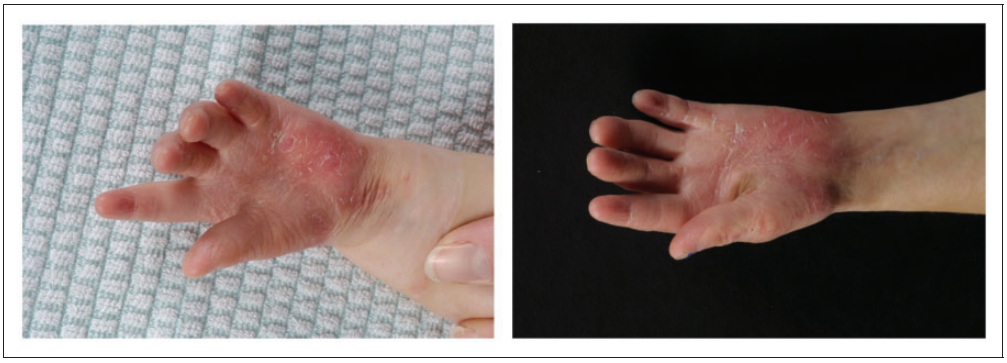

Figure 3 Thumb web space release in the left hand. (a) Two years before surgery. (b) One year after surgery.

asymmetrical accentuation of the synovium. Lab results showed positive antinuclear antibodies (ANA). Oligoarticular JIA was diagnosed and treated with nonsteroidal anti-inflammatory drugs (NSAIDs), with good response. At the age of three years and a half she was diagnosed with bilateral anterior uveitis. Treatment with topical glucocorticoid was insufficient, so oral methotrexate was started and continued (10 mg/m^2/week). At the age of five years the patient has a good quality of life, and despite the scars on her face, trunk and extremities, is able to perform all tasks required for her age.

Discussion

The clinical manifestations of NL occasionally vary from the typical forms presented in the literature. Slightly atrophic and teleangiectic lesions can remain in up to 10% to 20% of children who present with cutaneous NL.[3] Severe skin atrophy after cutaneous NL has rarely been described, especially in CL cases.[10–13] To date, this is the first case report that showed hands- and feet-disabling scarring due to cutaneous CL involvement.

Atypical presentations of NL make the diagnosis a challenge, especially if the cutaneous involvement is the unique manifestation of the disease. A biopsy of the skin should be performed for diagnosis and to rule out other causes, such as epidermolysis bullosa and aplasia cutis congenita. The major histopathology features of the NL cutaneous lesions are identical to those of subacute cutaneous lupus, being keratinocyte damage and superficial mononuclear cell infiltrate. Neutrophils may occasionally be the predominant inflammatory cell type. The characteristic immunofluorescence of cutaneous lesions is deposits of immunoglobulins. However, as in adult subacute cutaneous lupus, it isn't always present.[2,6]

Corticosteroids may promote the resolution of the rash, but it does not prevent scars or teleangectasia.[3] Slightly atrophic lesions have been treated with laser therapy.[2] Unfortunately, there is no effective clinical treatment for severe scarring. In our patient, two successful surgical procedures

were performed in order to improve the function of her hands and feet.

Although the cutaneous involvement of this girl was very severe, her other manifestations showed a good outcome. The risk of congenital heart block (CHB) recurrence in subsequent pregnancies is approximately 20% when maternal antibodies are present.[7–9] Cutaneous manifestation without cardiac involvement is present in 7% of the pregnancies subsequent to the birth of a child with CHB.[9] Despite the fact that our patient's older brother had showed third-degree heart block at birth due to NL, this manifestation was not present in our patient. The transitory hypertension and minimal ventricular hypertrophy in her first weeks of life were probably due to the corticoid treatment, and resolved completely after tapering of steroids. The hepatobiliary and hematological findings resolved in a few months, following the child's clearance of maternal antibodies.

It is still debated whether children who present with NL have an increased risk for autoimmune diseases during their lives. In a follow-up study of 49 children with previous diagnosis of NL and their 45 unaffected siblings, six of 49 previous NL children (12%) developed an autoimmune disease at the mean age of 12 years old, compared to none of their siblings. This study suggests that children who present with NL have an increased risk for autoimmune diseases, and should be under continued follow-up.[6,14] Our case report showed one more case of autoimmune disease in a patient with a previous diagnosis of NL.

Conclusion

Although cutaneous manifestations of NL are recognized as benign and self-limiting, some reports have shown that it is possible to present with a severe course of cutaneous involvement, with permanent skin lesions.[10–13] This is the first case report of cutaneous CL leading to severe scarring of extremities. Plastic surgery led to improvement of the function of hands and feet. A single follow-up study has shown that NL diagnosis increases the risk of future autoimmune diseases.[6,14] Our case report is in accordance with this finding, as we described a CL patient who developed ANA-positive oligoarticular JIA and uveitis.

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All the information in this concise report can be accessed by the electronic file of the patient, located at Wilhelmina Children's Hospital/University Medical Centre Utrecht, the Netherlands.

Declaration of conflicting interests

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