ANDES PEDIATRICA
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Andes pediatr. 2023;94(2):240-245
DOI: 10.32641/andespediatr.v94i2.3889

CLINICAL CASE

Neonatal lupus erythematosus, a clinical case

Lupus eritematoso neonatal, caso clínico

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Received: April 8, 2022; Approved: January 6, 2023

What do we know about the subject matter of this study?

Neonatal lupus erythematosus (NLE) is a rare autoimmune disease that can cause severe complications such as complete heart block. In many cases, the cutaneous clinical manifestations allow early diagnosis and treatment of the newborn and detection of pathology in previously asymptomatic mothers.

What does this study contribute to what is already known?

This article describes a characteristic clinical case of neonatal lupus erythematosus in a patient born to a mother with no history of connective tissue disease. Early suspicion, based on the cutaneous manifestations, made it possible to follow up on the newborn to rule out complications and the maternal diagnosis of systemic lupus erythematosus (SLE).

Abstract

Neonatal lupus erythematosus (NLE) is a very rare autoimmune disease, occurring in neonates born to mothers who present auto-antibodies to cytoplasmic antigens of Sjögren's syndrome. In most cases, the clinical course is benign toward spontaneous resolution, but there is a group of patients who develop severe involvement of the cardiac conduction system, therefore, early detection is critical. **Objective:** To describe a clinical case of neonatal lupus erythematosus emphasizing the importance of timely diagnosis in the patient and the mother. **Clinical Case:** A 33-year-old woman, with a history of hypertension, came to the dermatology department for her 15-day-old male neonate who presented a recent onset of round, erythematous, raised-edged, and non-scaling plaques consistent with NLE. Cardiac conduction involvement was ruled out. Newborn's laboratory tests showed moderate neutropenia, mild increase of transaminases, and positive anti-Ro and anti-La antibodies. On directed anamnesis, the mother reported a personal history of symptoms consistent with connective tissue disease, such as fatigue, alopecia, and xerophthalmia. Antinuclear antibodies from the mother showed titers of 1/1280 in a speckled pattern, positive anti-double-stranded DNA antibodies, and anti-Ro and Anti-La antibodies. Schirmer Test was consistent with dry eye, therefore, Systemic Lupus Erythematosus associated with Sjögren's Syndrome was diagnosed. The infant was followed up for 5 months with remission of cutaneous manifestations and normalization of laboratory tests. **Con-**

Keywords:
Neonatal Lupus Erythematosus;
Newborn;
Sjögren's syndrome;
Connective Tissue Disease

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Edited by:
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How to cite this article: Andes pediatr. 2023;94(2):240-245. DOI: 10.32641/andespediatr.v94i2.3889

clusion: Although cutaneous manifestations of NLE are benign and transient in the newborn, these can be associated with other life-threatening manifestations that require an active search and prompt management by the medical team. A 25% of mothers of newborns with NLE are asymptomatic or unaware of their SLE diagnosis before delivery, so timely diagnosis of NLE leads to the diagnosis of asymptomatic mothers, improving their follow-up and treatment.

Introduction

Neonatal lupus erythematosus (NLE) is an acquired autoimmune disease associated with the presence of maternal autoantibodies that cross the placenta, especially anti-Ro(SSA) and anti-La(SSB)[1]. The incidence varies between 1 in 12,500 and 1 in 20,000 live births[2]. It is called neonatal lupus because its cutaneous manifestations are similar to those of systemic lupus erythematosus (SLE) in adults[3]. The main clinical manifestations are cutaneous and cardiac, and the most severe complication is complete heart block[4].

NLE occurs in children of mothers with anti–Sjögren's-syndrome-related antigen A and B autoantibody. It is estimated that approximately 2% of mothers with these autoantibodies will have children affected by the disease, with a recurrence of 20% in successive pregnancies[3]. Since this is an uncommon disease, it is necessary to know the cutaneous clinical manifestations in order to promote early diagnosis. The most reported manifestations in the literature are cutaneous and cardiac ones, but hematologic and hepatobiliary involvement can also be observed[5,6].

Although, in most cases, the evolution of NLE is benign, there is a risk of severe heart conduction alteration, so its timely detection is essential.

The objective of this report is to describe a characteristic clinical case of NLE, highlighting the clinical manifestations and the complementary study necessary to confirm the diagnosis and evaluate possible complications in addition to highlighting the diagnostic timeliness of maternal pathology from the diagnosis of the disease in the newborn.

Clinical Case

A 33-year-old woman with a history of essential hypertension attended a dermatology evaluation for her 15-day-old male neonate due to the recent appearance of rounded, erythematous, raised-edged, non-desquamative plaques that began in the retroauricular area (Figure 1) 5 days after birth and later appeared in the abdomen (Figure 2), posterior trunk, and both inguinal folds (Figure 3). The neonate, born in winter, did not receive phototherapy at any time. The mother, who had a monitored physiological pregnancy, with no relevant perinatal history, had no personal or family history of connective tissue diseases.

Due to the high suspicion of neonatal lupus, both the mother and the newborn were studied. The mother presented positive antinuclear antibodies titer 1/1280, with a speckled pattern, positive anti-(double-stranded)-DNA antibodies titer 1/20, and positive anti-RO and anti-LA antibodies with values higher than 200 U/ml. She was evaluated in rheumatology and, by directed anamnesis, she reported a history of fatigue, alopecia, xerophthalmia, acrocyanosis, and recurrent non-painful ulcers on the labial mucosa. Physical examination revealed malar rash and livedo reticularis in both upper limbs. The diagnosis of systemic lupus erythematosus with associated Sjogren's syndrome (SS) was proposed, supported by a Schirmer test compatible with severe dry eye due to hypolacrimia. Steroid

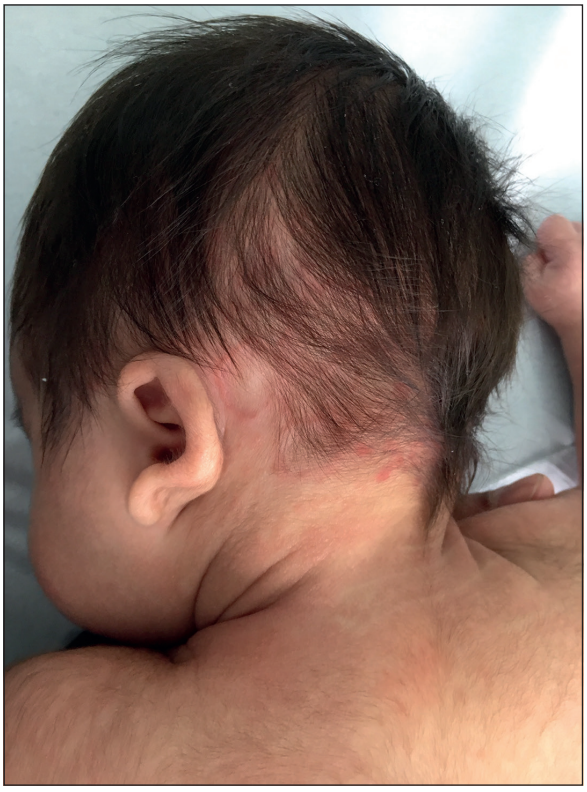

Figure 1. Erythematous, anular plaques on the occipital and retroauricular area.

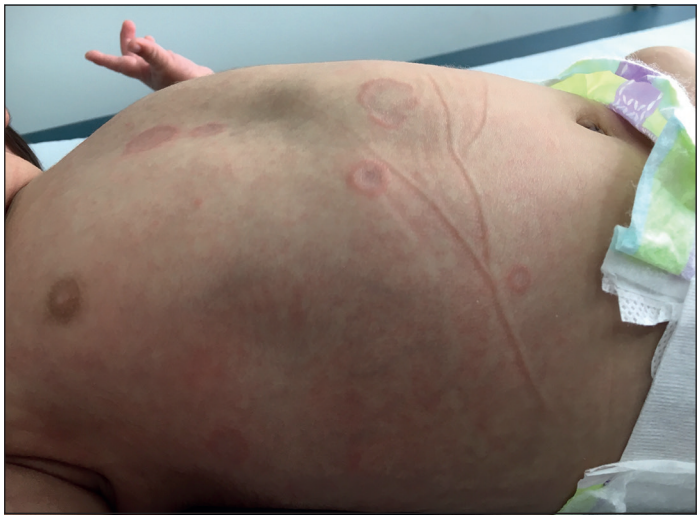

Figure 2. Erythematous, anular plaques with raised borders on the abdomen and trunk

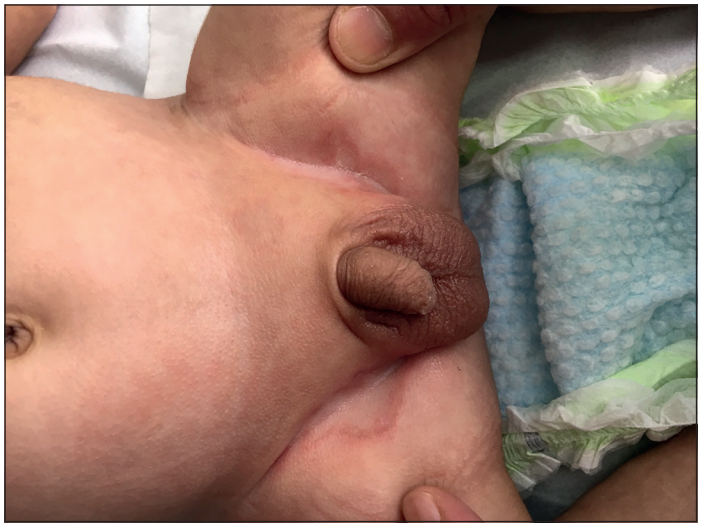

Figure 3. Polyciclic, anular erythematous plaques on both inguinal folds

therapy was started with prednisone at 20 mg dose daily for 30 days, then decreasing doses for 8 weeks until its suspension associated with hydroxychloroquine at 200 and 400 mg doses every other day, with good response and improvement of the general condition. The mother remains stable in her baseline disease and is currently in follow-up with rheumatology.

In the study of the newborn, an initial electrocardiograph was within normal limits, a Holter monitoring test showed normal atrioventricular and intraventricular conduction, and a Doppler echocardiography showed a patent foramen ovale. Blood tests showed moderate neutropenia (ANC 620), altered liver tests with mild transaminases elevation (AST/GOT 95 IU/L and ALT/GPT 130 IU/L), and the presence of positive anti-Ro and anti-La antibodies. Photoprotection was indicated and follow-up examinations at 2 and 5 months of life showed recovery of neutropenia, normalization of liver tests, and decrease of the aforementioned antibody titers. Dermatological check-ups showed complete regression of skin lesions at 2 months of follow-up.

Discussion

Although the prognosis of NLE is favorable when there is exclusively cutaneous involvement, the presence of heart conduction involvement worsens this prognosis[7]. Regarding the organs affected by this disease, the most common manifestations are skin lesions in approximately 40% of cases and heart conduction involvement in 25% of cases[3], so it was expected that, in our case, the diagnostic suspicion arose from the cutaneous manifestations. Other systems that may be involved are hematologic, hepatobiliary, central nervous, and pulmonary ones[3,5,8]. NLE is the most common cause of congenital complete heart block, which most often develops between 18 and 26 weeks of gestation and very rarely begins after 26 to 30 weeks[3].

Although this condition may result in a lower-than-expected heart rate, approximately half of the infants with heart block due to NLE do not require treatment and the other half will require pacemaker implantation[6]. This is the importance of a timely diagnosis since it allows searching for manifestations related to the disease that may imply an increase in the patient's morbidity and mortality. In our case, the patient did not present signs of heart block either antenatally or postnatally, and this complication was ruled out by electrocardiogram, Holter monitoring test, and echocardiogram.

Within the hematological manifestations, it is possible to detect anemia, neutropenia, thrombocytopenia, and, very infrequently, aplastic anemia. These manifestations are generally transient and occur in 20% of cases and rarely occur in isolation[3]. Regarding hepatic manifestations, the asymptomatic elevation of aminotransferases, cholestasis, or hepatomegaly may be observed in 15-25% of patients[3]. Some patients may present macrocephaly with or without hydrocephalus, but these findings are extremely rare[9].

The characteristic skin lesions are rounded or elliptical erythematous plaques, frequently scaly, with regular and sometimes raised edges. Macular lesions may also be observed. The lesions measure approximately 1 cm in diameter and may coalesce to form large polycyclic erythematous areas. They occur most frequently in photo-exposed areas, such as the face and scalp and,

occasionally, occur in the periorbital and malar region taking the classic "raccoon eye" shape. Sun exposure usually exacerbates the lesions, which may explain why they appear more frequently in photo-exposed areas. Occasionally, the involvement is more extensive, even in photo-protected areas, which shows that sun exposure is not absolutely necessary for skin lesions to appear[6].

The lesions usually disappear in weeks to months, being 6 months the most frequently described period, which coincides with the clearance of maternal antibodies from the newborn's circulation[3,7].

A cohort including 47 mothers and their 57 newborns diagnosed with NLE showed that 14 of the neonates developed skin involvement following exposure to sunlight. The mean age of presentation was 6 weeks and the mean duration of rash was 17 weeks. All patients presented involvement of the facial region, followed by the scalp, trunk, limbs, neck, and intertriginous areas. In most of the newborns, the rash resolved without sequelae; however, a quarter of the patients presented residual lesions such as telangiectasias and depigmentation[10].

Regarding the cutaneous manifestations, our patient presented a cutaneous eruption of similar characteristics to those described in the literature, however, the distribution of this is not the most characteristic since, apart from the retroauricular lesions, he did not present other lesions on the face and scalp, showing a predominance on the trunk and inguinal area where the latter is protected from sun exposure. In addition, the lesions appear in a winter month and without another triggering factor such as phototherapy.

The diagnosis of NLE is made when the mother presents anti–Sjögren's-syndrome-related antigen A and B autoantibody and the fetus or newborn develops some of the characteristic manifestations. In our case, the cutaneous manifestations of early onset made it possible to study and rule out more serious manifestations in the newborn, to perform the appropriate follow-up and the pertinent study of the mother[3]. The differential diagnosis of annular lesions in the neonatal period includes NLE, atopic eczema, trauma, or fungal infection. In neonates with suspected NLE, it is recommended to perform serological evaluation, hemogram, liver function tests, and electrocardiogram to look for the different alterations that can be expressed in this pathology[3]. Occasionally, although it is not necessary for diagnosis, a skin biopsy is performed which shows alterations similar to those of SLE, including interface dermatitis, vacuolar degeneration of the basal layer, dermal edema, skin atrophy, hyperkeratosis, follicular plugging, increased thickness of the basement membrane, mucin dermal deposition, and variable lymphocytic infiltrate with granular immunoglobulin G deposition at the dermal-epidermal junction[3,8].

Approximately, one-quarter of mothers are asymptomatic at the time of birth of their first child with NLE[3], although some studies describe this value as high as 50%[3,8]. This highlights the importance of identifying the clinical picture of the neonate to diagnose the mother, who may eventually develop SLE or Sjögren's syndrome[3,11]. One study showed that the probability of an asymptomatic mother developing SLE 10 years after delivery was 18.6% and of developing Sjögren's syndrome was 27.9%[12]. In our case, the maternal diagnosis was made at the time of the child's diagnosis. Although, when she underwent an anamnesis with a specialist, she presented symptoms of the disease and was unaware of her diagnosis. Given the above, the diagnosis of NLE should be considered a marker of autoimmune disease in the mother, so when NLE is suspected, antibodies should be looked for in both the mother's and the child's blood. In 95% of cases, anti-Ro/SSA antibodies are found[6].

Regarding treatment, as the non-cardiac manifestations of NLE resolve spontaneously, in most cases, only observation and sun protection are suggested (3). In cases of residual telangiectasia, it can be resolved with laser therapy[3]. Topical corticosteroids have not been shown to change the course of skin lesions (3). In our case, clinical and laboratory follow-up of the patient was performed until the cutaneous and laboratory alterations spontaneously remitted. In cases of symptomatic anemia and/or thrombocytopenia, transfusion may be necessary, and, in the case of atrioventricular block, management is performed by pediatric cardiology[3].

Conclusion

As described in this clinical case, the timely and accurate diagnosis of NLE in the newborn allows for ruling out vital complications in the patient and making the diagnosis of autoimmune diseases in the mother.

It is important to raise awareness of this disease since the diagnosis of NLE favors timely treatment and screening for complications in both mother and child.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the parents (tutors) of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

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