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From a mosquito bite to neonatal lupus: primary care initial diagnosis and multidisciplinary evaluation (case report)

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RESUMO

Introduction: This clinical case demonstrates that a common lesion like an insect bite can often be much more than it appears. It also illustrates the approach taken to pathology.

Case description: This case report describes a newborn who, on the 10th day of life, developed skin lesions with characteristics resembling insect bites. Three weeks later, at 45 days of life, the lesions progressed in size and dimension, leading to an urgent referral to Dermatology. The infant was admitted for a differential diagnosis, undergoing several studies, including skin biopsies and autoimmune studies. The mother's autoimmune study revealed positive anti-SSA and anti-SSB antibodies, confirming the diagnosis of neonatal lupus. He performed topical treatment with hydrocortisone, which helped stabilize and reduce some lesions. However, after discharge, due to clinical aggravation, the infant returned to the hospital, with impetiginization of the lesions. Antibiotic therapy (topical with fusidic acid and oral with amoxicillin + clavulanic acid) was thus initiated, topical corticosteroid (hydrocortisone) reintroduced, and oral corticosteroid (deflazacort) initiated, and breast-feeding was temporarily suspended due to the presence of antibodies in breast milk (anti-SSA and anti-SSB antibodies). After five months of topical and oral corticoid, maintenance, and cessation of breastfeeding, there was significant improvement in the lesions, and the infant exhibited appropriate psychomotor development. The mother began follow-up in a Rheumatology appointment, where she was diagnosed with Sjögren's syndrome and initiated appropriate treatment. She also received counseling regarding future pregnancies, particularly about the higher likelihood of the baby experiencing manifestations of neonatal lupus, potentially affecting other systems besides the skin.

Comment: This case highlights the deceptive simplicity of the initial diagnosis and the role of a multidisciplinary team in addressing complex conditions. The family physician plays a crucial role in supporting and guiding families throughout their healthcare journey. In this case, the cessation of breastfeeding and the potential impact on future pregnancies posed additional challenges for the mother, and the family doctor played a key role in addressing her concerns and providing emotional support.

Keywords: Neonatal lupus; Differential diagnosis; Skin diseases; Case report.

INTRODUCTION

Neonatal lupus erythematosus is an autoimmune disease acquired during fetal life as a result of transplacental passage of A or B antigens related to Sjögren's syndrome (anti-SSA/Ro or anti-SSB/La, respectively) or anti-U1 ribonucleoprotein (anti-U1-RNP) autoantibodies. The clinical presentation includes skin lesions (around 40% of cases) similar to those observed in systemic lupus erythematosus, hepatobiliary disease (around 35% of cases), and hematological abnormalities, like cytopenias, in 35% of cases, which disappear with the elimination of maternal autoantibodies. The

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neurological involvement is self-remitting and may also manifest as macrocephaly with or without associated hydrocephalus.[1-4]

Around 25% of neonates experience irreversible cardiac arrhythmias, which are the most distinctive and hazardous features.[4] In this way, mothers with affected offspring that tested positive for autoantibodies to Sjögren syndrome auto-antigens types A or B, should be assessed for an underlying autoimmune disease and should be counseled about the 2% risk of having an affected newborn. If there is a history of a previous offspring with neonatal lupus, the risk increases to 20% with subsequent pregnancies. The risk of AV block is higher if there is a history of previous infants with cardiac manifestations. A fetal echocardiography, after 16 weeks of pregnancy, is a helpful tool for the assessment of the heart structure, rhythm, and function.[4]

Postnatal management of neonatal lupus erythematosus depends on the degree of heart block observed during pregnancy and neonatal electrocardiogram (ECG) findings. Neonates born to mothers with anti-Ro/SSA and/or anti-La/SSB antibodies should have an ECG, even without apparent prenatal cardiac issues; consultation with a pediatric cardiologist is advised if *in utero* monitoring indicated heart block or if the neonatal ECG is abnormal. Infants with first- or second-degree heart block detected after birth require vigilant monitoring due to the risk of progressing to complete heart block. Similarly, those with transient *in utero* second-degree block should be assessed within the first three months of life, as they remain at risk of developing third-degree heart block, while infants with transient first-degree block may need an ECG and echocardiogram at one year. Complete heart block in infants may necessitate a cardiac pacemaker, especially if the heart rate at delivery is below 55 beats per minute. Even asymptomatic infants may require pacemakers later in life, with the absence of pacing potentially leading to exercise limitations or even death. Nevertheless, the prognosis following pacemaker implantation is generally favourable for most children.[3]

Neonatal lupus patients with noncardiac manifestations and no evidence of heart block at birth are unlikely to develop cardiac issues, but those who do should be referred to cardiology.[3]

Neonatal adrenal insufficiency, a rare complication, should be anticipated and tested for in neonates with prolonged exposure to corticoids. It can be treated with hydrocortisone if neonatal hypotension occurs.[3]

The neonatal lupus rash typically resolves by the age of six months, although some may have persistent atrophy for several years; however, without permanent sequelae.[5]

Finally, children who had neonatal lupus may have a slightly elevated risk of developing autoimmune or rheumatic diseases, though this is rare and typically not systemic lupus erythematosus.[3]

This clinical case demonstrates that a presentation of such a common lesion as an insect bite can often be much more than it seems and that the family physician is often the first to initiate an investigation into a condition with significant implications for the patient and their family, and gives support along the way.

CASE DESCRIPTION

This case report describes an infant male, a member of a nuclear family, in phase II of Duvall's Life Cycle. He was born of a term pregnancy and monitored without complications, with eutocic delivery and an uneventful early neonatal period, with exclusive breastfeeding since birth. There was no significant family history, including autoimmune diseases.

At the first consultation at the Family Health Unit, at 10 days of life, the newborn presented two pinpoint lesions on the left plantar region and frontotemporal region, resembling insect bites, without fever or other symptoms (Figure 1).

Over three weeks, with 45 days of life, the lesions progressed to erythematous, annular exanthema with desquamating borders, scattered on the scalp and limbs, with daily progression (Figures 2 and 3).

For this reason, the infant was referred to the dermatology clinic, which considered the following diagnostic hypotheses: granuloma annulare, histiocytosis, subacute lupus, porokeratosis, congenital syphilis, pityriasis rosea or cutaneous tinea.

The infant was hospitalized for further investigation, including mycological examination of skin scrapings, biopsy of the lesions, electrocardiogram, and autoimmune studies to exclude neonatal lupus. At this point, the tests did not reveal any abnormalities. At the

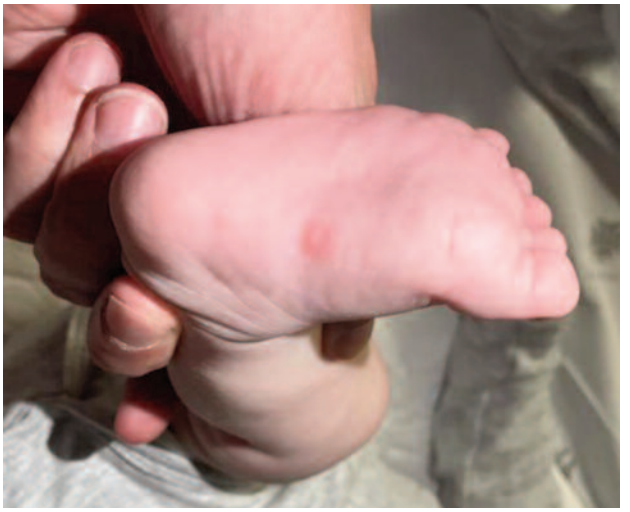

Figure 1. Erythematous pinpoint lesion located on the sole, at 10 days of age (2022).

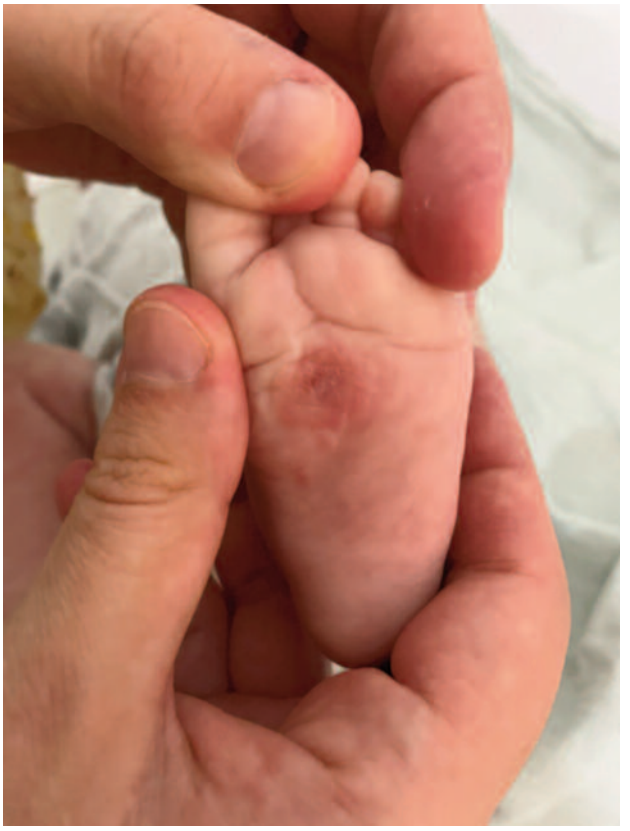

Figure 2. Circular erythematous lesions with mild scaling located on the sole. No skin infection of the lesions (2022).

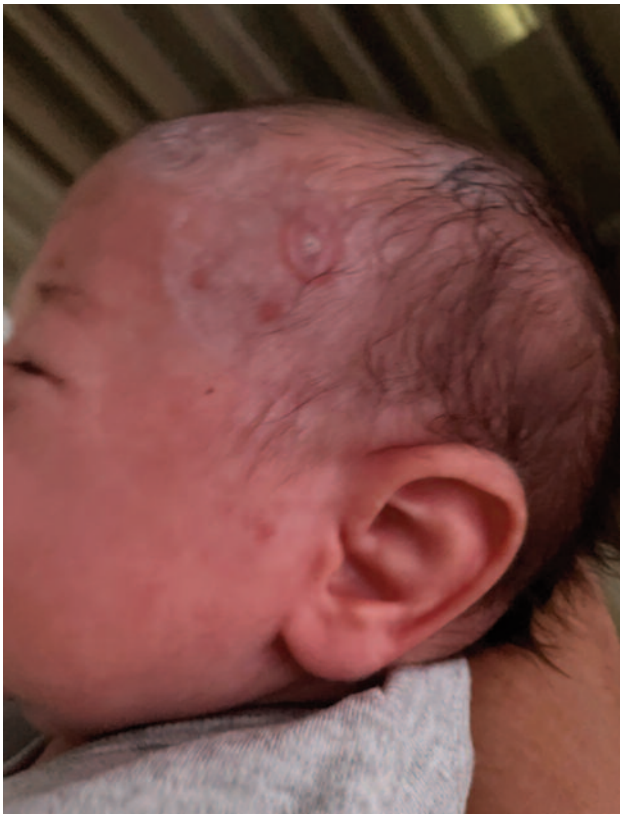

Figure 3. Circular erythematous lesions with mild scaling in the left frontotemporal region. No skin infection of the lesions (2022).

hospital, the mother also underwent general laboratory testing and screening for syphilis and lupus.

During the hospitalization period, there was growth and extension of the lesions. Topical treatment with hydrocortisone was initiated, leading to stability and involution of some lesions. On the seventh day of hospitalization, the mother's autoimmune study revealed positive anti-SSA and anti-SSB antibodies, establishing the diagnosis of neonatal lupus.

At the time of discharge, the infant was referred to pediatric dermatology, general pediatrics, pediatric cardiology, and rheumatology, while his autoimmune blood tests remained in course.

There was a favorable progression in the two weeks following discharge, which led to the suspension of topical therapy.

At the three-month appointment, the lesions had been changing in appearance since discharge,

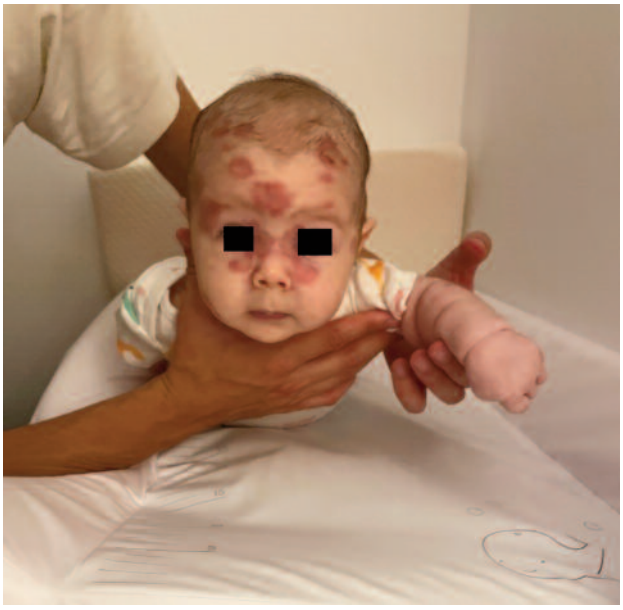

Figure 4. Erythematous rash with scaly borders in the bilateral malar region forming a "butterfly wing" pattern, and multiple well-defined, slightly infiltrated, and scaly erythematous annular lesions with honey-coloured crust, located in the frontotemporal region and scalp. The perioral region and nasolabial folds are spared (2022).

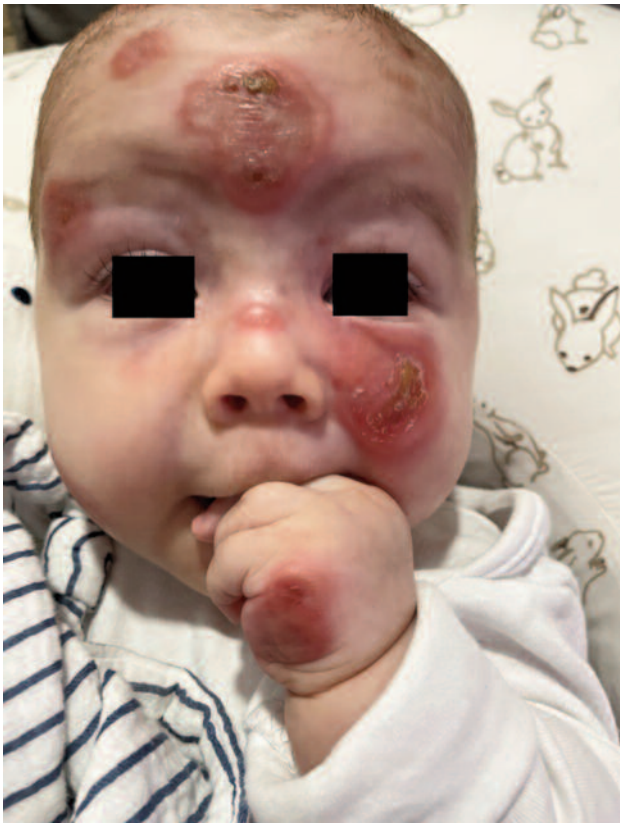

Figure 5. Disseminated erythematous-scaly lesions in the frontotemporal region, the hand palm, and the left malar region. Impetigo of the lesions despite topical and oral corticoid therapy instituted (2022).

presenting as an erythematous rash with desquamating borders in the bilateral malar region in a 'butterfly wing' pattern (Figure 4). The pending autoimmune blood tests were positive (anti-ENA – ANAs 1/>1000 and positive anti-SSa/Ro).

One month later, at four months of age, the male infant returned to the emergency department due to clinical aggravation, with impetiginization of the lesions. He presented disseminated erythematous-scaly lesions in the frontotemporal region, the hand palm, and the left malar region (Figure 5).

Topical and oral, with fusidic acid and with amoxicillin + clavulanic acid, respectively, was thus initiated, topical corticosteroid (hydrocortisone) was reintroduced, and oral corticosteroid (deflazacort) was initiated.

Meanwhile, the mother's milk was tested at the outpatient clinic, and it showed positive antibodies (positive anti-SSA and anti-SSB antibodies). Therefore, the decision was also made to suspend breastfeeding at this time. For this reason, the mother developed feelings of sadness and guilt.

At five months of age, there was a significant improvement in the lesions, with no other relevant changes on physical examination and appropriate growth and psychomotor development (Figure 6).

Cardiac and rheumatological complications were ruled out. Therefore, the patient was discharged from cardiology.

The mother received counseling regarding future pregnancies, particularly about the higher likelihood of the baby experiencing manifestations of neonatal lupus, potentially affecting other systems besides the skin.

At six months of age, a reassessment was conducted by dermatology, which determined a significant improvement. As a result, oral corticosteroids were discontinued, and only topical corticosteroids were maintained on an as-needed basis. At 12 months of age, due

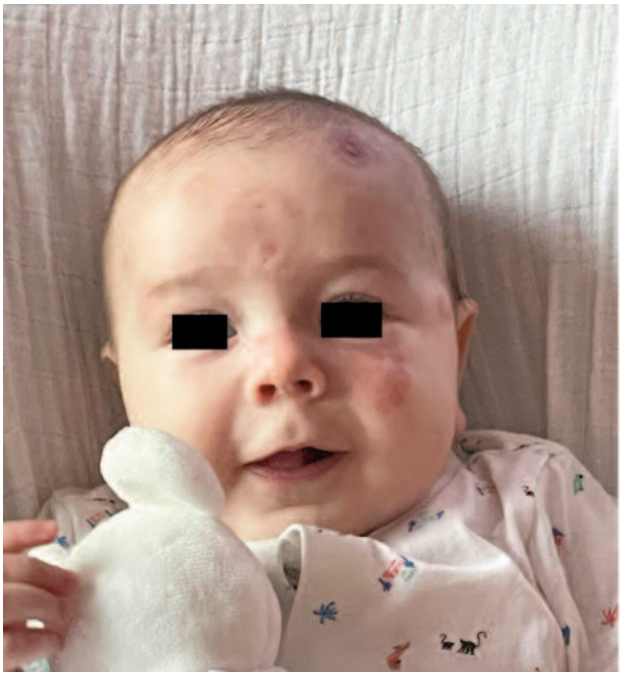

Figure 6. Disseminated erythematous-scaly lesions in a clear phase of resolution (2022).

to the complete resolution of the lesions, the child was discharged from the dermatology clinic but continues to take vitamin D and hydrocortisone cream on an as-needed basis. The child was advised to avoid sun exposure to prevent worsening of the injuries.[5]

Follow-up with the Rheumatology department was maintained, and although the antibodies remain positive, they have shown a decreasing trend (ANAs 1/160 and negative anti-ENAs).

Given the stability of the condition and normal growth and psychomotor development, the child will continue to have annual appointments with both the rheumatology and general pediatrics departments. Regular check-ups will also be continued with the primary care pediatrician according to the recommended age-specific surveillance guidelines.

The mother was also evaluated in a Rheumatology appointment and repeated autoimmune markers, which remained positive (ANA >1/1000 speckled, anti-SSA/Ro-52 positive). The histological examination of the salivary glands revealed seromucous salivary glands (8 mm^2) with preserved architecture. Six foci of lymphocytes were identified (Focus score=3), leading to the diagnosis of Sjögren's syndrome. Therefore, she was prescribed hydroxychloroquine 400/200 mg on alternate days and monthly calcifediol 0.226 mg. She will continue to follow up in the rheumatology clinic.

COMMENT

A 'keen eye' for the child, within the context of their family and psychosocial environment, allows them to value seemingly insignificant details of their daily life that may provide clues for diagnosis. Furthermore, it emphasizes the need for a cohesive and unified multidisciplinary team capable of managing and guiding families and their conditions. The family physician plays a role in managing the expectations and concerns of parents, providing clarification and support, particularly for the mother who felt a crucial bond with her baby, breastfeeding, had been disrupted. The family healthcare team's involvement in supporting the parents during challenging future pregnancies will also be crucial.

The complexity of pathologies such as the one described in this case report underscores the importance of the attentive approach of each healthcare professional involved in different phases of a family's life. The family physician holds a privileged position in the responsibility of caring for and guiding each member of the family.

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AUTHORS CONTRIBUTION
Conceptualization, IGC, and SAO; methodology, IGC, and SAO; writing – original draft, IGC, and SAO; project administration, SAO.

INTEREST CONFLICTS
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ABSTRACT

DE UMA PICADA DE MOSQUITO AO LÚPUS NEONATAL: DIAGNÓSTICO INICIAL NOS CUIDADOS DE SAÚDE PRIMÁRIOS E AVALIAÇÃO MULTIDISCIPLINAR (RELATO DE CASO)

Introdução: Este caso clínico demonstra que uma lesão tão comum como uma picada de inseto pode ser muito mais do que aparenta, ilustrando a abordagem adotada à patologia.

Descrição do caso: Este relato de caso descreve um recém-nascido que, no 10.º dia de vida, desenvolveu lesões cutâneas com características semelhantes a picadas de inseto. Três semanas mais tarde, aos 45 dias de vida, as lesões progrediram em tamanho e dimensão, o que levou ao encaminhamento urgente para a especialidade de dermatologia. O lactente foi internado para diagnóstico diferencial, tendo sido submetido a vários exames, incluindo biópsias de pele e estudos de autoimunidade. O estudo autoimune da mãe revelou anticorpos anti-SSA e anti-SSB positivos, confirmando o diagnóstico de lúpus neonatal. Realizou tratamento tópico com hidrocortisona, que ajudou a estabilizar e a reduzir algumas lesões. Porém, após a alta, por agravamento clínico, o lactente retornou ao hospital, tendo-se verificado impetiginização das lesões. Foi, assim, iniciada antibioterapia (tópica com ácido fusídico e oral com amoxicilina + ácido clavulânico), reintroduzido corticoide tópico (hidrocortisona), iniciado corticoide oral (deflazacorte) e suspensa temporariamente a amamentação devido à presença de anticorpos no leite materno (anticorpos anti-SSA e anti SSB). Após cinco meses de manutenção com corticoide tópico e oral e suspensão da amamentação verificou-se melhoria significativa das lesões e o lactente apresentou um desenvolvimento psicomotor adequado. A mãe iniciou acompanhamento em consulta de reumatologia, tendo sido diagnosticada com síndroma de Sjögren e iniciado tratamento apropriado. Recebeu também aconselhamento sobre futuras gestações, nomeadamente sobre a maior probabilidade de o bebé ter também manifestações de lúpus neonatal, podendo afetar outros sistemas para além da pele.

Comentário: Este caso realça a enganosa simplicidade do diagnóstico inicial. Destaca o papel de uma equipa multidisciplinar na abordagem de condições complexas. O médico de família tem um papel crucial no apoio e orientação das famílias ao longo do seu percurso de cuidados de saúde. Neste caso, a interrupção da amamentação e a possível influência aquando de gestações futuras apresentaram desafios adicionais para a mãe e o médico de família desempenhou um papel fundamental na resposta às suas preocupações e no apoio emocional.

Palavras-chave: Lúpus neonatal; Diagnóstico diferencial; Doenças de pele; Relato de caso.