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Case report

Bullous systemic lupus erythematosus in a pregnant woman: a case report[☆]

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ARTICLE INFO

Article history:

Received 21 September 2011

Accepted 14 May 2013

Keywords:

Systemic lupus erythematosus
vesiculobullous skin diseases
Pregnant women

ABSTRACT

Systemic lupus erythematosus (SLE) can cause numerous skin lesions. Despite being rare, lupus-specific bullous lesions demonstrate characteristic clinical and immunopathological features and require differential diagnosis among numerous bullous conditions that may overlap with SLE. The present study presents a case of bullous systemic lupus erythematosus (BSLE) in a pregnant woman.

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Lúpus eritematoso sistêmico bolhoso em gestante: relato de caso

RESUMO

O lúpus eritematoso sistêmico pode apresentar inúmeras lesões cutâneas. As lesões bolhosas específicas do lúpus, apesar de raras, apresentam características clínicas e imunopatológicas próprias e implicam em diagnóstico diferencial entre inúmeras patologias bolhosas que podem sobrepor-se ao lúpus eritematoso sistêmico. Apresenta-se um caso de lúpus eritematoso sistêmico bolhoso em gestante.

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Palavras-chave:

Lúpus eritematoso sistêmico
Dermatopatias vesiculobolhosas
Gestantes

Introduction

The skin lesions caused by systemic lupus erythematosus (SLE), such as malar rash, oral ulcers, discoid lesions and photosensitivity, are among the most common manifestations

of the disease. However, bullous eruptions are rare and occur in less than 5% of SLE patients.¹⁻⁴ For this type of collagenosis, the vesiculobullous lesions that display distinct clinical and immunopathological features are described as bullous systemic lupus erythematosus (BSLE) and are part of the differential diagnosis for numerous bullous diseases, such as

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dermatitis herpetiformis, bullous pemphigoid, epidermolysis bullosa acquisita and gestational pemphigoid. Here, we present the case of a patient with SLE who presented with vesiculobullous lesions during the third trimester of pregnancy.

Case report

The patient was a 25-year-old-woman who had been diagnosed with SLE, according to the criteria of the American College of Rheumatology (ACR), approximately one year previously. The patient regularly used chloroquine diphosphate 250 mg/day, prednisone 5 mg/day and enalapril 40 mg/day. Ten months prior, the patient received a routine consultation for a confirmed 12-week pregnancy and presented a malar rash. Enalapril was then replaced by methyl dopa, chloroquine was replaced by hydroxychloroquine, and the prednisone dose was increased to 20 mg/day. The patient's rash subsequently improved.

Four months later, she presented with extensive erythematous-squamous lesions on sun-exposed areas, with mild pain and itching. The prednisone dose was increased to 60 mg (approximately 1 mg/kg), and an early outpatient reassessment with laboratory tests was scheduled. On the follow-up visit, the patient demonstrated bullous, hyperaemic and squamous lesions on the face, trunk and upper limbs (Fig. 1). She did not report any association between the disease onset and concomitant infections or use of other drugs.



Fig. 1 – View of the back of the pregnant patient with SLE presenting bullous lesions.

There was also no hypertension, abdominal pain or lower extremity oedema.

Blood count analysis showed mild anaemia and lymphopenia, with normal platelet numbers. No alterations were observed in the peripheral blood analysis. Liver enzymes and renal function were normal. Lactate dehydrogenase, uric acid and C3 and C4 levels were also normal. The anti-DNA antibody titre was 1:80. The extractable nuclear antigen (ENA) profile was negative, and partial urine samples were normal. A skin biopsy was performed, and it showed significant necrosis of keratinocytes in the epidermis and a subepidermal cleft with a perivascular lymphocytic inflammatory infiltrate at the dermis/epidermis interface (Fig. 2). The direct immunofluorescence (DI) results showed granular, dense and continuous deposits of moderate IgG positivity in the basement membrane zone.

The patient developed fever due to secondary skin infection. Prednisone 60 mg/day was maintained, and therapy with broad-spectrum antibiotics was initiated. Because the foetus had a severe intrauterine growth restriction, an emergency caesarean was performed. The surgery was uneventful, and the child did not demonstrate any complications.

During hospitalisation, there was slight progression of the injuries to the lower limbs and involvement of the oral mucosa. The high dose of corticosteroids was maintained, with gradual improvement of the skin condition. After two months, the prednisone dose was tapered. The patient has since been monitored as an outpatient, and her skin symptoms did not return, leaving only hyper- and hypochromic scars on the upper limbs and trunk.

Discussion

Skin involvement occurs in 70-85% of all patients with SLE. Cutaneous manifestations can be classified as specific and non-specific, according to morphological and histological assessment,⁵ and BSLE is classified as a specific acute cutaneous manifestation.^{5,6}

In 1973, Pedro and Dahl described the first case of BSLE.⁴ This rare form of skin involvement in SLE occurs at an inci-

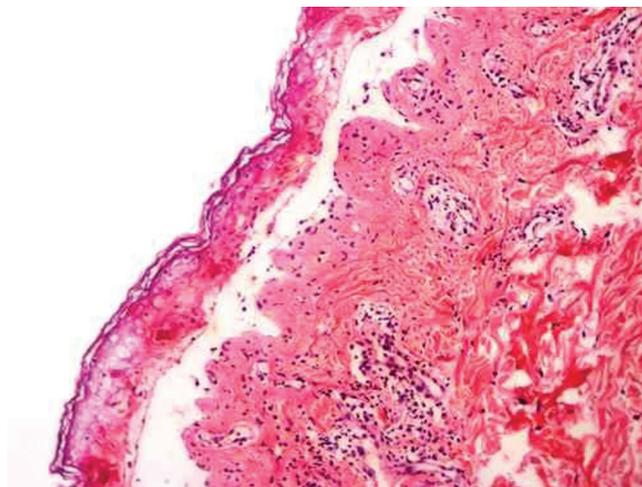


Fig. 2 – Back skin biopsy showing a subepidermal cleft.

dence of less than 0.2 cases per million/year.^{3,7} The clinical condition is characterised by vesicles or bullae with serous or haemorrhagic content,^{4,7} in areas both exposed and non-exposed to the sun. Mild to severe itching and mucosal involvement may also be found.⁴ In addition, the bullae can progress without scarring⁴ or with hypo- or hyperpigmented scarring.⁷

The histopathology of BSLE is characterised by subepidermal bullae with microabscesses of neutrophils in the dermal papillae, similar to those found in dermatitis herpetiformis. There is also dermal oedema with a perivascular inflammatory infiltrate and a predominance of lymphocytes. Some cases present with leukocytoclastic vasculitis and extravasation of erythrocytes.^{2,4,6,8,9} In our patient, biopsy revealed necrotic keratinocytes in the epidermis, lymphocytic infiltration at the dermis/epidermis interface and in the subepidermal cleft and a perivascular inflammatory infiltrate in the dermis. These findings can also be found in erythema multiforme and in Rowell's Syndrome, the latter being described as an association of lupus and erythema multiforme in patients with anti-Ro/SS-A antibodies and rheumatoid factor.^{1,10} Because the DI results for our patient showed a moderate degree of IgG deposition in the basement membrane zone, which is characteristic of BSLE, and because the antibodies often present in Rowell Syndrome were not detected, the diagnosis of BSLE was the most suitable.

The diagnostic criteria for BSLE proposed by Camisa and Sharma include a diagnosis of SLE based on the following criteria of the ACR: vesicles and bullae mainly located on sun-exposed areas; histopathological findings similar to those found in dermatitis herpetiformis; and deposition of IgG, IgM or both and often IgA in the basement membrane zone.^{4,8,9} Gammon and Buggaman classified BSLE into two different subtypes: type 1, in which patients have circulating anti-collagen VII antibodies, and type 2, in which no specific antibodies are present.^{8,9}

The pathology of BSLE is thought to be associated with antibodies against the non-collagenous domain of collagen VII, as well as other antibodies against different components of the basement membrane. In particular, these immunoglobulins are thought to block the connection between the basement membrane and the dermal papillae by complement activation and recruitment and activation of neutrophils, resulting in the formation of a subepidermal bulla.^{3,8,9,11}

It remains unclear whether there is a relationship between bullous eruptions and symptom flares in SLE. Vesiculobullous lesions can develop without clinical or laboratory evidence of disease worsening; however, in some cases, there is a clear association between skin manifestations and renal activity.^{2,4,7,9} The patient described herein demonstrated no other signs of SLE activity in other organs.

The behaviour of SLE during pregnancy has been discussed,^{12,13} and most patients are believed to exhibit exacerbation of skin lesions during pregnancy, with a 60% chance of prematurity and 2- to 4-fold increased likelihood of miscarriage when the disease is active. One important differential diagnosis in the context of bullous diseases in pregnancy is gestational pemphigoid, also known as herpes gestationis. This clinical presentation is very similar to BSLE, including histopathology results showing subepidermal bulla, which, in this case, contained numerous eosinophils. The DI results

generally also show linear deposition of C3 in the basement membrane. In general, however, pregnancy does not seem to be a risk factor for the appearance of bullous lesions, given that we did not find other case reports of BSLE in pregnant women.

Dapsone is the drug of choice for BSLE treatment.^{2,3,9,11} Patients generally respond dramatically to this drug, as the formation of new bullae is interrupted within 1-2 days of treatment and the existing lesions are healed in a few days, even with low doses of 25-50 mg/day.^{3,9} Dapsone has been assigned to pregnancy category C. Other drugs such as prednisone, azathioprine, cyclophosphamide, mycophenolate mofetil and antimalarial drugs may also be effective for BSLE treatment.³ For example, Malcangi et al. described the case of a BSLE patient who demonstrated a good response to the use of methotrexate.¹⁴ However, because our patient was pregnant and using hydroxychloroquine, we opted for treatment with high-dose corticosteroids and obtained a satisfactory response.

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