Bullous systemic lupus erythematosus (BSLE) is a rare but distinct disease, characterized by vesiculobullous skin eruptions in systemic lupus erythematosus (SLE). It can arise either before or after a diagnosis of SLE has been established. BSLE is characterized by a dermatitis herpetiformis-like histology and an autoimmunity to type VII collagen. It must be differentiated from other autoimmune vesiculobullous diseases such as epidermolysis bullosa acquisita, dermatitis herpetiformis, linear IgA disease, and bullous pemphigoid. A combination of clinical, histological, and immunofluorescence findings are necessary to establish a diagnosis of BSLE. We present a case of BSLE to illustrate and emphasize the need for an integrative diagnostic approach.

Introduction

Bullous systemic lupus erythematosus (BSLE) is a rare dermatosis that is regarded as a distinct variant of systemic lupus erythematosus (SLE) (1–4). It is characterized by widespread vesiculobullous eruptions, a dermatitis herpetiformis-like histology, immunologic features resembling epidermolysis bullosa acquisita (EBA), and striking response of cutaneous lesions to dapsone treatment. We present a case of BSLE to illustrate and emphasize the need for an integrative diagnostic approach, to include clinical, histological, and immunofluorescence findings.

Case report

A 16-year-old boy presented in June 2007 with “butterfly” facial erythema, accompanied by vesicles and bullae. Similar lesions subsequently developed on the trunk and proximal parts of the upper extremities. The vesicles and bullae quickly ruptured and crusted (Fig. 1). Oral ulcers developed in July 2007. The patient had an elevated body temperature up to 39 °C for three weeks before being admitted to the rheumatology department at the end of July 2007. Apart from the changes to his skin described above, physical examination showed no abnormalities. The results of laboratory tests revealed a mildly elevated sedimentation rate (32 mm/h; normal <15 mm/h), normal C-reactive protein levels (< 5mg/l), leucopenia (1.3 × 10⁹/l; normal 4.0–10.0 × 10⁹/l), mild thrombocytopenia (105 × 10⁹/l; normal 140–340 × 10⁹/l), mild Coombs positive anemia (106 g/l; normal 140–180 g/l), and proteinuria (0.77 g / 24 hours). Immunological blood testing showed positive antinuclear antibodies (titer > 1:640), whereas the patient was shown...
A skin biopsy from a lesion on the shoulder was performed in July 2007. The histology revealed subepidermal clefting with the formation of subepidermal vesicle containing neutrophils, fibrin, and nuclear dust with mild inflammatory infiltrate in the dermis (a, b), and deposition of mucin in the reticular dermis (c).

Figure 1. Vesiculobullous lesions with crusting arising from an area affected by erythema on the face (a), trunk, and proximal parts of the upper extremities (b). Note the “butterfly” facial erythema.

Figure 2. Subepidermal vesicle containing neutrophils, fibrin, and nuclear dust with mild inflammatory infiltrate in the dermis (a, b), and deposition of mucin in the reticular dermis (c).

to be negative for antibodies against soluble nuclear antigens, dsDNA, cardiolipin, and beta2-glycoprotein I. Lupus anticoagulant was negative. Two episodes of convulsions developed on the third day of admission, which were successfully treated with sedation.

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Figure 3. Granular deposition of IgG along the epidermal basement membrane.

mal vesicles containing fibrin, neutrophils, and nu-
clear dust (Figs. 2a and 2b). In addition, neutrophilic
microabscesses were present in the papillary dermis.
The epidermis showed focal interface changes with
vacuolar degeneration and apoptosis of basal kerati-
ocyes. In the dermis, there was a mild perivascular
and perifollicular infiltrate composed of lymphocytes,
macrophages, and neutrophils. A deposition of mu-
cin was demonstrated in the dermis by alcian blue
histochemical staining (Fig. 2c). Direct immunofluo-
rescence revealed a granular deposition of IgG, IgA,
IgM, and complement components C1q and C3 along
the epidermal basement membrane and within the
vesel walls of the superficial dermis (Fig. 3).

Based on clinical, histopathological, and immu-
nofluorescence findings, the diagnosis of BSLE was
established. Therapy was commenced using 6-
methylprednisolone and pulse cyclophosphamide (1 g
monthly for six months), followed by mycophenolate
mofetil 1 g bid, which was administered for one year
and then discontinued. The skin and oral lesions re-
gressed, the proteinuria disappeared, and there were
no further convulsions. Two years after the onset of
the disease he remains in full remission on low-dose
corticosteroids and hydroxychloroquine.

Discussion

Patients with SLE rarely (in less than 1%) develop
widespread vesiculobullous eruptions that cannot be
classified as either of the primary bullous dermatoses
and are not merely a manifestation of extreme basal
cell hydrotic degeneration and the resulting epider-
mal-dermal separation. In such cases, it is referred to
as BSLE, a unique dermatosis that is regarded as a
distinct variant of SLE (1–4). It is characterized by
dermatitis herpetiformis–like histology, immunologic
features resembling EBA, and a striking response of
cutaneous lesions to dapsone treatment.

Similarly to SLE, BSLE most often affects young
patients, predominantly female, in the second to
fourth decades of life. Although any sun-exposed
or non-sun-exposed areas can be affected, the upper
trunk, neck, supraclavicular areas, and proximal ex-
tremitities are predilection sites (1, 2). The skin eruption
comprises bullae arising either from areas affected by
diffuse erythema or on an urticarial base resembling
bullous pemphigoid, or as grouped vesicular lesions
mimicking dermatitis herpetiformis (1, 2, 4). The
onset of vesiculobullous cutaneous lesions can pre-
cede, coincide with, or follow the diagnosis of SLE,
as defined by the revised American Rheumatism As-
sociation criteria for classification of SLE (3, 5). Our
patient met several diagnostic criteria: skin lesions in-
cluding malar rash, oral ulcers, renal, hematological,
and neurological disorders, and a positive result for
antinuclear antibodies. The patient was treated with
systemic corticosteroids and pulse cyclophosphamide,
followed by mycophenolate mofetil due to the severe
systemic involvement, and did not receive dapsone
treatment.

Bullous changes in lupus erythematosus have two
basic histological patterns: neutrophilic and mononu-
clear (6). The neutrophilic pattern typical of BSLE is
characterized by subepidermal vesicles or bullae con-
taining fibrin, mixed inflammatory cell infiltrate with
a predominance of neutrophils, and nuclear debris.
These histological features simulate dermatitis herpe-
tiformis or linear IgA disease (1). In contrast to der-
matitis herpetiformis and linear IgA disease, BSLE
frequently includes the deposition of mucin in the
dermis. On the other hand, bullous changes with a
mononuclear inflammatory pattern can develop in the
cutaneous lesions of lupus erythematosus as a result
of extensive damage to the epidermal basal layer. This
is due to intense interface dermatitis, which can result
in epidermal-dermal separation and vesicle formation.
Such bullous changes, which can clinically resemble
erythema multiforme or toxic epidermal necrolysis,
represent a spectrum of changes resulting from cuta-
necous lupus erythematosus and are not referred to as
BSLE (1, 6).

Patients with SLE can produce a myriad of autoan-
tibodies, resulting in diverse clinical manifestations.
Similarly to EBA, the pathogenesis of BSLE is associ-
ated with autoantibodies reacting with collagen type
VII (2, 4). Multiple classes of immunoglobulins are of-
ten detected along the basement membrane by direct
immunofluorescence: IgG has been found in nearly
100% of patients with BSLE, IgA in about 70%, and
IgM in 50%. Deposition of immunoreactants along
the basement membrane has been reported to be
granular in 40% of cases, similar to the lupus band in non-bullous cutaneous lupus, or linear in 60%, similar to the deposits in bullous pemphigoid or EBA (1, 3). In addition to deposits along the basement membrane, deposition of immunoreactants within vessel walls can be identified in BSLE (1).

The differential diagnosis of BSLE includes other autoimmune vesiculobullous diseases such as EBA, dermatitis herpetiformis, linear IgA disease, and bullous pemphigoid (1, 3–6). EBA generally occurs in older patients than does BSLE, and it is associated with the formation of bullae at the sites of previous trauma or mechanical rubbing. These bullae heal with scarring and do not respond to dapsone treatment. Despite similar histological features, dermatitis herpetiformis can be distinguished from BSLE by observing granular deposits of IgA in dermal papillae (3). Linear IgA dermatosis is characterized by the linear deposition of IgA along the basement membrane in perilesional skin (5).

REFERENCES


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