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Subacute Cutaneous Lupus Erythematosus:

Two Cases of Delayed Diagnosis

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Two cases of subacute cutaneous lupus erythematosus are described. Features which delayed diagnosis are discussed. The potential clinical and histopathological overlap between this condition and erythema multiforme is emphasized, drawing attention to the histological features which allow distinction. The possibility that some cases of Rowell's syndrome may be manifestations of subacute lupus erythematosus is discussed. ***Key words: erythema multiforme; Rowell's syndrome; Sjögren's syndrome.***

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Subacute cutaneous lupus erythematosus (SCLE) (1) manifests clinically with symmetrical, non-scarring, erythematosquamous lesions, which are typically in a photo-aggravated distribution. Annular, psoriasiform, erythema multiforme-like, pityriasiform and vitiligo-like lesions (2) may develop singly or in combination, resulting in a potential for diagnostic confusion. SCLE has been described in association with other systemic conditions, in particular connective tissue diseases, most notably primary Sjögren's syndrome. This has been reported in between 18% (3) and 44% (4) of patients.

A variety of antinuclear antibody patterns have been described, although antibodies to the Ro/La antigen are the most frequent serological abnormality, occurring in between 50% (5) and 71% (6) of cases. There are no pathognomonic histological findings, and assigning the diagnosis requires appraisal of the features of the history, examination, serological and histopathological findings.

SCLE may mimic other cutaneous reaction patterns both clinically and pathologically. We describe 2 cases of SCLE, each occurring on a background of mild Sjögren's syndrome and both of which manifest clinical and histological features which delayed diagnosis.

CASE REPORTS

Case 1

A 64-year-old woman with a 15-year history of primary, anti-Ro/La positive Sjögren's syndrome (SS) presented to our department with a widespread erythema multiforme-like rash. Over the preceding 20 years she had occasionally suffered from a mild, maculopapular, pruritic erythema, occurring in a photosensitive distribution during hot weather. She was receiving no regular medications; her daughter had systemic lupus erythematosus (SLE) and her grandmother suffered from an undiagnosed, symmetrical, deforming arthropathy. Histopathological examination of a skin biopsy was consistent with erythema multiforme and all features resolved with a 7-day course of oral corticosteroids. During the succeeding 3 years she reported two milder recurrences of the rash, each of which resolved spontaneously without medical intervention. She also suffered for 18 months from a mild symmetrical small-joint oligo-arthropathy for which she consulted a rheumatologist, who diagnosed SS-related arthropathy rather than primary rheumatoid disease. Having been entirely asymptomatic for more than 1 year, she was admitted acutely unwell with a florid, ulcerating recrudescence of her rash. This was associated with a purpuric papular rash on the lower legs (Fig. 1). She had been receiving no medications. Initial haematological investigations revealed pancytopaenia haemoglobin 10.5 g/dl; WCC 2.7×10^9/l; PLT 30×10^9/l; marrow hypoplasia was confirmed on biopsy. Her erythrocyte sedimentation rate (ESR) was elevated at 76 mm/hr and autoimmune screen (Hep 2a cells) confirmed the presence of rheumatoid factor and anti-Ro/La antibodies. Immune complexes were detected and there was a transient, mild depression of complement C3 and C4. Antineutrophil cytoplasmic antibodies (ANCA) were not detected and immunoglobulin levels were normal. Renal and liver function tests were normal. She complained of proximal leg weakness and despite a normal CK, biopsy confirmed myositis.

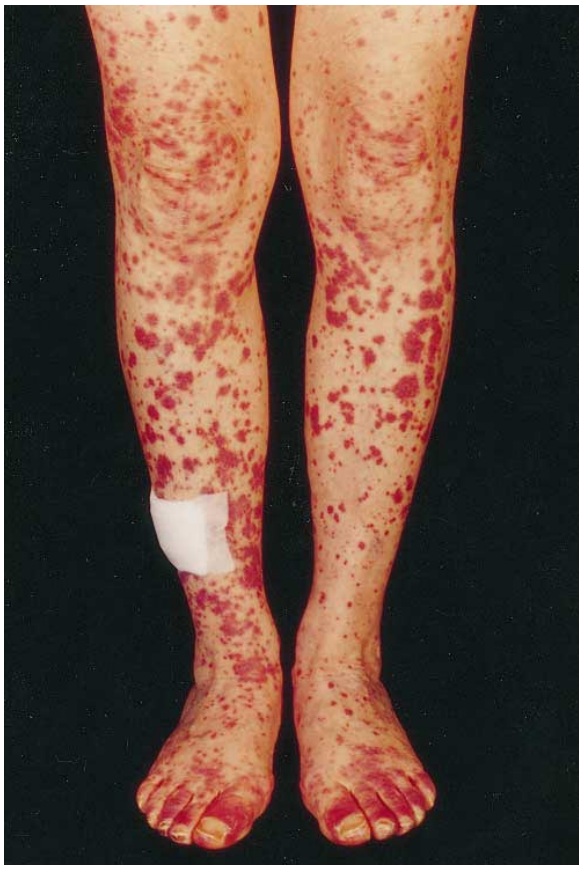

Fig. 1. Case 1. Generalised nummular erythema and lower-leg purpura.

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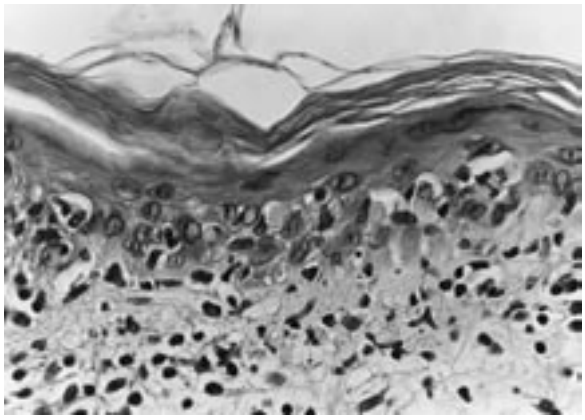

Fig. 2. Skin histology, case 1. The epidermis is atrophic; there is an interface dermatitis with vacuolation of the basal epidermal cells, satellite-cell necrosis and numerous cytoid bodies typical of SCLE.

The rashes, haematological abnormalities and muscle weakness improved with oral prednisolone but recurred on reducing the dose. Reappraisal of the history, examination and laboratory findings suggested SCLE and this was supported by a further skin biopsy (Fig. 2). Direct immunofluorescence examination of the skin was consistently negative. Her recovery was complicated by the neuropsychiatric side-effects of corticosteroids, which resolved on reducing the dose. She is receiving cyclosporine 50 mg daily only and continues well and symptom-free 6 months after discharge from hospital. HLA testing has subsequently found her to be HLA A1,3 B8 C6,7 DQ1,2 DR2,3.

Case 2

A 66-year-old woman presented to clinic in the summer with a 6-week history of a progressive, mildly haemorrhagic, erythematous rash on the arms, neck and face in a photo-aggravated distribution. Morphologically it was defined by confluent nummular plaques (Fig. 3). She also had a pruritic, asteatotic eczematous rash over the right thorax and flank, most severe at the site of a recently resolved, T10 thoracic herpes zoster. She was well apart from mild malaise and gave a history of similar, if much milder and more short-lived eruptions occurring during the previous two summers. For more than 5 years she had suffered from a dry, gritty sensation in the eyes and Schirmer's test demonstrated diminished tear secretion. There was no significant family history and she took no medications. The initial differential diagnosis included polymorphic light eruption, photo-contact eczema and SLE. Histological examination of a skin biopsy specimen showed only non-specific eczematous changes and negative direct immunofluorescence. Renal and liver function tests were normal, but ESR was elevated at 120 mm/hr. She was anaemic (haemoglobin 9.3 g/dl) and mildly lymphopaenic at 1.3×10^9/l (normal >1.5). Bone marrow examination revealed only mild hypocellularity, consistent with the anaemia of chronic disease. Autoimmune screen (Hep 2a cells) demonstrated the presence of antibodies to Ro and La together with antinuclear antibody (IgG) 40 units. Rheumatoid factor and ANCA were not detected and immune complexes were present. Complement C4 was reduced at 0.14 g/l (normal >0.22) and C3 was within normal limits. Immunogenetic studies have not been undertaken, but C4 levels have subsequently returned to normal, making it unlikely that her predisposition to SCLE results from a primary C4-deficiency such as the presence of a C4 null-allele. Further skin biopsy to look for evidence of lupus erythematosus was consistent with a diagnosis of SCLE (Fig. 4). Once again immunofluorescence staining for immunoreactants was negative. Therapy with topical mometasone and systemic prednisolone 30 mg daily was associated with a marked improvement in the rash. We continued to monitor her as an outpatient and she is currently well on no medication.

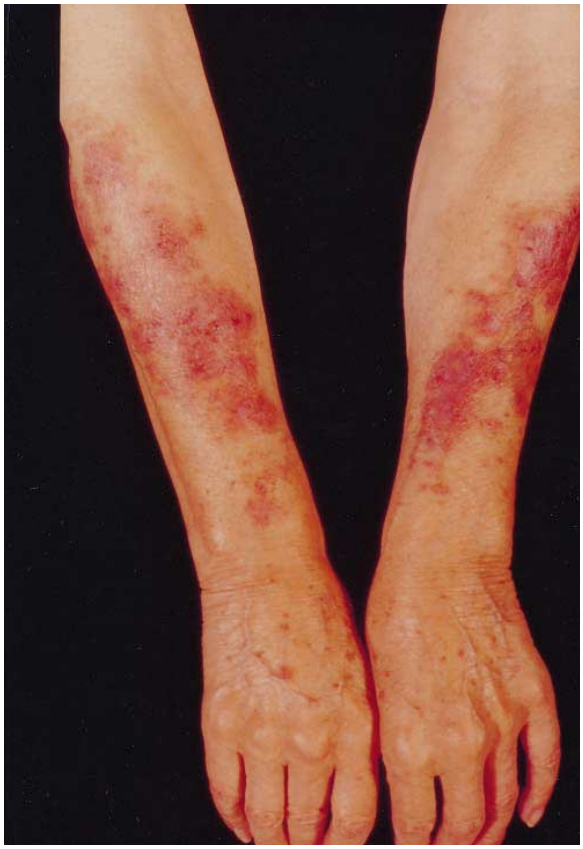

Fig. 3. Case 2. Photo-aggravated erythema.

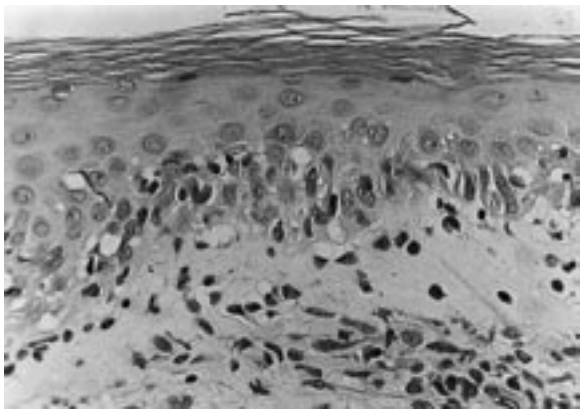

Fig. 4. Skin histology, case 2. There is vacuolation of the basal epidermal cells, dermal oedema and a mild lymphoid infiltrate, consistent with SCLE.

DISCUSSION

Both women described here fall into a category described by Provost et al. (7). They reported a group of anti-Ro-positive

patients who, over a period of some years, developed either SS and subsequently SCLE lesions or vice versa. The lesions are more frequent on sun-exposed skin and a previous history, sometimes of several years, of recurrent photosensitive erythemas is typical. SCLE is associated with a generally good prognosis (2, 3), having significantly less systemic sequelae than is seen with SLE. However, as our first case shows, this is not universal. Both cases presented a typical spectrum of the clinical features of SCLE. They also demonstrate that none of these is pathognomonic, and unless SCLE is suspected and investigated with autoimmune screening and skin histology, the diagnosis may be delayed.

The histological features require correlation with the clinical and laboratory findings, since taken in isolation they can indicate other diagnoses. Given a confident clinical impression of erythema multiforme the pathologist may well find histological support for the diagnosis and overlook the possibility of SCLE. In fact the two conditions share a number of histological features (8) and correct diagnosis demands attention to rather subtle details and an appreciation of the wider clinical picture. We feel that this has not been adequately emphasised in the literature.

The basic histological process in both erythema multiforme and SCLE is inflammation at the dermo-epidermal interface, with vacuolar degeneration of basal epidermal cells (interface dermatitis), and in both conditions there is oedema of the upper dermis, some lymphocytic exocytosis into the epidermis and "spotty" necrosis of individual cells in the epidermis. In both processes the inflammatory damage can progress to a subepidermal blister. Whilst direct immunofluorescence is typically negative in erythema multiforme, it can also be negative in SCLE. Unlike erythema multiforme, the epidermis in SCLE is often strikingly atrophic and many cytoid bodies are present at the dermo-epidermal junction and throughout the thin epidermis. In advanced lesions, the "spotty" necrosis in erythema multiforme tends to become confluent and may be accompanied by vesiculation, unlike SCLE. The necrotic cells in erythema multiforme tend to show homogenous eosinophilic cytoplasm, with pyknotic nuclear remnants, rather than typical cytoid bodies or "satellite-cell necrosis" of SCLE. "Satellite-cell necrosis" refers to a necrotic epidermal cell cuffed by a lymphocyte. Like cytoid bodies, "satellite-cell necrosis" is seen in various other inflammatory skin conditions, particularly lichen planus.

In case 1 the histology was, in retrospect SCLE, but reported initially as erythema multiforme in the light of the clinical impression. In case 2, initial biopsies showed mild chronic inflammation and oedema. Perhaps the pigmentary incontinence might have been a clue to interface dermatitis. The later biopsy of case 2 showed a clear interface dermatitis leading to epidermal separation, but no cytoid bodies. Whilst the diagnosis of SCLE can sometimes be strongly suspected from the histology alone (case 1), the diagnosis can only be made in the presence of a typical clinical picture. Nevertheless, the pathologist must be aware of the histological subtleties of SCLE and the clinician should not rely on histology alone to provide the correct diagnosis.

The association between erythema multiforme, anti Ro/La antibodies and SS/SLE is well described (9–11) (Rowell's syndrome). Our first case highlights the features shared by SCLE and Rowell's syndrome which have led some to question the existence of a separate syndrome of erythema multiforme plus lupus erythematosus (9). In two of these reports (9, 10), which together describe 5 cases, many of the features reported, including a negative lupus band test, were similar to our first case. Whilst many of the features presented by case 1 suggested erythema multiforme, we feel that both of our patients satisfactorily fulfil the criteria for a diagnosis of SCLE. It is interesting to speculate that many other patients with lupus erythematosus with EM-like rashes designated as Rowell's syndrome may in fact be usefully redefined as manifesting SCLE.

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