Recurrent Subacute Cutaneous Lupus Erythematosus Following Exposure to Different Drugs

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Lupus erythematosus (LE) is a multifaceted autoimmune disease with a wide spectrum of manifestations, ranging from skin lesions alone in some cases of cutaneous LE (CLE), to multiple organ involvement in the most severe form, systemic LE (SLE). Both SLE and CLE can be induced by several families of drugs (1–3).

CASE REPORT

A 70-year-old woman presented with multiple infiltrating, erythematous scaly plaques on her chest and back (Fig. 1a). She also had a personal history of xerostomia and xerophthalmia, but no other symptoms were reported. The differential diagnosis included CLE, pityriasis rosea, autoimmune bullous dermatosis, and contact dermatitis following external application of a homeopathic tincture to the affected areas. Her medical history revealed four new drugs; amiodarone (an anti-arrhythmic), torasemide (a loop diuretic), losartan (an angiotensin II antagonist – anti-hypertonic), and phenprocoumone (a vitamin K antagonist – anticoagulant), initiated 10 days before the appearance of the lesions, prescribed due to an aortic valve replacement operation with biological prosthesis. The patient was also on long-term medication with bisoprolol (a β-blocker) and acetylsalicylic acid. The specific laboratory investigation detected an antinuclear antibody titre of 1:1280 (normal < 1:160) anti-Ro/SS-A autoantibodies > 240 units/ml (normal < 10 units/ml) and circulating immune complexes 70.9 g/ml (normal < 45.0 g/ml). ds-DNA, anti-histone and anti-nucleosome antibodies, myoglobin, creatine kinase, transglutaminase and gliadin antibodies, as well as complement and antibodies characteristic for autoimmune bullous diseases, were either normal or negative. Skin biopsies demonstrated superficial interface dermatitis, thus subacute CLE (SCLE), lichenoid drug reaction and erythema exsudativum multiforme came into consideration histologically. However, the associated increase in dermal mucinous material following application of Alcian blue stain favoured LE, namely SCLE of papulosquamous (psoriasiform) form, according to the classification of Gilliam & Sontheimer (4).

The medical history also revealed similar clinical signs in 2005, after administration of terbinafine because of a tinea. Laboratory investigation had also detected an increased antinuclear antibody (ANA) titre at that time (1:1280), along with an increased anti-SS-A antibody titre. After discontinuation of terbinafine the patient rapidly became symptom-free. At the current admission, the suspected drugs could not be discontinued or replaced, due to the recent aortic valve replacement operation. The patient was treated with oral chloroquine, 250 mg/day, and mild and potent topical corticosteroids and antiseptics. Three months later there was marked improvement of the skin lesions, but complete healing did not occur (Fig. 1b).

DISCUSSION

Drug-induced LE is characterized by clinical manifestations and immunopathological serological findings similar to those of idiopathic LE, but it is temporally related to continuous drug exposure and usually resolves after discontinuation of the responsible drug. Similar to idiopathic lupus, drug-induced LE can be divided into SCLE and SLE (5, 6). The cutaneous features of drug-induced SLE include purpura, erythema nodosum and photosensitivity, and the typical laboratory profile consists of positive ANA and anti-histone antibodies. The drugs most frequently implicated in the development of drug-induced SLE are hydralazine, procainamide, isoniazid and minocycline. On the other hand, the less common drug-induced SCLE usually presents with annular polycyclic or papulosquamous lesions, but blisters or targetoid lesions mimicking erythema multiforme may also be associated with this condition. ANA and anti-Ro/SSA antibodies are usually present, whereas anti-histone antibodies are uncommonly found. Drugs associated with SCLE include, in particular, calcium-channel blockers, angiotensin-converting enzyme inhibitors, thiazide diuretics, ter-

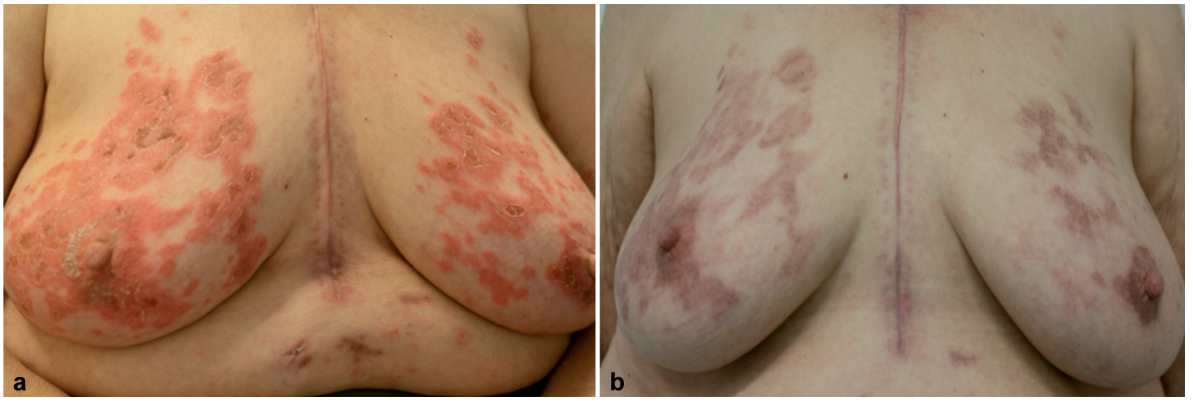

Fig. 1. (a) Erythematous scaly patches on the chest on admission. (b) Regression of the lesions 3 months later.

binafine and the recently reported tumour necrosis factor-α antagonists (6, 7).

Terbinafine, the responsible drug in the first presentation of the disease in our patient, can induce symptomatology or aggravation of SLE or SCLE (8, 9). Among the four new drugs our patient was taking, amiodarone has been reported to cause SCLE or SLE (10, 11). Of her additional long-term medication, bisoprolol has also been associated with the development of LE (12, 13). To our knowledge this is the first report of recurrent LE following exposure to different drugs. It is therefore worth observing whether one, or more, of these four drugs is found to induce LE in the future. It is important to note that our patient experienced drug-induced LE twice, being ANA and SS-A positive, with no clinical signs prior to the first presentation or in the interval. This implies the existence of LE-prone patients, who may develop a similar reaction of clinically manifest lupus under repeated drug exposure.

The authors declare no conflict of interest.

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