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CASE REPORT

Ticlopidine-induced subacute cutaneous lupus erythematosus: A case report and literature review

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ABSTRACT

Many drugs have been reported to induce lupus in a minority of patients. Ticlopidine hydrochloride inhibits platelet aggregation and is widely used for the prevention of thrombosis. There have been only a few reports of ticlopidine-induced lupus. Here, we review 13 previously reported cases and describe the case of a 71-year-old man with ticlopidine-induced subacute cutaneous lupus erythematosus. His diagnosis was supported by the appearance of papulosquamous skin lesions on sun-exposed areas and detectable anti-Ro/SS-A antibodies, shortly after drug initiation as well as the gradual resolution of these symptoms after the discontinuation of ticlopidine. Our case highlights that when a patient presents with subacute cutaneous lupus erythematosus-like skin lesions, ticlopidine should be considered as a potential causative agent.

Introduction

Since the report of skin reactions to hydrochlorothiazide in conjunction with Ro⁄SS-A autoantibody after the drug was first introduced in 1985,[1] more than 40 types of drugs have been reported to induce subacute cutaneous lupus erythematosus (SCLE).[2–4] Ticlopidine hydrochloride is a platelet aggregation inhibitor used as a substitute for aspirin in patients who cannot tolerate the side effects of aspirin.[5] It is commonly prescribed for stroke prevention[6] or after coronary artery stenting to prevent thrombosis based on Food and Drug Administration-labeled indications. Common adverse drug reactions of ticlopidine are diarrhea, exanthematus eruptions, and rarely neutropenia or bone marrow aplasia.[7] Ticlopidine-induced SCLE is extremely rare. Here, we describe the case of a patient with ticlopidine-induced SCLE who was diagnosed based on his clinical medication history, and the clinical, histological, and immunopathological results.

Case report

A 71-year-old man suffered from multiple skin rashes on his trunk and limbs for 2 months. The rashes did not respond to topical steroid treatment. On physical examination, many scaly reddish papules and plaques were observed on the scalp, face, forearms, upper chest, and upper back (Figure 1A–C). He showed no sign of fever, arthralgia, myalgia, pleurisy, or pericarditis. The distribution of the skin rash was mainly on sun-exposed areas, and thus, SCLE or photosensitive lichenoid drug eruption was considered. Blood tests, urine tests, and incisional biopsy for pathology and immunofluorescence were performed.

Based on the medical and medication history, he had suffered from essential hypertension, benign prostate hyperplasia, and type 2 diabetes mellitus for many years. He was persistently treated with losartan, isosorbide dinitrate, propranolol, tamsulosin, desmopressin, bromazepam, acarbose, glimepiride, and sitagliptin without change for more than 1 year. He was diagnosed with cardiovascular disease after coronary artery stenting that occurred 2 years prior to admission. Subsequently, he had taken aspirin for thrombus prevention until 4 months ago when he was prescribed ticlopidine hydrochloride as an aspirin substitute due to gastrointestinal discomfort.

The blood test results revealed anemia (hemoglobin: 9.8 mg/dL) and the urine test results suggested proteinuria. The other test items, including liver and renal functions, were within the normal

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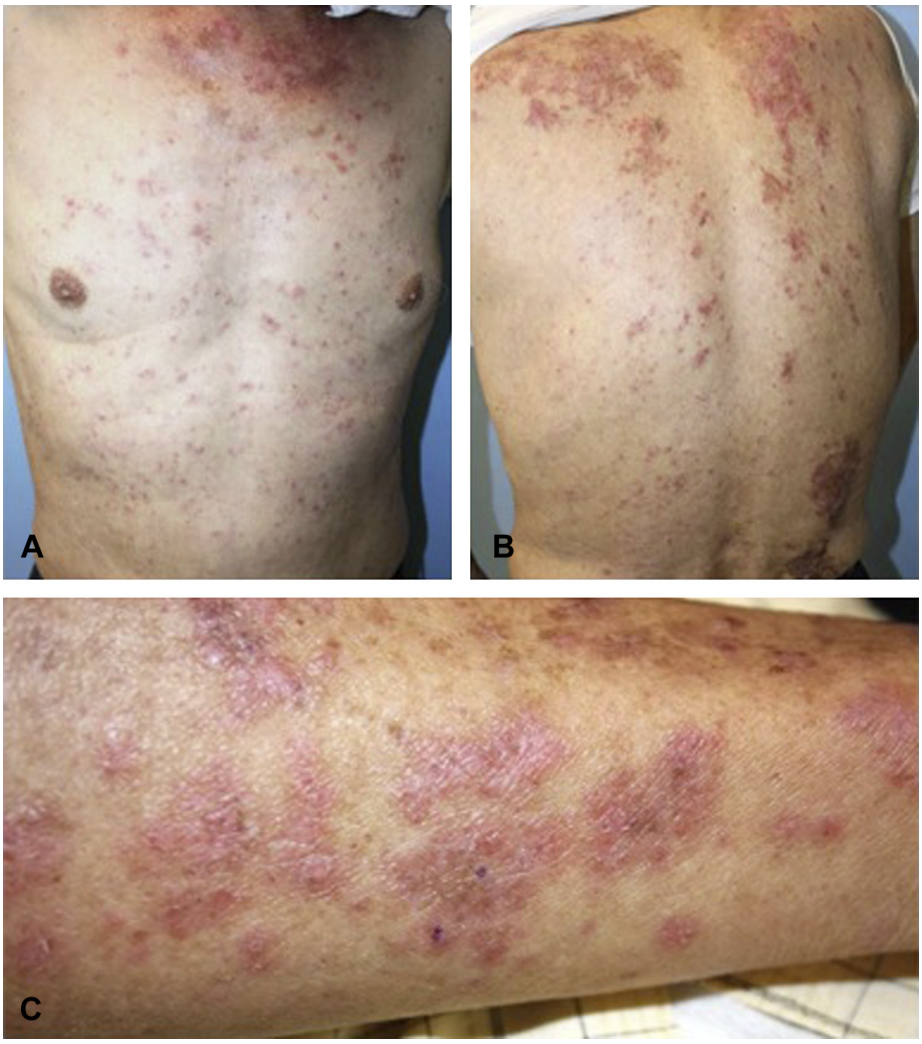

Figure 1 Multiple scaly erythematous plaques on the (A) upper chest and (B) upper back. (C) A close view of the reddish papulosquamous papuloplaques on the extensor side of the right forearm.

range. Circulating antinuclear antibodies (ANAs) were detected (antinuclear factor 40X; speckled/centromere) and identified as anti-Ro antibodies (anti-Ro 347 AU/mL; normal range: <120 AU/mL). Other tests to survey for connective tissue disease were within normal limits, including C3, C4, and anti-double-stranded DNA.

Histological examination revealed diffuse vacuolar degeneration of the basal layers of keratinocytes (Figure 2A and B) and mild to moderate lymphocytic perivascular infiltrates in the upper dermis. There was focal parakeratosis and lymphocytic exocytosis in the epidermis, but neither an increase in dermal mucin deposition nor basement membrane thickening was observed. Eosinophils were rare. Direct immunofluorescent tests of the involved skin showed deposition of cytoid bodies that expressed immunoglobulins (Ig), including IgA, IgG, and IgM (Figure 2C and D). There was also fibrinogen deposition along the dermal–epidermal junction. The overall features represented interface dermatitis and were consistent with a connective tissue disorder such as lupus erythematosus or dermatomyositis.

Dermatomyositis was less likely because of the absence of muscle weakness and normal blood tests for muscle enzymes. The diagnosis after clinicopathological correlation was SCLE. The presence of anti-Ro antibody and his medication history raised the possibility of drug-induced SCLE. Ticlopidine hydrochloride, the only recent addition to the medical regimen, was highly suspected. He was asked to discontinue oral ticlopidine, and a topical potent steroid (0.05% fluocinonide) was prescribed without oral medication. After discontinuation of ticlopidine, the skin lesions rapidly improved and completely subsided 4 weeks later. Therefore, no further blood test was performed. Lesions did not recur during the 1-year follow-up period.

Discussion

There have been only 12 cases of ticlopidine-induced lupus and only two cases of ticlopidine-induced SCLE reported in the literature (Table 1).[8,15–20] The time from ticlopidine exposure to the onset of drug-induced lupus varied from 1 week to 4 years. Most patients started to feel better after discontinuing ticlopidine for several weeks and completely recovered after several months. ANAs and antihistone antibodies are a common finding in drug-induced lupus and are detected in almost all ticlopidine-induced systemic lupus cases. ANAs and Ro/SS-A autoantibodies were detected in both cases of ticlopidine-induced SCLE. The case of ticlopidine-induced SCLE reported in Poland[8] shares many similar