DERMATOLOGICA SINICA 29 (2011) 63–66

Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

CASE REPORT

# Myocarditis in dapsone-induced drug reaction with eosinophilia and systemic symptoms—a case report and review of the literature

Wei-Hsuan Li, Han-Nan Liu, Ding-Dar Lee*

*Department of Dermatology, National Yang-Ming University & Taipei Veterans General Hospital, Taipei, Taiwan*

ARTICLE INFO

*Article history:*
Received: Mar 30, 2010
Revised: Jun 29, 2010
Accepted: Sep 13, 2010

*Keywords:*
Dapsone
Drug hypersensitivity
Myocarditis

ABSTRACT

Dapsone (4,4′-diaminodiphenylsulfone) has been used for a variety of dermatological conditions. Dapsone-induced drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but severe drug reaction characterized by fever, cutaneous eruption, and systemic involvement. We present a case of dapsone-induced DRESS, which resulted in fever, maculopapular eruptions progressing to exfoliative dermatitis, cervical lymphadenopathy, transaminitis, and hypersensitivity myocarditis resulting in congestive heart failure. This patient was withdrawn from dapsone and treated with systemic corticosteroids, but he finally passed away despite aggressive intensive care. We report this rare case and review the literature concerning DRESS with cardiac involvement.



## Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but severe drug reaction characterized by fever, skin eruption, and systemic involvement, including lymphadenopathy, abnormal liver function, renal impairment, pulmonary or pericardial infiltrates, and hematologic abnormalities, mainly hypereosinophilia and lymphocytosis. Symptoms typically begin between 2 weeks and 6 weeks after initiation of drug therapy and mostly subside after discontinuing the drug.[1] However, potentially life-threatening events have been reported. The 10% mortality rate associated with DRESS is usually secondary to hepatotoxicity or myocarditis.[2]

Dapsone is the drug of choice for treatment of leprosy and dermatitis herpetiformis and can be used for various kinds of inflammatory skin diseases. Dapsone-induced DRESS with myocarditis is a rare but potentially fatal complication. In this article, we present a case of dapsone-induced DRESS with hypersensitivity myocarditis and review previous reports of dapsone-induced DRESS with cardiac involvement.

## Case report

A 33-year-old man presented with fever, malaise, multiple oral ulcers, and generalized itchy erythematous maculopapular rash with scaling on the face, trunk, and limbs for 3 weeks (Figure 1). He had received dapsone 100 mg daily for 6 weeks because of chronic refractory urticaria. Dapsone-related drug eruption was suspected, and dapsone was therefore discontinued. Topical clobetasol cream and oral prednisolone (30 mg/d) were given in another medical setting but did not alleviate his symptoms. Then, he was transferred to our hospital.

On admission, his body temperature was 38.7°C, blood pressure 86/52 mmHg, and heart rate 135 beats/min. Other physical examinations of cardiovascular and respiratory system were unremarkable. Bilateral cervical lymphadenopathy was palpable. His skin biopsy showed spongiosis, necrotic keratinocytes, and a dense perivascular inflammatory infiltrate of lymphohistiocytes and eosinophils (Figure 2). Laboratory investigations revealed hemoglobin, 13.9 g/dL (normal range: 14–18 g/dL); platelet count, 495,000/μL (normal range: 150,000–450,000/μL); leukocyte count, 17,700/μL (eosinophil, 10%); total serum bilirubin, 0.3 mg/dL (normal range: 0.2–1.6 mg/dL); aspartate aminotransferase, 226 U/L (normal range: 0–40 U/L); and alanine aminotransferase, 252 U/L (normal range: 5–45 U/L). Hepatitis B surface antigen, hepatitis C virus antibody, anti-dsDNA, antimitochondrial antibody, anti-Jo-1 antibody, and extractable nuclear antigen were tested to rule out viral and autoimmune hepatitis. The workup was all negative. Subsequent laboratory studies for systemic infection, including cytomegalovirus (CMV), Epstein-Barr virus (EBV), toxoplasma, herpes simplex virus, and HIV, were all negative. Intravascular hydrocortisone 150 mg daily was then given under the impression of DRESS. However, the patient developed chest pain and dyspnea 1 week after admission. Cardiac ischemic change was detected by

* Corresponding author. Department of Dermatology, Taipei Veterans General Hospital, No. 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan.
*E-mail address:* ddlee@vghtpe.gov.tw (D.-D. Lee).

1027-8117/$ – see front matter 
doi:10.1016/j.dsi.2011.05.005

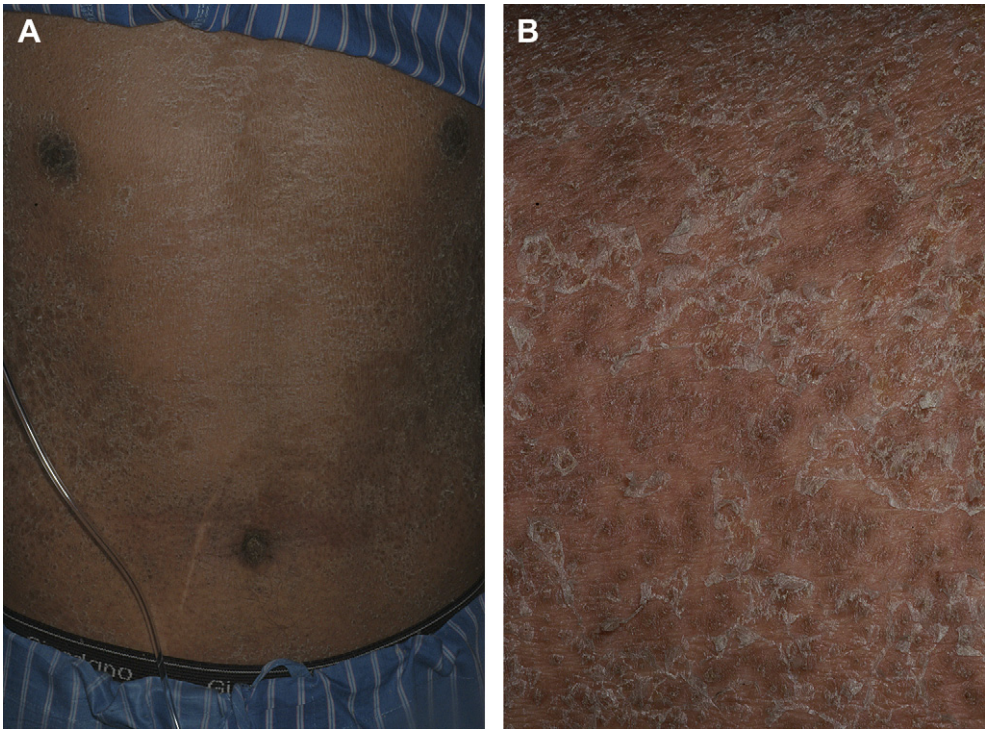


**Figure 1** A 33-year-old male patient presented with generalized exfoliative dermatitis involving most of the trunk and limbs. (A) Diffuse itchy scaly erythematous-to-brownish papulosquamous eruptions on the trunk. (B) A closer view of the patient's back showing confluent brownish papulosquamous lesions with moderate scaling.

abnormal electrocardiogram (ST elevation in leads V1, V2, and T-wave inversion in V3–V6) and elevated cardiac enzyme (creatinine kinase, 1074 U/L (normal range: 40–210 U/L)). Troponin-I level was 13.43 ng/mL (<1.5 ng/mL). The echocardiography revealed generalized hypokinesia and markedly declined left ventricular ejection fraction (from 64% to 11%). The patient's coronary angiography demonstrated patent coronary arteries. The endomyocardial biopsy revealed organizing endomyocarditis with eosinophilic infiltration (Figure 3). His condition deteriorated rapidly, and he passed away despite aggressive intensive care and extracorporeal membrane oxygenation support.

## Discussion

Dapsone (4,4′-diaminodiphenylsulfone) is the parent compound of the sulfones. It has a history of more than a century and remains a powerful therapeutic tool for many skin diseases, including leprosy, dermatitis herpetiformis, erythema elevatum diutinum,[3] linear immunoglobulin A dermatosis,[4] and the bullous eruption of systemic lupus erythematosus.[5] It is an alternative treatment for chronic idiopathic urticaria.[6]

The anti-inflammatory effects of dapsone are mainly associated with its interference with neutrophil chemotactic migration,

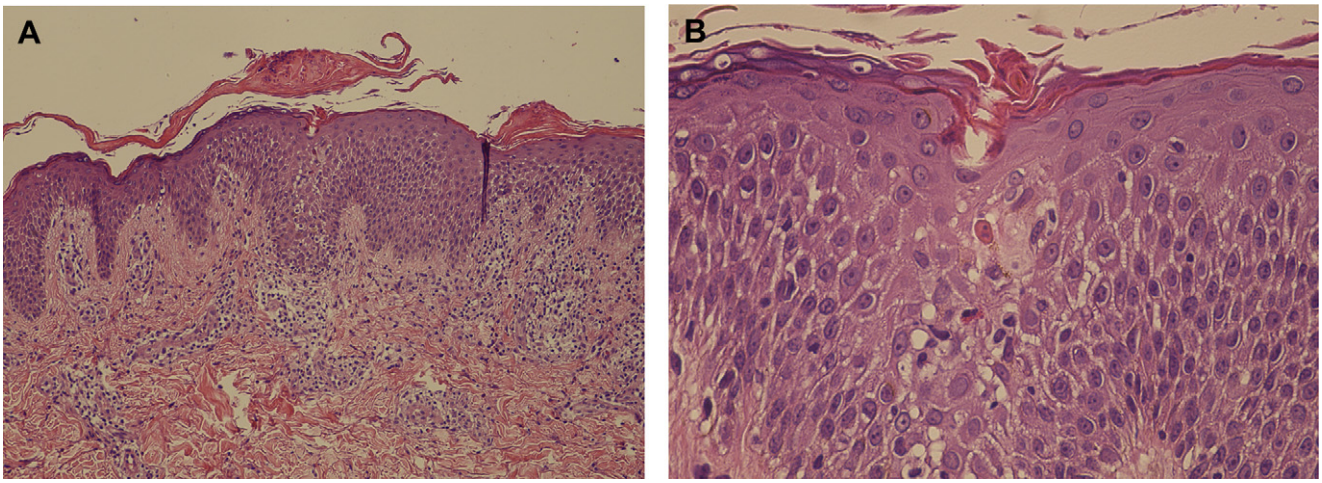


**Figure 2** Biopsy specimens from the exfoliative lesions. (A) These specimens demonstrate spongiosis, acanthosis with dyskeratotic cells in the epidermis, and a perivascular and interstitial mixed inflammatory cell infiltrate composed of lymphohistiocytes and eosinophils in the upper dermis [hematoxylin and eosin (H&E), original magnification ×100]. (B) Dyskeratotic cells in the epidermis (H&E, original magnification ×400).