

# Sulphasalazine-induced DRESS

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## ABSTRACT

**Drug rash with eosinophilia and systemic symptoms (DRESS) is a hypersensitivity syndrome. It presents with severe cutaneous eruption, fever, lymphadenopathy, hepatitis, haematological abnormalities with eosinophilia, atypical lymphocytes and may also involve other organs. The multi-organ involvement differentiates this entity from other common drug eruptions. DRESS has been associated with higher morbidity and mortality compared to other adverse drug reactions. Sulphasalazine hypersensitivity is rarely reported and we wish to highlight a case of sulfasalazine-induced DRESS presenting as leukocytoclastic vasculitis, hepatitis and haematological abnormalities in a 49-year-old Indian woman.**

**Keywords:** drug eruption, drug rash, eosinophilia, hypersensitivity, sulphasalazine

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## INTRODUCTION

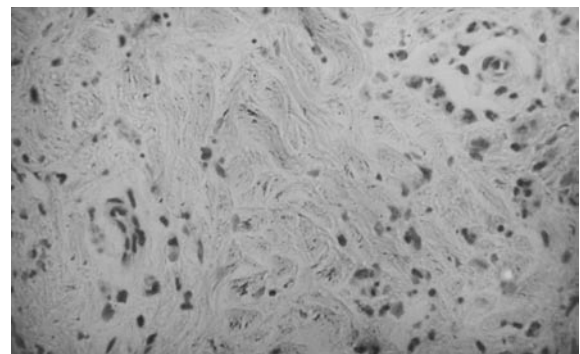
Drug rash with eosinophilia and systemic symptoms (DRESS) is recognised as a hypersensitivity syndrome presenting with severe cutaneous eruption, fever, lymphadenopathy, hepatitis, haematologic abnormalities with eosinophilia, atypical lymphocytes, and may involve other organs. We describe a case of sulfasalazine-induced DRESS presenting as leukocytoclastic vasculitis, hepatitis and haematological abnormalities.

## CASE REPORT

A 49-year-old Indian woman presented with a sudden onset of a generalised maculopapular rash that lasted four days. As the old lesions began to subside, new purpuric rashes appeared gradually over three weeks. She described the new skin lesions as painless and non-pruritic. The patient has rheumatic arthritis and was on prednisolone 5 mg daily for several months. She only began taking



**Fig. 1** Clinical photograph shows multiple purpuric papules and plaques on both lower limbs.



**Fig. 2** Photomicrograph shows endothelial swelling with surrounding neutrophilic infiltrates and extravasation of red blood cells, suggestive of leukocytoclastic vasculitis. (Haematoxylin & eosin, x40)

sulfasalazine 500 mg daily, one month prior to the skin eruption. On further questioning, she recalled transient red rashes that developed after taking co-trimoxazole a year before. Physical examination revealed bilateral, multiple, dusky red to purpuric

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papules and plaques on the trunk, upper and lower limbs (Fig. 1). Multiple 1-2 cm cervical lymph nodes were palpable. She was afebrile and there was no oral, genital, nail, hair or scalp involvement. The rest of her examination was essentially normal.

A 5 mm punch biopsy taken from her right thigh revealed a spongiotic dermatitis with a predominant lymphocytic infiltrate in the epidermis. There was extravasation of red blood cells and necrosis of superficial vessels with surrounding neutrophilic infiltrate suggestive of leukocytoclastic vasculitis (Fig. 2). Direct immunofluorescence yielded non-specific deposition of C3 in the walls of the dermal vessels. The initial full blood count revealed leukocyte count of  $29.1 \times 10^9/L$  (normal range  $4-10 \times 10^9/L$ ), haemoglobin 11.0 g/dL (normal range 14-18 g/dL), platelets  $424 \times 10^9/L$  (normal range  $140-400 \times 10^9/L$ ), polymorphs 27% (normal range 40-70%), lymphocytes 49% (normal range 20-45%), monocytes 12% (normal range 2-10%), and eosinophils 10% (normal range 1-5%). Erythrocyte sedimentation rate was mildly elevated at 25 mm/hr (normal range 0-20 mm/hr). Liver function test revealed a transaminitis – protein 73 g/L (normal range 62-82 g/L), alanine transaminase 171U/L (normal range 7-36 U/L), aspartate transaminase 103 U/L (normal range 15-33 U/L), alkaline phosphatase 115 U/L (normal range 32-103 U/L). Urea and electrolytes, blood and urine cultures were unremarkable. Hepatitis B, C, Epstein Barr virus serology and antinuclear antibody were also negative.

The rash improved after discontinuation of sulfasalazine and a tapering dose prednisolone 30 mg was prescribed over four weeks. Her haematological and liver abnormalities subsided without clinical recurrence.

## DISCUSSION

Sulfasalazine is a compound consisting of sulphapyridine (a sulphonamide) and 5-aminosalicylic acid<sup>(1)</sup>. Sulfasalazine is administered orally and is useful in many inflammatory diseases. DRESS is recognised as a distinct hypersensitivity syndrome presenting with severe cutaneous eruption, fever, lymphadenopathy, hepatitis, haematological abnormalities with eosinophilia, atypical lymphocytes and may involve other organs<sup>(2)</sup>. The hypersensitivity syndrome usually develops within one to two months of initiating therapy. Fever and a skin rash are frequently the first signs. It has been recently classified under a delayed type IVb hypersensitivity reaction where T-helper type 2 cells play a significant role<sup>(3)</sup>. Tissue cells produce high levels of interleukin-

5 and eotaxin that result in the maculopapular rash with eosinophilia.

Sulfasalazine allergy has been reported to present with photosensitivity<sup>(4)</sup> and fixed drug eruption<sup>(2)</sup>. However, sulphasalazine hypersensitivity has rarely been reported. In two earlier reports of sulfasalazine hypersensitivity<sup>(5,6)</sup>, the patients presented with maculopapular rash, hepatitis and atypical lymphocytosis. Our patient similarly had hepatitis and atypical lymphocytosis but differs in the cutaneous presentation. In addition to DRESS, we had considered viral eruption, vasculitis, cutaneous T cell lymphoma and pseudolymphoma as differential diagnoses<sup>(7)</sup>. However, the combination of clinical and laboratory features satisfy the criteria for DRESS.

In our patient, the current adverse reaction was most likely due to the sulphonamide component of sulphasalazine as supported by a previous cutaneous eruption to co-trimoxazole. However, the pathophysiological mechanisms involved in DRESS appear to be due to a whole host of factors that interact closely and not just due to the culprit drug alone. Genetic predisposition, comorbidities that can affect drug metabolism and transient hypogammaglobulinaemia, among others, have some part to play<sup>(8,9)</sup>. Recently, reactivation of the human herpes virus-6 (HHV-6) has been indicated as high on the list as aetiological factors for DRESS. HHV-6 IgG and HHV-6 DNA were present in two patients with sulphasalazine-induced DRESS in a recent review of cases<sup>(9)</sup>. Even though successful sulfasalazine desensitisation have been reported<sup>(10,11)</sup>, we felt that desensitisation and drug rechallenge in DRESS is inappropriate as it could precipitate organ failure.

In summary, we highlight a case of sulfasalazine-induced DRESS presenting as leukocytoclastic vasculitis. Even though sulfasalazine hypersensitivity is rare, increase in awareness enables early recognition and treatment so as to reduce morbidity in these patients.

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