

Relapsing Course of Sulfasalazine-Induced Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Complicated by Alopecia Universalis and Vitiligo

Dear Editor,

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a drug-related severe cutaneous adverse reaction characterised by a delayed latency, multi-organ involvement, reactivation of human herpes virus as well as a chronic relapsing course. Various autoimmune associations following the development of DRESS have been described—including autoimmune thyroid disease and type 1 diabetes.^{1,2} The exact pathogenesis of autoimmunity remains unclear although a delayed dysfunction of T reg cells and association with viral reactivation have been postulated.²⁻⁵ We present a case of sulfasalazine-induced DRESS that is complicated by a relapsing course and concurrent vitiligo and alopecia universalis.

Case Report

The patient is a 59-year-old male with a history of rheumatoid factor-positive erosive rheumatoid arthritis, initially treated with methotrexate for a duration of 10 months and subsequently switched to sulfasalazine. Two months after starting sulfasalazine of progressively increasing doses (1 g daily for 1 week, then 1.5 g daily for 1 week, then 2 g daily for 6 weeks), he developed a generalised, pruritic scaly dermatosis characterised by facial oedema and swelling with confluent erythema affecting 70% of his body. Over the course of the next 2 months, he developed fever, absolute eosinophil count of $2.99 \times 10^9/L$ (upper limit of normal: $0.04 \times 10^9/L$), renal impairment: creatinine 127 $\mu\text{mol/L}$ (reference: 37-75 $\mu\text{mol/L}$), mild hepatic impairment: alanine aminotransferase 78 IU/L (reference: 6-66 IU/L), aspartate aminotransferase 29 IU/L (reference: 12-42 IU/L) and cytomegalovirus (CMV) reactivation. Skin biopsy performed showed mild spongiosis with neutrophil extension into the superficial epidermis; the papillary dermis was oedematous with proliferated capillaries and a diffuse interstitial as well as perivascular polymorphous inflammatory cell infiltrate. A diagnosis of DRESS was made. The calculated RegiSCAR diagnostic score⁶ was 6 (based on: eosinophilia, skin rash >50%, oedema and scaling, 1 internal organ involved, 3 biological investigations done and negative to exclude alternative diagnosis). He was initially treated with systemic corticosteroids (prednisolone: 40 mg daily, 0.5 mg/kg) which was gradually tapered, with

cyclosporine (highest dose of 225 mg daily, 3 mg/kg) being added 2 months later.

However, he continued to have intermittent flares characterised by erythematous scaly plaques which was associated with CMV reactivation based on polymerase chain reaction (PCR). CMV titres were noted to decrease with improvement in the skin. Six months after the onset of the rash, he developed diffuse non-scarring alopecia affecting his scalp, axilla, genitals and eyebrows consistent with alopecia universalis (Fig. 1); as well as depigmented macules over his lower back and abdomen consistent with vitiligo (Fig. 2). At that time, his treatment consisted of prednisolone 12.5 mg daily and cyclosporine 100 mg daily. Thyroid function and glucose levels done prior were normal. Although this improved his cutaneous flares, the alopecia and vitiligo remained. He had no further recurrences of DRESS although the depigmentation and hair loss remained permanent. Both prednisolone and cyclosporine were stopped 19 months after onset of the rash.

Discussion

DRESS is a drug-related severe cutaneous adverse reaction characterised by a variable cutaneous eruption with blood eosinophilia and visceral organ involvement.⁶ Patients with DRESS are often treated with the use of systemic corticosteroids.⁷ Clinical improvements with the use of corticosteroids are believed to suppress excessive immune responses to drug metabolites and/or inhibit the



Fig. 1. Development of alopecia universalis with gradual loss of scalp hair and eyebrows at 3 and 5 months from onset of rash.



Fig. 2. Presence of vitiligo over the chest and abdomen at 6 months from onset of rash.

production of cytokines caused by massive replication of viruses.⁸ However, the use of corticosteroids and concomitant immunosuppression give rise to an increased risk of infectious complications.⁹ CMV reactivation after the onset of DRESS has been previously reported³ and was seen in our patient. This discordance between controlling the immune response and viral reactivation in DRESS makes therapy difficult and a careful balance must be struck while adjusting the corticosteroids.

DRESS has also been associated with the development of long-term autoimmune sequelae such as Graves' disease, Hashimoto's thyroiditis, type 1 diabetes mellitus and autoimmune haemolytic anaemia.^{3,4} Reports regarding autoimmune dermatological sequelae following DRESS are limited. Our patient developed a combination of alopecia universalis and vitiligo. The underlying pathophysiology for the development of autoimmune sequelae are unclear at present. Studies done have posited viral infection or reactivation and the subsequent dysfunction of regulatory T cells as possible mechanisms underlying such sequelae.^{3,5}

In view of sequelae of viral reactivation and autoimmune complications after onset of DRESS, the monitoring of patients even after resolution of the cutaneous eruption is essential.

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Bertrand SY Lian,¹MBBS, Inny Busmanis,²MBBS, FRCPA, FAMS,
Haur Yueh Lee,^{1,3}MBBS, MRCP, FAMS

¹Department of Dermatology, Singapore General Hospital, Singapore

²Department of Pathology, Singapore General Hospital, Singapore

³Duke-National University of Singapore Graduate Medical School, Singapore

Address for Correspondence: Dr Lee Haur Yueh, Department of Dermatology, Singapore General Hospital, Outram Road, Singapore 169608.
Email: lee.haur.yueh@singhealth.com.sg