

DRESS syndrome: A life-threatening complication of dapsone therapy

*Manori Nayanakantha Gamage¹, Kanishka Thilakarathne², Eranga Wicramanayake², N M Marcellin²

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Introduction

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is an idiosyncratic hypersensitive (type IV) drug reaction which is associated with some groups of drugs¹. Some of the commonly used drugs reported with DRESS syndrome (DS) are anticonvulsants, sulpha drugs, ACE inhibitors, antidepressants, beta blockers (atenolol) and some antibiotics². The diagnosis DS is mainly clinical. Two panels of diagnostic criteria are described in DS¹.

1. The *RegiSCAR criteria for diagnosis of DS* comprise the following: Fever >38⁰ C, lymphadenopathy at a minimum of 2 sites, involvement of at least 1 internal organ and blood count abnormalities (lymphocytes above or below normal limits, eosinophils above laboratory limits, platelets below laboratory limits). **Three out of the 4 criteria are required for diagnosis.**
2. The *Japanese group's criteria for diagnosis of DS* comprise the following: Maculopapular rash developing >3 weeks after starting suspected drug, prolonged clinical symptoms 2 weeks after discontinuation of the suspected drug, fever >38⁰C, liver abnormalities, leucocytosis (>11x10⁹/L), atypical lymphocytes (>5%), eosinophilia (>1.5x10⁹/L), lymphadenopathy, leucocyte abnormalities and human herpes 6 reactivation. **The diagnosis is confirmed by the presence of 7 criteria.**

¹Faculty of Medical Sciences University of Sri Jayawardenapura, Sri Lanka, ²Colombo South Teaching Hospital, Sri Lanka

*Correspondence: manorigamage@sjp.ac.lk



orcid.org/0000-0003-3836-5945

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Case report

An 11 year old girl was brought to the paediatric ward with a history of fever for 6 days and a generalized, erythematous, itchy, maculopapular rash and lip ulcers of 1 day duration. She also had dark yellow coloured urine and yellowish discolouration of the sclera for five days prior to admission. She was a diagnosed patient with lichen planus and was on dapsone 200 mg daily for the last one month. With the onset of this febrile illness on the 3rd day mother has withheld the dapsone therapy.

On examination, she was febrile (>38⁰C), and ill looking. An intensely itchy, generalized erythematous macular papular rash was seen mainly over the trunk and both upper limbs. She was mildly icteric and was noted to have bilateral cervical lymphadenopathy. In addition, there were crusted lesions over the lips but the oral mucosa and vulval mucosa were normal. Her blood pressure was normal with normal pulse volume. There was hepatomegaly (2cm below the right costal margin) but no splenomegaly.

Initial laboratory investigations revealed leucocytosis (white cell count 22x10⁹/L) associated with eosinophilia. (N 45%, L 37%, E 12%). Platelet count was 335x10⁹/L and there were atypical lymphocytes in the blood picture. There was evidence of hepatic involvement (alanine aminotransferase: 217 IU/L, aspartate aminotransferase: 122 IU/L, total bilirubin 78 micromoles/L with the direct fraction 60.2 micromoles/L) but her urine analysis and renal functions were normal. Abdominal ultrasonography showed mild hepatomegaly with grade 1 fatty liver, with normal biliary tree. Portal venous system appeared normal. Tests for hepatitis A (anti-HAV IgM), hepatitis B (HBsAg), Epstein-Barr virus and cytomegalovirus were negative. Markers for autoimmune hepatitis were also negative

Initially she was managed with antihistamines (chlorpheniramine) and antibiotics. As there was no improvement, a dermatological referral was made. Based on the clinical features, history and laboratory findings, a diagnosis of DS due to dapsone use was made. By that time dapsone was already withheld so she was started on oral prednisolone 1 mg/kg/day. With the commencement of prednisolone she improved dramatically. Other manifestations were managed symptomatically. She was discharged after

completing a one week course of antibiotics with a plan to continue tapering oral prednisolone over 6 weeks.

Discussion

In 1996 Bocquet *et al* described a drug induced reaction presenting with high grade fever, generalized rash, lymphadenopathy, hepatic, renal, heart or lung involvement and eosinophilia. He termed it as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)³. This is an idiosyncratic condition with a high mortality rate². Commonest cause of death is liver failure². The incidence of DS is 1 per 5,000 to 10,000 drug exposures¹. The pathogenesis of DRESS syndrome is not well understood, but the following are identified as possible factors².

1. A genetic factor which alters immune response
2. A viral infection as a possible trigger
3. A defect in drug metabolism

Occurrence of DS has been reported with dapsone in published case series^{1,4}. In our patient, the presence of fever >38⁰ C, bilateral cervical lymphadenopathy, hepatic involvement and blood count abnormalities fulfilled the RegiSCAR criteria for diagnosis of DS. The presence of fever >38⁰ C, maculopapular rash developing >3 weeks after starting dapsone, liver abnormalities, leucocytosis, atypical lymphocytes, eosinophilia and lymphadenopathy fulfilled the Japanese group's criteria for diagnosis of DS.

Management of DS involves early diagnosis with prompt discontinuation of the culprit drug, systemic steroids (prednisolone 1mg/kg/day) and supportive care. During the course of drug therapy, gradual tapering of steroids over a period of more than one month is recommended. The French Society of Dermatology further recommends IVIG (2g/kg/over 5 days) for patients with renal failure and respiratory failure². It has been reported that earlier the drug withdrawal, the better the prognosis. Other than steroids there are reported cases who have demonstrated beneficial effects of concomitant use of N-acetyl cysteine^{5,6}. Other management options found in the literature are plasmapheresis and cyclosporine therapy^{7,8}. Clinicians who prescribe dapsone for different clinical conditions should have awareness about DS and its presentation.

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