

CASE REPORT

DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME ASSOCIATED WITH SULFASALAZINE WITHOUT EOSINOPHILIA

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Abstract

A 28-year-old previously healthy woman presented with fever and constitutional symptoms for one week duration. Prior to the hospital admission, she had been treated for an inflammatory arthritis with sulfasalazine for three months duration. On examination, she had a generalized maculopapular rash mainly on extremities with bilateral posterior cervical lymphadenopathy and mild hepatomegaly. Her full blood count showed leukocytosis without eosinophilia and her liver transaminases were elevated. An ultra sound scan of the abdomen showed hepatosplenomegaly, mild free fluid and a small right sided pleural effusion. She was treated with intravenous steroids. Her liver enzymes gradually decreased to normal and she subsequently improved with therapy. According to the diagnostic criteria for drug-induced hypersensitivity syndrome (DIHS) established by a Japanese consensus group, she fulfilled the first 6 criteria without eosinophilia. Therefore, this case is an atypical presentation of DRESS syndrome. There are a limited number of case reports on DRESS syndrome without eosinophilia in the literature. To our best knowledge, this is the first case report on sulfasalazine induced DRESS syndrome without eosinophilia in Sri Lanka.

Key words: DRESS Syndrome, Sulfasalazine, Liver enzymes, Maculopapular rash

Introduction

The Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a severe, potentially life-threatening adverse drug reaction which includes features of a severe skin eruption, fever, haematological abnormalities and internal organ involvement¹. Here, we report a case of DRESS syndrome without eosinophilia in a young woman fulfilling the first six diagnostic criteria of DRESS syndrome established by a Japanese consensus

group². There are a limited number of case reports on DRESS syndrome without eosinophilia in the literature³. This case report highlights an atypical presentation of DRESS syndrome.

Case History

A 28-year-old previously healthy woman presented with fever and constitutional symptoms for one-week duration. She had been treated for an inflammatory arthritis with sulfasalazine for three months



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duration. There was no history of allergies to food, drugs or plasters. On examination she was febrile. Her pulse rate was 92 beats per minute and blood pressure was 100/60 mmHg. She had a generalized maculopapular rash mainly on the extremities with bilateral posterior cervical lymphadenopathy and mild hepatomegaly (Figure 1).

Her full blood count showed leukocytosis ($16.81 \times 10^3 \text{ mm}^3$ -Normal range 4×10^3 - $11 \times 10^3 \text{ mm}^3$) without eosinophilia (4%-Normal range 0%-6%). Her inflammatory markers were (ESR- 45 mm/1st hour, CRP-47.3 mg/L), liver enzymes were elevated (AST 182 U/l, ALT 402 U/l) and renal function tests were normal. Septic screening was negative. An ultra sound scan of the abdomen was performed which revealed

hepatosplenomegaly, mild free fluid and a small right sided pleural effusion. The

diagnosis of DRESS syndrome was made based on fulfilling the first six diagnostic criteria of DRESS syndrome established by a Japanese consensus group. She was treated with intravenous steroids (Figure 1). Her liver enzymes gradually decreased to normal and she subsequently improved with therapy. Further follow-up was arranged at clinic level.

Discussion

The Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a potentially life-threatening syndrome with features of a severe skin eruption, fever, hematologic abnormalities and internal organ involvement¹. The term "Drug Rash with Eosinophilia and Systemic Symptoms" was coined by Bocquet⁴. It was first recognized in 1950 by Chaiken¹. Anticonvulsants such as phenytoin and phenobarbital are important

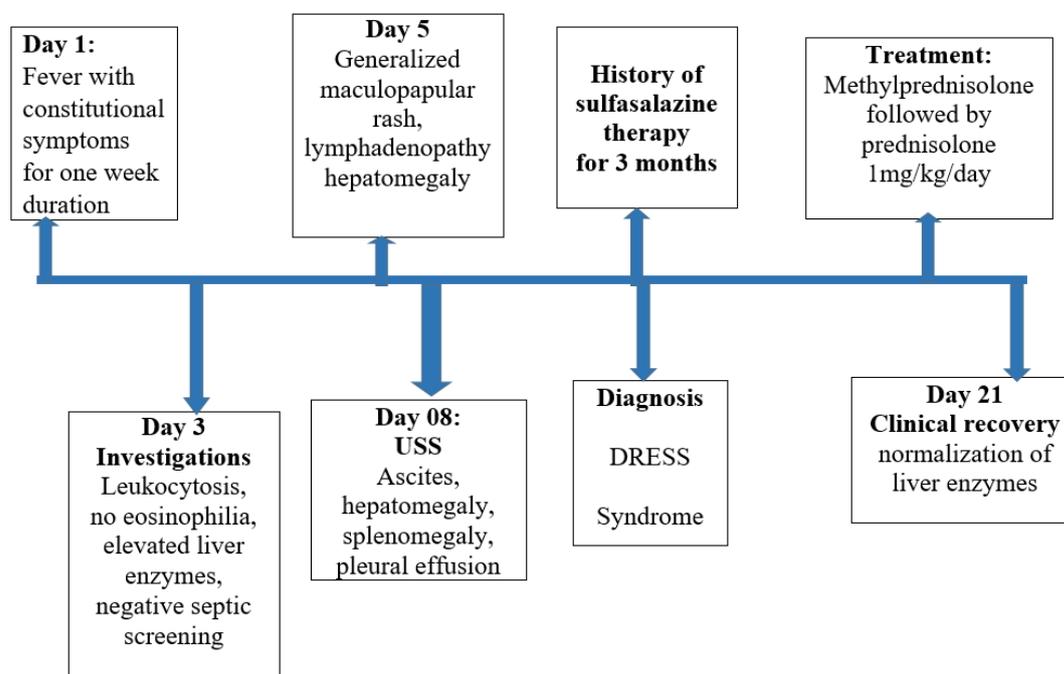


Figure 1: Timeline of the case history

etiologies⁵. It usually appears $\geq 2-8$ weeks after administration of the causative drug and the symptoms may persist or aggravate despite the discontinuation of the causative drug. This patient developed DRESS syndrome 3 months after the commencement of sulfasalazine therapy.

The pathogenesis of DRESS syndrome is not well understood. However a genetic component that alters immune response, a triggering factor such as a viral infection and a defect in drug metabolism resulting in failure to eliminate drug intermediates are described as essential components in its pathogenesis⁶. It has been suggested that drugs may cause a type 4 hypersensitivity reaction due to abnormalities in detoxification of its active metabolites in drug metabolism pathways. It has been demonstrated that the drug can induce reactivation of HHV 6 and EBV even in patients taking sulfasalazine therapy⁷.

Patients present with fever followed by a maculopapular rash and a variable degree of lymphadenopathy⁸. Subsequently, the rash may become a generalized severe exfoliative dermatitis or erythroderma. Mucocutaneous involvement is not seen in DRESS syndrome making it distinguishable from other severe drug eruptions such as Stevens Johnson Syndrome⁹. There may be visceral involvement include hepatitis, pneumonitis, myocarditis, pericarditis, nephritis and colitis. The most commonly found haematological abnormality is eosinophilia⁸. The onset of eosinophilia may get delayed up to 1-2 weeks and even up to the time where elevations in liver enzyme levels return to baseline⁹. The mainstay of treatment is withdrawal of the offending drug and corticosteroids⁹. The outcome is better if the corticosteroids are started at the acute stage. This patient was also treated with intravenous steroids and withdrawal of the offending drug. Her full

blood count did not show eosinophilia. According to the Diagnostic criteria for drug-induced hypersensitivity syndrome (DIHS) established by a Japanese consensus group, she fulfilled the first 6 criteria² without eosinophilia. Therefore, this case is an atypical presentation of DRESS syndrome.

Conclusion

Clinicians should think about possibility of DRESS syndrome among highly suspicious cases without eosinophilia, considering the presence of other diagnostic criteria for drug-induced hypersensitivity syndrome. It will be helpful to discontinue the offending drug and to start appropriate therapy to prevent harmful consequences of the syndrome.

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