CASE REPORT

DRESS syndrome potentially induced by allopurinol and triggered by influenza vaccine

Berna Solak,¹ Bahar Sevimli Dikicier,² Rabia Oztas Kara,¹ Teoman Erdem¹¹Department of Dermatology, Sakarya University, School of Medicine, Sakarya, Turkey²Department of Dermatology, Sakarya University Training and Research Hospital, Sakarya, Turkey

Correspondence to

Dr Berna Solak,
bernasolakmd@gmail.com

Accepted 15 March 2016

SUMMARY

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, also known as drug-induced hypersensitivity syndrome (DHIS), is an acute, potentially life-threatening disease that includes skin rash, fever, haematological abnormalities and multiorgan involvement. Although its aetiopathogenesis is not exactly known, it is thought that inefficient drug detoxification leading to the accumulation of drug reactive metabolites causes autoimmune responses in skin and some internal organs, alters immune responses and induces reactivation of viral infections in people who have genetic predisposition. To the best of our knowledge, only one case of DRESS syndrome has been reported after delivery of the influenza vaccine, but the drug that induced the reaction in that case was sulfasalazine. We report a case of a 64-year-old woman, receiving allopurinol, who developed DRESS syndrome after taking the influenza vaccine.

alkaline phosphatase 740 IU/L, serum creatinine 5.3 mg/dL and C reactive protein 104 mg/L. Serum total immunoglobulin E level was within normal limits. Urinalysis showed pyuria. Serological tests for hepatitis B, C, cytomegalovirus, toxoplasma, rubella and HIV were negative. Skin biopsy showed vacuolisation of the epidermal basal cell layer and perivascular lymphocytic infiltrate in the dermis. We diagnosed the patient as having Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, meeting all the diagnostic criteria of DRESS syndrome except human herpes virus 6 (HHV-6) reactivation in our patient. However, one should consider viral exanthemas and, particularly, life-threatening conditions such as sepsis syndrome in the differential diagnosis of DRESS syndrome. Common viral serology and blood cultures refuted these potential diagnoses in our patients. We supposed that the syndrome is induced by allopurinol and triggered by influenza vaccine.

BACKGROUND

Although Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome can occur due to many different aetiological factors, to the best of our knowledge, this is the first case of DRESS syndrome induced by allopurinol and triggered by the influenza vaccine.

CASE PRESENTATION

A 64-year-old woman was referred to the emergency department, with a maculopapular skin rash and facial oedema, dysuria and dyspnoea. She had chronic kidney disease, hypertension and diabetes mellitus, but no history of hypersensitivity was reported. She had been on insulin therapy for 5 years, and metformin and thiazide diuretics for 6 years. Allopurinol had been prescribed for hyperuricaemia 45 days prior to admission. One week before admission, the patient underwent immunisation with an influenza vaccine (Vaxigrip) as well. Dermatological examination revealed a maculopapular rash on the face, chest, abdomen, back, arms, thighs and legs (figure 1), and crusted lesions around the mouth (figure 2). Vital signs were: body temperature 38.5°C, pulse rate 88 bpm, respiration rate 20 breaths/min and blood pressure 105/70 mm Hg. There were bibasilar inspiratory crackles and two palpable lymph nodes at the submandibular region bilaterally. Biochemistry studies and complete blood counts showed eosinophilia $1.2 \times 10^3/\mu\text{L}$, white cell count $13\,700/\text{mm}^3$, aspartate aminotransferase 95 IU/L, alanine transaminase 232 IU/L, γ -glutamyl transpeptidase 748 IU/L,

OUTCOME AND FOLLOW-UP

One mg/kg/day intravenous methylprednisolone, 45.5 mg pheniramine maleate twice a day orally and 1 g ceftriaxone intravenous, was administered for the skin rash and cystitis. Two days after the therapy, the skin rash, facial oedema and fever started to ameliorate. However, the patient developed acute kidney injury—requiring dialysis therapy—as well as impaired hepatic functions. Subsequently, the hepatic and renal functions fully recovered. Methylprednisolone therapy was stopped with tapering. The facial oedema and skin rash resolved completely with desquamation.

DISCUSSION

DRESS syndrome is an atypical late onset drug reaction secondary to ingestion of a suspected drug. The aetiopathogenesis of the syndrome is not exactly known.^{1–3} Despite discontinuation of the offending medication, the reaction continues and clinical and laboratory findings may exhibit a presumptive viral infection. It is suggested that inefficient drug detoxification leads to accumulation of reactive metabolites of the drug, which cause autoimmune responses in skin and some internal organs in vulnerable individuals who have genetic predisposition. Then, transient alteration in immune responses may induce reactivation of viral infections. The latter explains why the clinical findings continue after the patient stops taking the medication.^{2,3}

In our case, allopurinol was being used over a month but the clinical manifestations appeared

CrossMark

To cite: Solak B, Dikicier BS, Kara RO, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-214563

Figure 1 Maculopapular rash on the back and leg.

1 week after vaccine application. Hence, we believe that the viral antigens in the vaccine (VAXIGRIP) might have contributed to trigger the disease. VAXIGRIP is an inactivated Influenza trivalent vaccine containing influenza A and B subtypes (split virion). However, we could not determine the HHV-6, HHV-7 and Epstein-Barr virus reactivation, due to lack of the measurement kits at our laboratory. Those viral reactivations also might have occurred in our patient besides the influenza vaccine. To the best of our knowledge, there has only been one patient

diagnosed with DRESS syndrome after immunisation with H1N1 vaccination. In that case, the patient had been treated for 12 months with sulphasalazine, and had undergone H1N1 vaccination 4 days prior to the symptoms. HHV 6 reactivation had been confirmed with a serological test.⁴

Learning points

- ▶ Drug Reaction with Eosinophilia and Systemic Symptoms syndrome has a late onset after ingestion of a suspected drug. Thus, it is important to take a comprehensive drug history of patients.
- ▶ Despite discontinuation of the offending medication, the reaction continues and clinical and laboratory findings show a presumptive viral infection.

Figure 2 Facial oedema and crusting around the mouth.

Contributors BS conducted the dermatological examination and wrote the manuscript. BSD and TE conducted the dermatological examination and contributed to writing the manuscript. ROK captured the images and performed the literature review. All the authors have seen and approved the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Cacoub P, Musette P, Descamps V, *et al*. The DRESS syndrome: a literature review. *Am J Med* 2011;124:588–97.
- 2 Pritchett JC, Nanau RM, Neuman MG. The link between hypersensitivity syndrome reaction development and human herpes virus-6 reactivation. *Int J Hepatol* 2012;2012:723062.
- 3 Criado PR, Avancini J, Santi CG, *et al*. Drug reaction with eosinophilia and systemic symptoms (DRESS): a complex interaction of drugs, viruses and the immune system. *Isr Med Assoc J* 2012;14:577–82.
- 4 Hewitt N, Levinson M, Stephenson G. Drug reaction with eosinophilia and systemic symptoms associated with H1N1 vaccination. *Intern Med J* 2012;42:1365–6.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow