# Case Report

# Co-Trimoxazole-Induced DRESS Syndrome: A Case Report

Paitorn Limvorraphan MPharm*

** Department of Pharmacy, Rajavithi Hospital, Bangkok, Thailand*

*Drug Rash with Eosinophilia and Systemic Symptoms (DRESS syndrome) is a severe adverse drug reaction. The drugs, which most commonly induce this condition, are anti-convulsants and sulfonamides. A 15-year-old Thai woman with no known underlying disease was prescribed co-trimoxazole, and two months after initiation, DRESS was diagnosed by RegiSCAR's score. Her clinical symptoms were fever, laboratory abnormalities and maculopapular rash on her face, trunk and extremities. She was treated with antipyretics, antihistamines and steroid therapy, and her clinical and laboratory findings were restored to normal by the 10th day of treatment. Early diagnosis, discontinuation of the culprit drug, and management with steroids therapy can reduce the severity of DRESS syndrome.*

***Keywords:*** *Co-trimoxazole, DRESS syndrome, Hypersensitivity syndrome*

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Drug rash with eosinophilia and systemic symptoms (DRESS syndrome) is also known as drug hypersensitivity syndrome[1,2]. The mechanism of this idiosyncratic reaction is not yet fully understood, but it has been used to describe the combination of symptoms that arise from severe hypersensitivity reaction, and it carries a mortality rate of 10-20%[3]. DRESS is characterized by a clinical triad of early onset of fever, skin eruption and internal organ involvement which emerges 1-8 weeks after exposure to drug therapy. In case of relapse, symptoms may occur on the first day of initiation of therapy. Prodromal symptoms of DRESS include high-grade fever (38-40°C) with eosinophilia ($\geq$1,500 cell/mm$^3$) for a week and possibly longer even after discontinuation of the suspected culprit drug. Myalgia, cough, and enlarged lymph nodes can also be present and can lead to misdiagnosis. And approximately 90% of DRESS cases have skin eruption along with fever. Involvement of at least one internal organ is normally found, such as elevation of liver function tests, hepatomegaly, hematuria, nephritis, pancreatitis, pneumonitis, and myocarditis[4,5]. The common differential diagnoses include acute viral infection, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), idiopathic hyper-eosinophilic syndrome, Kawasaki disease and lymphoma[6] which have diagnostic criteria that are very similar to those of DRESS. The exact incidence of DRESS syndrome cannot be conclusively established because of its multiple-organ involvement, but the estimated incidence of this syndrome ranges from 1 in 1,000 to 1 in 10,000 drug exposures[6]. Aromatic anticonvulsants and sulfonamides are the most common causes of this syndrome[5]. Here, the authors report a case of co-trimoxazole-® induced DRESS syndrome found in Rajavithi Hospital, Bangkok, Thailand.

***Correspondence to:***
*Limvorraphan P, Department of Pharmacy, Rajavithi Hospital, 2, Phyathai Road, Rajathewi, Bangkok 10400, Thailand.*
*Phone: +66-2-3548108 ext. 2239*
*E-mail: amh8220@hotmail.com*

**Case Report**

A 15-year-old Thai woman with no known underlying disease visited the hospital on February 15, 2014, presenting with a rash on her face, trunk and extremities. One day earlier, she had facial and eyelid swelling and took 1 chlorpheniramine (CPM) tablet. Three days previously, she had fever and rash with an itch that started on her face, trunk and extremities. Patient interview and history revealed that she had been taking 2 co-trimoxazole® tablets once per day for 2 months together with 1 Roacutane® tablet daily. She had no history of medication or food allergies. The following laboratory investigations were performed on 15th February: complete blood count, which revealed white blood count (WBC) 13,600 cells/uL, eosinophil 19.4%, and absolute eosinophil 2,640 cells/uL; liver function test which found aspartate aminotransferase

(AST) 198 U/L, alanine aminotransferase (ALT) 273 U/L, and alkaline phosphatase (ALP) 461 U/L; and renal function test which revealed blood urea nitrogen (BUN) 5 mg/dL, and Creatinine 0.77 mg/dL. Two days later, the patient was hospitalized with WBC 12,000 cells/uL; eosinophil 26%; absolute eosinophil 3,200 cells/UL; liver function test AST 128 U/L, ALT 215 U/L and ALP 379 U/L; renal function test BUN 7 mg/dL; and Creatinine 0.55 mg/dL. The doctor diagnosed DRESS syndrome, and Co-trimoxazole® was suspected to be the cause (Fig. 1).

DRESS syndrome management[7] was initiated with discontinuation of Co-trimoxazole®, and supportive care was started after which clinical presentation and laboratory manifestations improved. Two tablets of paracetamol (500 mg), intravenous dexamethasone (4 mg/ml) and intravenous chlorpheniramine (10 mg/ml) were promptly administered followed by CPM (4 mg) 1 tablet 3 times daily for ten days. Steroid therapy was started with prednisolone (5 mg) 2 tablets 3 times daily and topical triamcinolone 0.02% cream was applied twice a day during treatment. Eventually, her clinical condition improved, and after 10 days, she was discharged from hospital and issued with a drug allergy identity card.

**Fig. 1** Maculopapular rash affecting the trunk.

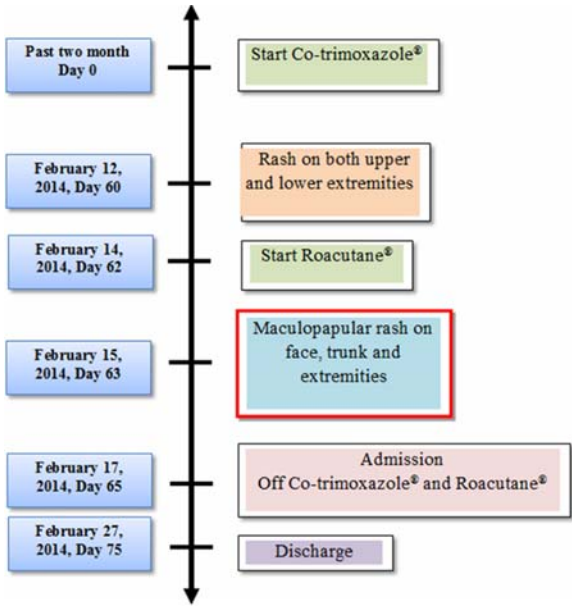


**Fig. 2** Timeline for reporting this case of DRESS from Co-trimoxazole®.

## Discussion

On February 15, 2014, the patient presented with fever and laboratory abnormalities, and she had a maculopapular rash on her face, trunk and extremities. The drugs associated with DRESS were evaluated by RegiSCAR's score[6,8,9], and in this case a score of 4 was arrived at from eosinophilia (2,640 cell/UL), skin involvement (>50% BSA), and liver involvement, and it was, therefore, classified as probable DRESS syndrome. Her medical history showed that she had been taking Co-trimoxazole® and Roacutane® (isotretinoin) as acne treatment. Co-trimoxazole® was suspected to be the probable offending drug, as she had been taking this medication for 2 months, and this is known to inhibit adequate activation of the immune system. Co-trimoxazole® contains sulfamethoxazole and trimethoprime[10], and sulfamethoxazole is associated with a high incidence of drug-induced DRESS. Naranjo adverse drug reaction probability scale was assessed and a score of 7 indicated probable DRESS (Fig. 2).

The exact incidence of DRESS syndrome is unknown, but it is estimated to be between 1 in 1,000 and 1 in 10,000 drug exposures[6], and clinical presentation can be expressed in many organ systems. The drugs most frequently associated with DRESS syndrome are antibiotics (41%), mainly penicillin and sulfonamides derivatives, and in some cases, minocycline; anti-inflammatories (11%); and anticonvulsants (10%). It has also been reported to be associated with other drugs such as allopurinol, gold salts, and dapsone[11]. A previous case report found a patient presenting with facial edema, fever, generalized erythematous morbilliform rash, drug-induced liver injury, and severe elevation of liver enzyme with RegiSCAR's score 6, indicating definite DRESS

syndrome. Past medical history showed that he had been treated with sulfamethoxazole/trimethoprim (Co-trimoxazole®) for acne vulgaris. His symptoms persisted for 6 months after he was diagnosed with DRESS syndrome, and his treatment was managed with pulsed intravenous methylprednisolone followed by intravenous hydrocortisone and oral prednisolone[12]. In this case, the patient had fever and rash with liver enzyme elevation similar to the previous case, but she had a shorter persistence of symptoms duration and higher RegiSCAR's score.

Clinical presentation, physician's diagnosis and medical history suggested that sulfamethoxazole was the cause of DRESS, which can produce complications and life threatening adverse reactions[13]. Healthcare providers should be aware of the importance of monitoring adverse drug reactions, and pharmacists have an important role to play in patient interview and medical reconciliation. Early diagnosis, discontinuation of the culprit drug, and management with steroid therapy can be life-saving in severe forms of DRESS. Moreover, patient education[14] in the form of information such as known adverse drug reactions can help to prevent adverse drug reactions, and drug allergy identity cards should be issued when appropriate.

**What this study adds ?**

Drug rash with eosinophila and systemic symptoms (DRESS syndrome) is a rare, acute and severe life-threatening systemic disease, which occurs in 12.5% of patients affected by adverse drug reaction. Anti-convulsants are the most implicated drugs in reported cases of DRESS due to Co-trimoxazole® so Co-trimoxazole®-induced DRESS was reported in this study.

**Potential conflicts of interest**

None.

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## *รายงานผู้ป่วยกลุ่มอาการ DRESS syndrome ที่เกิดจากยาโค-ไตรม๊อกซาโซล*

*ไพทร ลิมปวรพรรณ*

*กลุ่มอาการ DRESS เป็นปฏิกิริยาแพ้ยารุนแรง โดยยาที่มีส่วนเกี่ยวข้องมาก คือ กลุ่มยากันชัก และกลุ่มยาซัลโฟนาไมด์ ผู้ป่วยหญิงไทยอายุ 15 ปี ไม่ระบุโรคประจำตัว ได้รับยาโค-ไตรม๊อกซาโซล หลังจากได้รับยา 2 เดือน ผู้ป่วยถูกวินิจฉัยภาวะ DRESS โดยใช้การประเมิน RegiSCAR's ผู้ป่วยมาด้วยอาการไข้ ผลทางห้องปฏิบัติการผิดปกติและมีผื่นชนิด maculopapular rash บริเวณ หน้า ลำตัว แขนและขา อาการของผู้ป่วยรักษาโดยใช้ยาบรรเทาอาการไข้ ยาต้านฮีสตามีน และสเตียรอยด์ ต่อมาอาการและผลทางห้องปฏิบัติการผิดปกติของผู้ป่วยกลับมาเป็นปกติหลังจากได้รับการรักษา 10 วัน การวินิจฉัยและหยุดยาได้รวดเร็ว ร่วมกับการรักษาด้วยสเตียรอยด์สามารถช่วยลดความรุนแรงของกลุ่มอาการ DRESS ได้*