

Case Report



Paracetamol Induced Drug Reaction with Eosinophilia and Systemic Symptoms (Dress Syndrome): A Case Report

Nitishkumar D.Tank*, Bharti N. Karelia, Nishant B. Bhansali

Department of Pharmacology, P.D.U. Govt. Medical College, Jamnagar Road, Rajkot, India.

*Corresponding author's E-mail: drnitishtank@gmail.com

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ABSTRACT

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, acute and severe life-threatening systemic disease. The most commonly implicated drugs are anticonvulsants, sulfa derivatives and antidepressants. Reported case of DRESS syndrome due to Paracetamol is very rare, so here we would like to present a case of DRESS syndrome due to Paracetamol.

Keywords: DRESS, Hypersensitivity, Eosinophilia, Paracetamol.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, also known as drug-induced hypersensitivity syndrome (DIHS), is an under-recognized and potentially life-threatening hypersensitivity reaction.¹ It is associated with a variety of medications. It should be differentiated from Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The primary clinical manifestations are fever, lymphadenopathy, rash, hypereosinophilia, and involvement of systemic organs. Systemic organ involvement can present as hepatitis, interstitial pneumonia, interstitial nephritis, and carditis.¹ It carries a mortality rate of 10–20%, with most fatalities as a result of liver failure.² Reported case of DRESS syndrome due to Paracetamol is very rare, so here we would like to present a case of DRESS syndrome due to Paracetamol.

Case Report

A 27 year old male patient with fever was on Tab. Paracetamol 500 mg twice a day. On 2nd day of therapy, after prodrome of fever, generalized weakness the

patient developed multiple itchy reddish lesions over face, neck, chest, abdomen, back, and extremities.^{figure 1,2,3}

Bilateral pain in knee joint, periorbital swelling and watering of eyes were also present.

Bilateral anterior and posterior cervical, submandibular, axillary, inguinal, and femoral lymphadenopathies were present. For these symptoms, patient had consulted to our hospital.

Laboratory investigations revealed the following: hemoglobin- 12.9gm/dl, increased total WBC count- 11,720 cells/cumm (normal 4,000-10,000) with eosinophilia (DC-67/19/11/3/0), erythrocyte sedimentation rate-22 mm/hr. Hepatic function panel revealed an alkaline phosphatase (ALP) of 47 IU/L, and alanine transaminase (ALT) of 29 IU/L. Evaluation for acute and chronic hepatitis with serology was negative for hepatitis B.

Test for HIV-1 & 2, Rheumatoid Factor, S.ASO test and RPR Test were negative. Serum C-reactive protein level (>0.6 mg/dl) was elevated (normal range: <0.6 mg/dl) with normal renal function.



Figure 1: Picture showing multiple itchy reddish lesions over lower neck, front of chest, abdomen and upper extremities.



Figure 2: Picture showing multiple itchy reddish lesions over back side of the upper body and upper extremities.



Figure 3: Picture showing multiple itchy reddish lesions over lower extremities.

From above signs, symptoms, laboratory investigation and patient had not taken any drug other than Paracetamol, clinical diagnosis of Paracetamol induced DRESS syndrome was made and drug was withdrawn.

The patient was treated with Inj. Hydrocortisone 100 mg in 100 ml NS IV once daily for 1 day, Inj. Cefotaxime 1 gm IV three times a day for 6 days. Oral treatment with Tab. Prednisolone (20 mg) two times daily + Tab. Prednisolone 10 mg once daily for 5 days, Tab. Fluconazole 150 mg once daily for 2 days, Tab. Acyclovir 200 mg two tablets three times daily for 5 days and Capsule Multivitamin B Complex, Tab. Folic acid, Tab. Levocetirizine once daily and Tab. Famotidine 20 mg two times daily for 6 days. Local applications like Framycetin cream over skin lesion for 5 days, Fluocinolone Acetonide Lotion + liquid paraffin over Scaling twice daily for 4 days, Clotrimazole mouth paint four times daily for 5 days and liquid glycerin over lips four times daily for 6 days, Betamethasone cream + Clotrimazole cream two times daily over face for 2 days, Calamine lotion two times daily for 2 days, Benzocaine mouth gel before taking food for 3 days, Betadine gargles two times daily for 5 days and Ciprofloxacin eye drops two hourly for 4 days were also given. There was gradual improvement in patient's condition over next 6-7 days.

Re-challenge with Paracetamol was not performed as signs, symptoms and Laboratory investigations were most consistent with DRESS syndrome. The causality was assessed by World Health Organization Uppsala Monitoring Centre, a causality assessment criteria, which concurred this reaction as 'possible'. Naranjo's adverse drug reaction causality scale concluded the causality as 'probable'. The adverse drug reaction was moderate (Level-4B) in severity according to Hartweg severity scale, not preventable according to modified Schumock and Thronton preventability scale and not predictable.³

DISCUSSION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome described for the first time in 1936. The incidence ranges between 1 in 1000 and 1 in 10,000 drug exposures.

Adults are more affected than children, and although the precise incidence of drug reaction has not yet been determined, it is much more common than Stevens-Johnson syndrome, which has an incidence of 1.2–6 cases per million persons-years, and most cases are sporadic, with no gender predilection.⁴

The pathogenesis of DRESS syndrome is not yet well understood. Although it is considered an idiosyncratic reaction, three potential causative factors have been identified among multiple cases: 1) a defect in drug metabolism resulting in the failure to eliminate toxic reactive intermediates, 2) reactivation of human herpes virus 6 (HHV-6), human herpes virus 7 (HHV-7), Epstein-Barr virus (EBV), or cytomegalovirus (CMV), which may serve as a trigger for the reaction, and 3) a genetic predisposition that alters immune response.²

The drugs most often reported with DRESS include anticonvulsants (particularly those with aromatic structures), sulfa derivatives, antidepressants, nonsteroidal anti-inflammatory drugs, and antimicrobials.² Based on the literature search, Paracetamol have also potential to cause DRESS syndrome but it is very rare.^{5,6}

In this case, adult male patient suffering from pyrexia had taken Tab. Paracetamol only; no other concomitant drug had been taken. To our knowledge, this is the first case of DRESS syndrome induced by Paracetamol. In all the previously reported cases Paracetamol was always in conjunction with other drugs.⁵

Two groups have developed specific criteria for making the diagnosis of DRESS. (1) The RegiSCAR program was developed by an international study group investigating severe cutaneous reactions (SCAR). (2) A Japanese group that investigated severe cutaneous adverse reactions to drugs (SCAR-J) adopted other criteria. However, universal adoption of the Japanese criteria may be limited, since one of the criteria is the viral replication during the course of infection, and some tests, such as measurement of IgG titer anti-HHV-6, are not yet routinely available in all hospitals or laboratories.

Our patient was classified as a definitive DRESS case according to the RegiSCAR scoring system.

To meet the definition of DRESS, patients must have three of the four main RegiSCAR criteria: an acute rash, fever above 38°C, lymphadenopathy at two sites, involvement of at least one internal organ, and abnormalities in lymphocyte and eosinophil counts. Additional criteria include hospitalization and that the reaction is suspected to be drug-related.²

Kennebeck documented the frequency of clinical manifestations and laboratory data of the DRESS syndrome: fever (90–100%), cutaneous eruption (87–90%), lymphadenopathy (70%), hepatitis (50–60%), hematologic abnormalities (23–50%), periorbital and oro facial edema (25%), myalgia and arthritis (20%), nephritis (11%), pharyngitis (10%) and pulmonary manifestations (9%).⁴ According to it, in our patient fever, cutaneous eruption, lymphadenopathy, hematologic abnormalities, periorbital and oro facial edema and arthritis complain were present. Though liver is the most common organ involved which is absent in our patient, it is also important to bear in mind that internal organ involvement may not develop for 1-2 weeks into the reaction and even not until 1 month later.⁷

Rechallenging with the suspected drug is considered the gold standard for drug eruptions; however, it cannot be used to confirm the culprit drug for DRESS due to the possible life-threatening consequences. In an attempt to identify a more effective diagnostic test, Santiago et al., evaluated the safety and usefulness of patch testing in DRESS, thus attempting to identify a drug-dependent delayed hypersensitivity mechanism.⁸ In our patient



Patch test was not done but literature shows that Paracetamol give positive result with patch test in aqueous vehicle.⁶

Presence of lymphadenopathies, laboratory result showing eosinophilia and Nikolsky sign, which is further detachment of the epidermis with slight lateral pressure is negative in our patient, differentiate it from the SJS/TEN.^{9,10} Presence of eosinophilia, on examination absence of Strawberry tongue, fissured lips, edema of hands and there are no cardiovascular abnormalities or gastrointestinal symptoms differentiate our patient from Kawasaki disease.⁹

DRESS syndrome must be recognized promptly and the causative drug withdrawn. Treatment is largely supportive and symptomatic; corticosteroids are often used, but the evidence regarding their effectiveness is scant. Other immune suppressants, such as cyclosporin, may also be required.⁸

CONCLUSION

Paracetamol is a widely used over the counter analgesic and anti-pyretic for various indications so the physician should be aware of this rare adverse drug reaction and keep it in mind when he encounters one.

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