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DRESS Syndrome following Sulfasalazine Treatment and Chikungunya Infection: A Case Report

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ABSTRACT

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a life-threatening drug-induced hypersensitivity syndrome that can present with a rash, facial edema, systemic symptoms, lymphadenopathy, visceral organ involvement, and eosinophilia. There is limited literature on DRESS syndrome following Chikungunya infection with concomitant sulfasalazine exposure. As fever and rash can present similarly in both DRESS syndrome and Chikungunya infection, the diagnosis can be quite challenging. Here, we present a patient who presented with fevers, facial swelling, intense pruritus, and a worsening morbilliform rash. Investigation revealed acute Chikungunya infection, leukocytosis, acute renal failure, and transaminitis. She was diagnosed with DRESS, and steroids were initiated, which prompted improvement in her symptoms. This report describes a case of DRESS following treatment for Chikungunya infection, a possibly novel trigger.

Keywords: Drug reaction with eosinophilia and systemic symptoms (DRESS); Drug; Chikungunya

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe cutaneous adverse drug reaction that presents clinically with fever, cutaneous eruption, lymphadenopathy, hematologic abnormalities, and organ dysfunction[1,2] It can affect anyone, regardless of age, and is estimated to occur in approximately 1/1000 to 1/10,000 medication exposures. [3,4] DRESS is associated with both short-term and long-term morbidity, and patients who experience DRESS are also at an increased risk for later systemic autoimmune conditions and myocarditis.[2,3]

While the pathogenesis is not completely understood, DRESS is associated with the human herpes virus reactivation, particularly human herpes virus-6 and 7, cytomegalovirus, varicella zoster virus, and ebstein-barr virus. [2] A T-cell mediated hypersensitivity reaction to drugs plays a key role in the pathophysiology of DRESS, and it is assumed that these viral infections play a role in generation and activation of these cells. A genetic predisposition to DRESS has been established with the specific human leukocyte antigen (HLA) subtypes as well.[2,4]

DRESS is associated with the use of many drugs, but most notably has been reported with the use of allopurinol, anticonvulsants, sulfonamides, antibiotics, and antiviral agents.[2,5] The syndrome usually manifests two to six weeks after exposure to the insulting agent.[3,6] Treatment includes prompt withdrawal of suspected medication and early administration of systemic prednisolone for the best prognosis.[6] In this report, we describe a case of DRESS following sulfasalazine treatment for chikungunya virus infection and explore the possibility of chikungunya as a new viral trigger.

CASE PRESENTATION

A 57-year-old African-American woman with a history of hypertension presented with a complaint of facial swelling. She had traveled to Jamaica twenty-two days prior to this hospital visit and experienced malaise, watery diarrhea, and arthralgias during her trip. She initially presented to her primary care physician and was started on sulfasalazine. Two days later she developed a diffuse, erythematous, papular rash. She was admitted to another hospital, treated with cefepime, and had improvement in the rash before discharge. However, she was admitted to our institution seven days later with recurring fevers, facial swelling, intense pruritus, and a worsening morbilliform rash. She was also diagnosed with acute renal failure and transaminitis (Table 1). While she did not have eosinophilia, her symptoms and course were concerning for DRESS, and she had atypical lymphocytes (Table 1). She was started on oral prednisone 60 mg daily with improvement in symptoms and organ function and was later discharged on a prednisone taper. Given her diarrhea and arthralgias while in Jamaica, she was also tested for tropical infections at the time of admission and the results did not come in till after she was discharged, but they were positive for acute chikungunya infection.

Table 1: Patient Lab Values

Laboratory Parameter	Patient Value	Normal Value
Creatine, mg/dL	1.2	0.55 – 1.02
AST, U/L	73	15 – 37
ALT, U/L	120	13 – 56
Alkaline phosphatase, U/L	122	45 – 117
Atypical Lymphocytes	1	-
White blood cell count, K/µL	8.5	4.5 – 11.0
Segmented Neutrophils, %	76	40 – 60
Lymphocytes, %	18	20 – 40
Monocytes, %	3	2 – 8
Eosinophils, %	0	1 – 4
Basophils, %	2	0.5 – 1

DISCUSSION

This is a unique case of DRESS confounded by an early rash due to Chikungunya viral illness. To diagnose DRESS in a patient, the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) to Drugs and Collection of Biological Samples validation tool is used.[1] Our patient had a RegiSCAR DRESS score of 5, which suggested a diagnosis of DRESS, likely secondary to sulfasalazine.[7] The adverse cutaneous reaction in this case is likely due to the sulfapyridines in sulfasalazine, which can induce hypersensitivity via defects in the drug's metabolism leading to accumulation of toxic metabolites that are both cytotoxic and can indirectly trigger a T-cell medicated immune response.[4,6,8] In addition, concomitant medication use can also play a role in the pathogenesis of DRESS.[8] Our patient received cefepime prior to the presentation of DRESS. The literature describes antibiotic-induced DRESS flares in patients taking amoxicillin within days of the onset of symptoms.[8] Eliciting a thorough medication history is crucial in patients presenting with fever and a rash.

It is theorized that viral illnesses can act as triggers for DRESS. Literature review revealed a previous report of chikungunya serving as a trigger for DRESS. This virus can present with an acute febrile illness and cutaneous and constitutional symptoms mimicking DRESS.[4] Apart from the contribution of medications, reactivation of viruses should be considered as a persuader of DRESS.[6] Management of DRESS involves identifying and discontinuing the offending agent, supportive measures to control clinical manifestations, topical and/or systemic steroids to control inflammation, and monitoring for long-term complications.[2] There is still a lack of consensus for the treatment of DRESS, however, systemic corticosteroids remain as the first-line therapy for treatment of DRESS.[4,5] Our patient received IV methylprednisolone in the hospital with improvement in her symptoms and organ function, and she was then discharged with a prednisone taper.

CONCLUSIONS

In summary, it is important for providers to be cognizant of a possible correlation between DRESS syndrome and chikungunya virus, as early management can improve outcomes. Future studies are needed to explore Chikungunya virus as an etiological factor for DRESS.

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