

Letter

DRESS syndrome with suspected *Strongyloides* infection in a patient treated for hepatitis C

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe hypersensitivity reaction to medications and is characterized by skin rash, fever, lymphadenopathy, and multi-organ pathologic conditions. We report a case of DRESS syndrome that was associated with hepatitis C virus (HCV) treatment and possible *Strongyloides* infection. To our knowledge, this is the first case description regarding co-existence of DRESS syndrome and suspected *Strongyloides* infection.

A 55-year-old Puerto Rican male patient with a history of chronic HCV was administered peg-interferon alpha-2a, telaprevir, and ribavirin. Six weeks after treatment initiation, he developed a diffuse, erythematous, maculopapular rash that rapidly generalized, sparing the palms and soles. After 3 days of rash, he developed fever and chills and was admitted to our university-based medical center. He denied nausea, vomiting, diarrhea, abdominal pain, sick contacts, or recent antibiotic use, and reported no recent use of alcohol, tobacco, or other drugs. Besides the HCV medications, the patient was taking no other medication before admission.

On presentation, the patient was febrile to 102.1°F (38.9°C); physical examination was notable for bilateral submandibular lymphadenopathy. Laboratory evaluation revealed marked eosinophilia (1,000 cells/ μ L; baseline eosinophil count tested 1 year prior was 400 cells/ μ L), abnormal liver enzymes (aspartate aminotransferase/alanine aminotransferase, 120/123 IU/L; baseline aspartate aminotransferase/alanine aminotransferase before treatment was 18/18 IU/L, respectively), lymphopenia (600 cells/ μ L), and leukopenia (3,200 cells/ μ L). Hepatitis A and B serological tests were negative. Furthermore, the human herpes virus-6 (HHV-6) serum immunoglobulin G (IgG) level was increased (1:40), and total serum IgE was very high (13,110 IU/mL). Skin biopsy on admission indicated purpuric spongiotic and perivascular dermatitis with eosinophils, which was interpreted as compatible with a drug reaction (Fig 1). Chest x-ray on presentation demonstrated increased interstitial lungs markings, and a noncontrast chest computed tomography scan demonstrated bilateral hilar lymphadenopathy. Of note, the patient's serum angiotensin-converting enzyme level was found to be elevated (66; reference level, 8–52 μ g/L). The patient is undergoing pulmonary evaluation for possible sarcoidosis.

Given the diffuse maculopapular rash, fever, lymphadenopathy, transaminitis, hematologic abnormalities, and skin biopsy results, in the setting of recently started medications, DRESS syndrome was suspected based on the RegiSCAR inclusion criteria (Table 1). Furthermore, the patient's calculated Naranjo score of 5 suggested the probable presence of an adverse drug reaction.¹ Telaprevir was considered to be the most likely cause, because there no DRESS

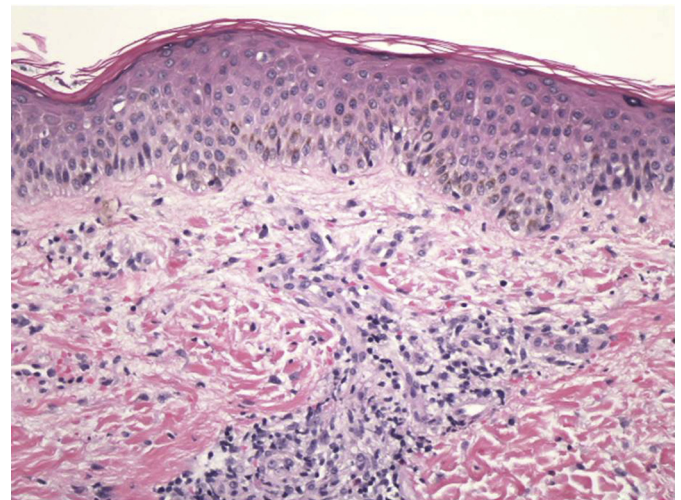


Figure 1. Purpuric spongiotic and perivascular dermatitis with eosinophils.

syndrome cases have been reported secondary to abacavir and peg-interferon alpha-2a. All HCV medications were discontinued, and the patient was treated with oral prednisone (40 mg for three days) starting on day 1 of admission. The viral load was undetectable 3 months and 7 months after stopping the antiviral medications; therefore, the patient was considered to be cured of HCV, and he will be followed every year in the hepatology clinic.

Table 1

The RegiSCAR-Group diagnosis score for drug reaction with eosinophilia and Systemic Symptoms (DRESS)

	No	Yes	Unknown
Fever ($\geq 38.5^{\circ}\text{C}$)	–1	0	–1
Enlarged lymph nodes (≥ 2 sites, >1 cm)	0	1	0
Atypical lymphocytes	0	1	0
Eosinophilia	0		0
700–1,499 or 10–19.9		1	
$\geq 15,00$ or $\geq 20\%$		2	
Skin rash	0		0
Extent $> 50\%$	0	1	0
At least 2 of: edema, infiltration, purpura, sacaling	–1	1	0
Biopsy suggesting DRESS	–1	0	0
Internal organ involved	0		0
One		1	
2 or more		2	
Resolution in > 15 days	–1	0	–1
At least 3 biological investigations done and negative to exclude alternative diagnosis	0	1	0

Final score: <2 , no case; 2–3, possible case; 4–5 probable case; >5 , definite case.

Disclosures: Authors have nothing to disclose.

Further evaluation of the eosinophilia revealed positive *Strongyloides* serum IgG. Two stool examinations for ova and parasites were negative. The patient was started on ivermectin (200 µg/kg/day for 2 days) on hospital day 2. After ivermectin and prednisone were started, the eosinophil count decreased to 2% (200 cells/µL) within 4 days, and the abnormal liver function tests and rash resolved within 7 days. One month after hospital discharge, the patient remained symptom-free with normal peripheral eosinophil count of 200 cells/µL.

Although glucocorticoids may have been effective against the DRESS syndrome, it is important to recognize *Strongyloides* in this setting, because glucocorticoids can cause hyperinfection syndrome, which is potentially life-threatening. Although this patient fulfilled the criteria for DRESS syndrome, fever, eosinophilia, and elevated liver enzymes may co-exist in other conditions, including other parasitic infections, Churg-Strauss syndrome, eosinophilia-myalgia syndrome, and eosinophilic leukemia/hyper-eosinophilic syndrome. Corticosteroids remain the mainstay of therapy for DRESS syndrome, and the co-existence of DRESS and *Strongyloides* can result in potentially disastrous consequences.

Strongyloides stercoralis, a soil-transmitted helminth that affects an estimated 30 million people worldwide, is endemic to Latin America, Southeast Asia, sub-Saharan Africa, and the Southeastern United States.² *Strongyloides* undergoes a complicated life cycle within humans, and it may cause autoinfection and thereby persist for decades.³ *Strongyloides* infections may cause eosinophilia, vague gastrointestinal or pulmonary symptoms, adult respiratory distress syndrome, hyperinfection syndrome, septic shock, or death.^{4–6} In hyperinfection syndrome, invasive filariform larvae cause leakage of gut flora from damaged bowel. This condition, which carries a mortality rate as high as 87%, might result in meningitis, pneumonia, gram-negative septicemia, or disseminated bacterial and fungal infections.^{4–6} Hyperinfection is most commonly seen in immunosuppressed patients, including those with human T-lymphotrophic virus infection, renal allograft recipients, or those using corticosteroids.⁷

The available serological test for *Strongyloides* infection is an IgG enzyme-linked immunosorbent assay test, which does not differentiate between current or previous infection. Sensitivity of stool examination is low, and multiple stool examinations can be negative in the setting of active infection, although the serological test may be positive. Also, the *Strongyloides* antibody test cross-reacts with other helminth infections, including filariasis, *Ascaris lumbricoides*, and acute schistosomiasis.

The occurrence of skin rash after retroviral therapy, the presence of an increased serum level of HHV-6 IgG, and the absence of hypereosinophilia before the beginning of retroviral therapy suggest that DRESS syndrome is the most likely diagnosis in this

case. Drug-specific T cells largely contribute to the systemic effects of DRESS syndrome, and multiple drugs such as allopurinol, sulfonamides, phenobarbital, sulfasalazine, carbamazepine, phenytoin, abacavir, and telaprevir have been implicated in causing DRESS syndrome.^{8,9} The HHV-6 reactivation in DRESS syndrome supports the theory that viruses may play a key role in this condition's pathogenesis, although the role of HCV is unknown.¹⁰ Moreover, the role of parasites in the immunopathogenesis of DRESS syndrome has not been well established. Whereas steroid therapy is often used to treat DRESS syndrome, this intervention carries a high mortality risk in the setting of *Strongyloides* infection. Therefore, physicians must maintain a high index of suspicion for parasitic infections before administering steroid therapy.

Lahari Rampur, MBBS*

Sunit Jariwala, MD*

Bijal Amin, MD*

Payal Patel, MD*

David L. Rosenstreich, MD*[†]

*Albert Einstein College of Medicine/Montefiore Medical Center

Bronx, New York

[†]Division of Allergy and Immunology

Director of the Bronx Asthma Project

Bronx, New York

lahari.j@gmail.com

References

- [1] Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30:239–245.
- [2] <http://www.cdc.gov/parasites/strongyloides/biology.html>.
- [3] Pelletier LL Jr, Baker CB, Gam AA, et al. Diagnosis and evaluation of treatment of chronic strongyloidiasis in ex-prisoners of war. *J Infect Dis*. 1988;157:573–576.
- [4] Siddiqui AA, Berk SL. Diagnosis of *Strongyloides stercoralis* infection. *Clin Infect Dis*. 2001;33:1040–1047.
- [5] Link K, Orenstein R. Bacterial complications of strongyloidiasis: *Streptococcus bovis* meningitis. *South Med J*. 1999;92:728–731.
- [6] Fodeman J, Jariwala S, Hudes G, et al. Scratching the surface. *Am J Med*. 2010;123:22–26.
- [7] Basile A, Simzar S, Bentow J, et al. Disseminated *Strongyloides stercoralis*: Hyperinfection during medical immunosuppression. *J Am Acad Dermatol*. 2010;63:896–902.
- [8] Camous X, Calbo S, Picard D, Musette P, et al. Drug reaction with eosinophilia and systemic symptoms: an update on pathogenesis. *Curr Opin Immunol*. 2012;24:730–735.
- [9] Criado PR, Criado RF, Avancini Jde M, et al. Drug reaction with Eosinophilia and Systemic Symptoms (DRESS)/Drug-induced Hypersensitivity Syndrome (DIHS): a review of current concepts. *An Bras Dermatol*. 2012;87:435–449.
- [10] Descamps V, Valance A, Edlinger C, et al. Association of human herpesvirus 6 infection with drug reaction with eosinophilia and systemic symptoms. *Arch Dermatol*. 2001;137:301–304.