CASE REPORT

A case of Vogt-Koyanagi-Harada disease as a sequela of drug reaction with eosinophilia and systemic symptoms

Katherine Altman, DO, MS, and Michi Shinohara, MD
Seattle, Washington

Key words: autoimmune; drug-induced hypersensitivity syndrome; drug reaction; drug reaction with eosinophilia and systemic symptoms.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe drug reaction with cutaneous, hematologic, and internal organ involvement and autoimmune sequelae. We report a case of DRESS complicated by Vogt-Koyanagi-Harada disease (VKHD), a rare autoimmune granulomatous syndrome targeting melanocytes.

CASE REPORT

A 32-year-old Asian-American man presented with 1 week of high spiking fevers and a pruritic rash. He started taking sulfamethoxazole-trimethoprim for acne 5 weeks prior. Initial therapy included oral antihistamines, topical steroids, and oral prednisone (60 mg/d) without improvement. Skin examination found facial edema, conjunctival injection, and diffuse confluent erythematous papules (Figs 1 and 2). No vesicles or bulla were present, and Nikolsky sign was negative.

Laboratory values were notable for an alanine aminotransferase of 419 U/L (normal, 10-64 U/L), aspartate aminotransferase of 85 U/L (normal, 9-38 U/L), and alkaline phosphatase of 123 U/L (normal, 35-109 U/L). Additionally, there was an elevated white blood cell count of 12.35k and no eosinophilia. DRESS was diagnosed, and oral prednisone was increased to 1 mg/kg/d (70 mg). Persistent pruritus required doxepin, 50 mg, and hydroxyzine, 50 mg, each once daily. Flaring of the rash occurred when attempts at prednisone taper reached 40 mg/d, and after 8 weeks of failed attempts, cyclosporine was added without improvement. Cyclosporine was started at a low dose and subsequently increased to 150 mg/d. Mycophenolate mofetil, 500 mg/d, was then started and eventually increased to 1 g twice a day with good control allowing cyclosporine to be tapered and stopped 6 months after starting. Eight months after initial presentation, while still requiring immunosuppressive medications, the patient had blurred vision in his right eye and abrupt-onset poliosis, with a white forelock. Consultation with a retinal expert revealed inflammatory scleritis and retinal detachment, consistent with VKHD. He was...

Fig 1. Initial presentation of our patient shows facial edema.

Abbreviations:

VKHD: Vogt-Koyanagi Harada Disease
DRESS: Drug reaction with eosinophilia and systemic symptoms

From the Department of Dermatology, the University of Washington.

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Katherine Altman, DO, MS, 1959 NE Pacific St, Seattle WA 98195. E-mail: kaltman@uw.edu.

JAAD Case Reports 2018;4:863-5.

2352-5126 © 2018 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
https://doi.org/10.1016/j.jdcr.2018.06.019
ultimately weaned off oral prednisone 2 years and 4 months after initial presentation and required about 3 years of treatment with mycophenolate mofetil.

DISCUSSION

DRESS is estimated to occur between 1 in 1000 to 1 in 10,000 cases of drug exposures. Because of the broad spectrum of clinical features of DRESS, the RegiSCAR scoring system was proposed to help standardize diagnosis. In our patient, features contributing to the diagnosis of DRESS were treatment with a known causative drug; long latency from drug initiation to onset of symptoms; extensive rash with facial edema, fever, and leukocytosis; and hepatitis with an alanine aminotransferase more than twice the upper limit of normal.

In addition to hematologic, liver, renal, pulmonary, and cardiac involvement, DRESS has been associated with autoimmune sequela, including type 1 diabetes, hypothyroidism and hyperthyroidism, autoimmune hemolytic anemia, and the development of antinuclear, anti-Sjogren syndrome A and anti-Smith antibodies. Our patient in fact also had Graves disease requiring thyroidectomy. Grave disease was diagnosed when he complained of difficulty sleeping and increased anxiety. Laboratory studies found a low thyroid-stimulating hormone level, elevated T3 and T4, and an iodine I-131 study confirming Graves disease. He also went on to have alopecia universalis and vitiligo.

VKHD is thought to be caused by T-helper cell 1-driven lymphocyte attack on melanocytes in genetically susceptible individuals carrying the HLA-DRB1*04 and HLA-DR4 alleles, although HLA specificities differ among races. Our patient expressed HLA-DRB1*04, HLA-DRB1*12, HLA-B3, HLA-B4, and HLA-DQ8B1*02 consistent with previous reports. By definition, ocular symptoms occur in 100% of cases and include blurred vision, panuveitis, and retinal detachment. Any tissue with melanocytes can be involved, including the meninges, causing neck stiffness, confusion, and headache; the inner ear, resulting in tinnitus, hearing loss and vertigo; and skin and hair leading to vitiligo and alopecia, which our patient also had (Fig 3).

Triggers of VKHD include viral illness, ocular trauma, or ocular surgery. Other case reports associated the development of VKHD with medications, specifically, pembrolizumab used to treat a patient with metastatic melanoma and interferon-α and ribavirin in patients treated for hepatitis C. However, these reports did not indicate that the patients described also had DRESS.

Autoimmune disease and specifically VKHD after DRESS may be explained by immunologic events that occur in both conditions. In DRESS, expansion...
of activated T lymphocytes is accompanied by reactivation of various herpes viruses. It is speculated that cytotoxic CD8 cells directed against virus-related antigens are the cause of tissue damage. Similarly, in VKHD, the most accepted mechanism of disease is that T lymphocytes develop in genetically susceptible individuals and damage melanocytes expressing antigens highly homologous to herpes virus antigens.

This case broadens the spectrum of autoimmune conditions that can occur as a result of DRESS. Furthermore, it strengthens the hypothesis that both DRESS and VKHD are caused by activated T lymphocytes that attack host tissues causing end organ damage.

REFERENCES
1. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: Part I. Clinical perspectives. J Am Acad Dermatol. 2013;68(5), 693.e1-4; quiz 706-698.
2. Kardaun SH, Sekula P, Valeyrle-Allanore L, et al. Drug reaction with eosinophilia and systemic symptoms (DRESS): an original multisystem adverse drug reaction. Results from the prospective RegiSCAR study. Br J Dermatol. 2013;169(5):1071-1080.
3. Matta JM, Flores SM, Cherit JD. Drug reaction with eosinophilia and systemic symptoms (DRESS) and its relation with autoimmunity in a reference center in Mexico. An Bras Dermatol. 2017;92(1):30-33.
4. Brown RJ, Rother KI, Artman H, et al. Minocycline-induced drug hypersensitivity syndrome followed by multiple autoimmune sequelae. Arch Dermatol. 2009;145(1):63-66.
5. Shi T, Lv W, Zhang L, Chen J, Chen H. Association of HLA-DR4/HLA-DRB1*04 with Vogt-Koyanagi-Harada disease: a systematic review and meta-analysis. Sci Rep. 2014;4:6887.
6. Baltm A, Lightman S, Tomkins-Netzer O. Vogt-Koyanagi-Harada syndrome - current perspectives. Clin Ophthalmol. 2016;10:2345-2361.
7. Duan J, Wang Y, Liu D, Ma J. Induction of Vogt-Koyanagi-Harada disease by interferon-alpha and ribavirin treatment in patients with hepatitis C: a case report and review of the literature. Ocul Immunol Inflamm. 2017;12:1-6.
8. Bricout M, Petre A, Amini-Adle M, et al. Vogt-Koyanagi-Harada-like syndrome complicating pembrolizumab treatment for metastatic melanoma. J Immunother. 2017;40(2):77-82.
9. Lavezzo MM, Sakata VM, Morita C, et al. Vogt-Koyanagi-Harada disease: review of a rare autoimmune disease targeting antigens of melanocytes. Orphanet J Rare Dis. 2016;11:29.