

Steroid Allergy in a Patient With Behçet's Disease

Bailey M. Harrison; R. John Looney, MD;
Zoë R. Williams, MD;
David A. DiLoreto Jr., MD, PhD

ABSTRACT: Immediate hypersensitivity reactions to systemic steroids are reported rarely in the literature. The authors present a case of Behçet's disease-associated panuveitis in a patient with skin test confirmed immunoglobulin E-mediated allergy to methylprednisolone and reported allergic reaction to prednisone. The patient tolerated prednisolone eyedrops for his anterior segment disease, as well as oral prednisolone for systemic therapy. This case demonstrates a challenge to conventional treatment, as it involves a hypersensitivity that is rarely reported. It also highlights class differences in corticosteroids with regard to immune reactivity.

[*Ophthalmic Surg Lasers Imaging Retina*. 2021;52:447-449.]

From University of Rochester School of Medicine and Dentistry, Rochester, New York (BMH); Allergy Immunology Rheumatology Division, Department of Medicine, University of Rochester Medical Center, Rochester, New York (RJM); Flaum Eye Institute, Department of Ophthalmology, University of Rochester Medical Center, Rochester, New York (ZRW, DAD); the Department of Neurosurgery, University of Rochester School of Medicine and Dentistry, Rochester, New York (ZRW); and the Department of Neurology, University of Rochester School of Medicine and Dentistry, Rochester, New York (ZRW).

Originally submitted February 1, 2021. Revision received February 13, 2021. Accepted for publication March 16, 2021.

The Department of Ophthalmology, Flaum Eye Institute, receives departmental funding for research from Research to Prevent Blindness. The authors report no relevant financial disclosures.

Address correspondence to David A. DiLoreto, Jr. MD, PhD, 601 Elmwood Avenue, Box 659, Rochester, NY 14642; email: david_diloreto@urmc.rochester.edu.

doi: 10.3928/23258160-20210727-07

INTRODUCTION

Ocular complications of noninfectious panuveitis include macular edema, retinopathy, and increased risk of cataract and glaucoma. Goals of treatment include inducing immunosuppression to subdue the ocular inflammation and its pathologic sequelae, and first-line treatment is often corticosteroids.¹ Other immunosuppressive agents are typically used for long-term management,² with a recent focus on biologic immunosuppressive treatment.³

Allergic reactions to systemic corticosteroids have been reported but are rare, even when compared to topical reactions; systemic allergy has an estimated prevalence of 0.3%.¹ Immediate reactions (≤ 1 hour) are classified as type I hypersensitivity, which is immunoglobulin E (IgE)-mediated and confirmed with antigen skin testing.⁴

There are case reports of hypersensitivity to specific corticosteroids; however, data are limited, and few cases have been reported since the early 2000s.⁵⁻⁹ There is some evidence that betamethasone and dexamethasone may be less likely to cause adverse reactions than other systemic agents.^{6,7,10} Recent evidence has suggested that additives in specific corticosteroids may also be associated with differences in reactions.¹¹

CASE REPORT

A 28-year-old male presented with vision loss in his right eye. Initial evaluation was consistent with neuroretinitis in the right eye. A thorough infectious and autoimmune laboratory work-up was initiated, which was negative except for elevated C-reactive protein (13.1 mg/L). His visual acuity improved over several weeks without systemic therapy.

Six months later, he reported worsening vision in the right eye. Exam revealed anterior uveitis, which was treated with prednisolone eye drops. There was no adverse reaction to prednisolone eye drops, even when dosing was increased to every hour while awake. The patient then developed anterior uveitis in the left eye, which was also successfully treated with prednisolone eye drops. Four weeks later, his vision significantly worsened, and vitritis was noted. A fluorescein angiogram revealed mild, diffuse vascular leakage. He was prescribed oral prednisone. A morbilliform rash on the face and neck developed 1 hour following the first dose (**Figures 1 and 2**). His rash resolved with diphenhydramine.



Figure 1. Distribution of the face and neck rash that developed following a single dose of oral prednisone.

Due to disease recurrence and adverse reaction to oral prednisone, rheumatology was consulted. Rheumatologic history revealed 5 years of recurrent sore throat, fever, skin rashes, oral ulcers, and Raynaud's phenomenon. Based on this history and the ocular findings, he was diagnosed with Behçet's disease. Allergy testing with intradermal methylprednisolone caused a large skin reaction. Since prednisolone eyedrops were tolerated, an oral prednisolone challenge was given, which caused no reaction. Oral prednisolone solution was initiated and caused no allergic reaction. Maintenance immunosuppressive therapy was planned with azathioprine; however, 4 hours after the first dose, he had facial flushing and redness, which resolved with diphenhydramine after 1 hour. Oral leflunomide was then chosen for long-term immunosuppression. He tolerated this well, and oral prednisolone was tapered.

DISCUSSION

Immediate hypersensitivity to systemic corticosteroids remains a rare entity. The largest case series to date, which included 23 patients, was described in 2015 and demonstrated that skin testing provided sufficient evidence for diagnosis.¹² However, challenge testing continues to be the only option to determine safe alternatives in cases of allergy.

Our patient had positive intradermal allergy testing to methylprednisolone and a rash after oral prednisone. He did not report associated shortness of breath or itching, so it is unclear whether his hypersensitivity reaction or his skin testing would suggest anaphylaxis upon exposure to corticosteroids in the future.



Figure 2. Close up of the neck showing the morbilliform nature of the rash.

He responded well to prednisolone eyedrops. However, with continued recurrence of uveitis progressing to panuveitis, systemic therapy was warranted. His lack of reaction to prednisolone oral solution is interesting, as it suggests a difference in reactivity based upon the agent. The difference structurally between methylprednisolone and prednisolone is a single methyl group, and it has been shown that even slight changes in molecular structure can significantly alter chemical properties and immune reactions.¹³ This patient did not have skin testing for betamethasone and dexamethasone, which are fluorinated agents and have previously been described as less likely to cause hypersensitivity reaction.

Interestingly, prednisolone is the active metabolite of oral prednisone, which suggests that the patient's reaction to prednisone may have been associated with properties of the prodrug or its excipient. In a sample of 64 patients with corticosteroid allergy diagnosis, Li et al. demonstrated true allergy with skin testing was confirmed in only 14% of patients, with the majority actually being allergic to excipients including carboxymethylcellulose and polyethylene glycol.¹¹ Skin testing of excipients in cases of suspected corticosteroid allergy may be helpful in estab-

lishing an accurate diagnosis,¹¹ although the clinical utility of this remains unknown.

To our knowledge, this is the first case report of Behçet's disease associated panuveitis in which hypersensitivity to systemic corticosteroids delayed acute treatment and resulted in the need for treatment with oral prednisolone solution. Further data on efficacy of prednisolone solution compared with conventional therapy may be needed to assess the impact his allergy may have on adequate treatment. This case also highlights that although rare, immediate IgE-mediated hypersensitivity reactions to systemic corticosteroids may be more prevalent than previously believed, and should be considered when treating ocular manifestations of systemic inflammatory diseases.

REFERENCES

1. Dick AD, Tundia N, Sorg R, et al. Risk of ocular complications in patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis. *Ophthalmology*. 2016;123(3):655-662. <https://doi.org/10.1016/j.ophtha.2015.10.028> PMID:26712559
2. Kempen JH, Daniel E, Gangaputra S, et al. Methods for identifying long-term adverse effects of treatment in patients with eye diseases: the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study. *Ophthalmic Epidemiol*. 2008;15(1):47-55. <https://doi.org/10.1080/09286580701585892> PMID:18300089
3. Leclercq M, Desbois AC, Domont F, et al. Biotherapies in Uveitis. *J Clin Med*. 2020;9(11):3599. <https://doi.org/10.3390/jcm9113599> PMID:33171664
4. Varti RR, Ali F, Teuber S, Chang C, Gershwin ME. Hypersensitivity reactions to corticosteroids. *Clin Rev Allergy Immunol*. 2014;47(1):26-37. <https://doi.org/10.1007/s12016-013-8365-z> PMID:23567983
5. Escibano-Rodríguez MM, González-Pol J, Muñoz-Bellido FJ, de la Calle-Toral A, Velázquez-Amor E, Conde-Hernández J. Immediate reaction to methylprednisolone with tolerance of other corticosteroids. *Allergy*. 1997;52(6):677-678. <https://doi.org/10.1111/j.1398-9995.1997.tb01054.x> PMID:9226068
6. Danley SG. Steroid allergy? A case report and review of the literature. *J Okla State Med Assoc*. 2007;100(1):28-31. PMID:17378500
7. Karsh J, Yang WH. An anaphylactic reaction to intra-articular triamcinolone: a case report and review of the literature. *Ann Allergy Asthma Immunol*. 2003;90(2):254-258. [https://doi.org/10.1016/S1081-1206\(10\)62151-5](https://doi.org/10.1016/S1081-1206(10)62151-5) PMID:12602676
8. Peng YS, Shyur SD, Lin HY, Wang CY. Steroid allergy: report of two cases. *J Microbiol Immunol Infect*. 2001;34(2):150-154. PMID:11456363
9. Borja JM, Galindo PA, Feo F, Gomez E. Urticaria to methylprednisolone sodium hemisuccinate. *Allergy*. 2001;56(8):791. <https://doi.org/10.1034/j.1398-9995.2001.056008791.x> PMID:11488681
10. Ventura MT, Calogiuri GF, Matino MG, et al. Alternative glucocorticoids for use in cases of adverse reaction to systemic glucocorticoids: a study on 10 patients. *Br J Dermatol*. 2003;148(1):139-141. <https://doi.org/10.1046/j.1365-2133.2003.05061.x> PMID:12534608
11. Li PH, Wagner A, Thomas I, Watts TJ, Rutkowski R, Rutkowski K. Steroid allergy: clinical features and the importance of excipient testing in a diagnostic algorithm. *J Allergy Clin Immunol Pract*. 2018;6(5):1655-1661. <https://doi.org/10.1016/j.jaip.2018.01.007> PMID:29408496
12. Baker A, Empson M, The R, Fitzharris P. Skin testing for immediate hypersensitivity to corticosteroids: a case series and literature review. *Clin Exp Allergy*. 2015;45(3):669-676. <https://doi.org/10.1111/cea.12441> PMID:25346233
13. Samuel S, Nguyen T, Choi HA. Pharmacologic characteristics of corticosteroids. *J Neurocrit Care*. 2017;10(2):53-59. <https://doi.org/10.18700/jnc.170035>

Reproduced with permission of copyright owner. Further reproduction prohibited without permission.