Successful treatment of drug reaction with eosinophilia and systemic symptoms syndrome relapse with oral pulsed dexamethasone

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INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe hypersensitivity reaction that can be life threatening. Long-term treatment with corticosteroids is required in the management of DRESS syndrome, and relapse or worsening of symptoms after a short course of steroids after initial improvement is common. Oral steroid pulse therapy has been used to treat various dermatologic conditions with the goal of reducing toxicity associated with sustained steroid use. The use of oral pulse therapy in the treatment of DRESS syndrome has not been reported. Here we present the case of a patient with allopurinol-induced DRESS syndrome relapse successfully treated with pulsed oral dexamethasone.

Abbreviation used:

DRESS: drug reaction with eosinophilia and systemic symptoms

CASE REPORT

A 74-year-old African-American woman with chronic kidney disease, secondary to longstanding hypertension and type 2 diabetes mellitus, presented to the emergency department with worsening facial swelling and a pruritic rash of 4 weeks' duration. Approximately 2 months prior, the patient was started on allopurinol (100 mg/d) after an acute gout flare. Four weeks after initiating allopurinol, the patient had a pruritic rash involving the face, trunk, and extremities. The patient was initially treated with diphenhydramine, but her rash worsened and progressed to facial swelling, at which time she presented to the emergency department for evaluation.

On presentation, the patient was afebrile, and vital signs were normal. Physical examination was remarkable for palpable cervical lymphadenopathy, swelling of the face/lips, and a desquamative morbilliform rash progressing to confluent erythroderma involving her face, neck, trunk, and extremities (Fig 1). There was no hepatosplenomegaly, skin tenderness, or mucosal involvement, and Nikolsky sign was negative. Laboratory results were notable for transaminitis (aspartate aminotransferase, 245 U/L; alanine aminotransferase, 1017 U/L), acute kidney injury (creatinine, 2.94 mg/dL; baseline creatinine, 1.7 mg/dL), and eosinophilia (7% on cell differential; white blood cell count, 8.25 μL), and atypical lymphocytes. Serology for viral hepatitis, Epstein-Barr virus, cytomegalovirus, and human herpesvirus 6 were negative. Biopsy of the right thigh found interface dermatitis with necrotic keratinocytes consistent with features of erythema multiforme-Steven-Johnson-TEN spectrum. Allopurinol was identified as the most likely culprit on medication review and was discontinued. The patient was started on intravenous methylprednisolone (125 mg/d) with rapid improvement over several days and was discharged on oral prednisone (120 mg/d).

At follow-up 1 week later, laboratory abnormalities and cutaneous findings had almost completely resolved, and rapid oral prednisone

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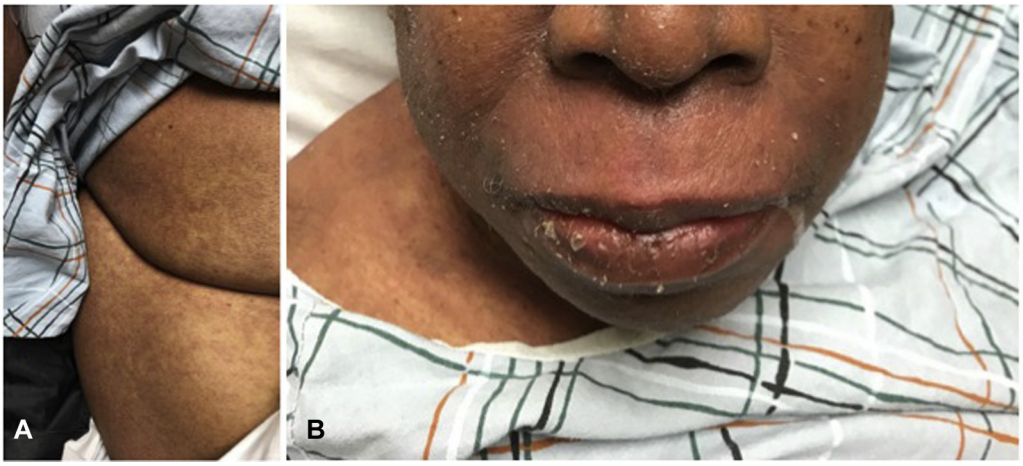

Fig 1. DRESS syndrome. **A**, Erythematous macules and papules on the right lower abdomen and thigh. **B**, Erythema, marked swelling, and desquamation involving the lower face at initial presentation.

taper (80 mg/d × 4 days, 60 mg/d × 4 days, 40 mg/d × 4 days, and 20 mg/d × 4 days) was initiated by another provider. Nine days after completion of the steroid taper, the patient presented to us with a diffuse erythematous maculopapular rash, skin desquamation, and facial swelling, consistent with DRESS syndrome relapse. The patient refused treatment with daily steroids because of the side effects she had previously experienced, including labile blood pressure, hyperglycemia, and weight gain. We discussed that DRESS syndrome requires long-term steroids for its management and offered a trial of pulse therapy with oral dexamethasone (12 mg/d) for 2 consecutive days per week. Symptoms completely resolved after 8 weeks of treatment and a slow taper of oral dexamethasone (8 mg/d for 2 consecutive days/7 days × 2 weeks; 4 mg/d for 2 consecutive days/7 days × 2 weeks) was initiated. The patient has maintained a good response and remains without symptoms 6 months after discontinuation of steroids.

DISCUSSION

DRESS syndrome is a severe idiosyncratic drug reaction characterized by generalized skin eruption, eosinophilia, lymphadenopathy, and end organ damage, usually 2 to 6 weeks after the initiation of the offending drug. Histopathology is polymorphic and associated with various inflammatory patterns.[1] Numerous medications are associated with DRESS syndrome, and allopurinol is among one of the most frequently reported culprits. In clinical practice, patients with DRESS are treated with high-dose long-term steroids. Although topical steroids are sufficient treatment in some cases, systemic steroids are usually required for patients with organ involvement and concerning laboratory findings.[2] Beyond this, consensus is lacking regarding the optimal steroid choice, dose, route of administration, and duration of therapy.

Long-term supraphysiologic doses of corticosteroids are needed to treat DRESS syndrome even after the patient appears to have improved. Relapses are frequent and commonly follow treatment discontinuation or a quick steroid taper as seen in this patient,[3,4] which can lead to increased patient morbidity and mortality. Unfortunately, prolonged treatment with high-dose corticosteroids can result in well-known adverse events and is more likely to cause serious complications such as hypothalamic-pituitary-adrenal axis suppression.

Oral and intravenous steroid pulse therapies have been used to treat various inflammatory and autoimmune conditions in an attempt to achieve a rapid therapeutic effect while avoiding the toxicities associated with daily or continuous systemic steroid use.[5] Long-term pulsing has also been used successfully, with similar benefit to sustained corticosteroid treatment, in the treatment of dermatologic conditions such as vitiligo, pemphigus vulgaris, and alopecia areata.

Serious adverse effects such as sudden cardiac death, arrhythmia, seizure, and electrolyte abnormalities have been described with intravenous steroid therapy.[5,6] Thus, hospitalization and cardiac monitoring are recommended.[5] However, oral pulse therapy appears relatively safe, with tolerable and reversible side effects reported.[5,7,8] This therapy can be used in the outpatient setting and is believed to have similar bioavailability to that of intravenous pulse therapy.[5,7,8] Because of the rapid clinical

effects observed with high-dose oral and intravenous pulse therapy, it is hypothesized that nongenomic mechanisms play an important role in these 2 forms of pulsing.[9] However, some effects are thought to be dose dependent, and the mechanism of oral pulsing at a low dose may differ.

Currently, no guidelines exist for oral pulse therapy in the treatment of dermatologic diseases. Dexamethasone and betamethasone are both long acting with good glucocorticoid potency and essentially no mineralocorticoid effects and are common choices.[5] Nonetheless, there is no clear recommendation for drug choice. Doses and pulsing schedules also vary widely, with pulse frequency ranging from weekly to monthly and duration of treatment ranging from several weeks to several months. Similarly, the role of tapering in this regimen has not been specified.

The use of pulsed oral steroids in DRESS syndrome relapse merits further investigation, as it may be an appropriate treatment for patients who cannot tolerate, or who do not wish to take, daily steroids. Furthermore, guidelines to standardize the dosing, choice of steroid, and pulsing schedule, while minimizing side effects and maximizing therapeutic benefit, are needed.

REFERENCES

1. Ortonne N, Valeyrie-Allanore L, Bastuji-Garin S, et al. Histopathology of drug rash with eosinophilia and systemic symptoms syndrome: A morphological and phenotypical study. *Br J Dermatol*. 2015;173(1):50-58.
2. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: Part II. Management and therapeutics. *J Am Acad Dermatol*. 2013; 68(5).
3. Turney R, Skittrall JP, Donovan J, Agranoff D. Drug Reaction, eosinophilia and systemic symptoms (DRESS) syndrome secondary to allopurinol with early lymphadenopathy and symptom relapse. *BMJ Case Rep*. 2015;2015: bcr2015211222.
4. Shalom R, Rimbroth S, Rozenman D, Markel A. Allopurinol-induced recurrent DRESS syndrome: pathophysiology and treatment. *Ren Fail*. 2008;30(3):327-329.
5. Wolverton SE. *Comprehensive Dermatologic Drug Therapy*. 3rd ed. Edinburgh: Saunders/Elsevier; 2013.
6. Natkunarajah J, Goolamali S, Craythorne E, et al. Ten cases of drug reaction with eosinophilia and systemic symptoms (DRESS) treated with pulsed intravenous methylprednisolone. *Eur J Dermatol*. 2011;21(3):385-391.
7. Toth G, van de Meer J, Jonkman M. Dexamethasone pulse therapy in pemphigus. *J Eur Acad Dermatol Venereol*. 2002; 16(6):607-611.
8. Kurosawa M, Nakagawa S, Mizuashi M, et al. A comparison of the efficacy, relapse rate and side effects among three modalities of systemic corticosteroid therapy for alopecia areata. *Dermatology*. 2006;212(4):361-365.
9. Bagga A, Sinha A. Symposium on steroid therapy pulse steroid therapy. *Indian J Pediatr*. 2008;75(7510):1057-1066.