A generalized fixed drug eruption associated with mycophenolate

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INTRODUCTION

Mycophenolate is a reversible inhibitor of inosine monophosphate dehydrogenase, which plays an important role in the production of DNA. This drug is commonly used in several autoimmune and inflammatory conditions, including connective tissue diseases, immunobullous disease, and atopic dermatitis, and in the setting of organ transplantation. Mycophenolate is considered first-line therapy in many patients because of its relatively minimal side effect profile when compared with other immunosuppressive agents. Most common side effects include diarrhea, gastrointestinal distress, peripheral edema, and high blood pressure. Less common side effects include pancytopenias and risk of infection.[1] Given the overall prevalence of mycophenolate use, we present a rare case of a generalized fixed drug eruption caused by mycophenolate.

Abbreviation used:

FDE: fixed drug eruption

CASE REPORT

A 45-year-old woman with history of an undifferentiated systemic rheumatic disease (characterized by idiopathic orbital inflammation and lacrimal gland involvement, diffuse lymphadenopathy, membranoproliferative glomerulonephritis, erythema nodosum, arthralgias, oral and vaginal ulcers, sicca symptoms, Raynaud's phenomenon, photosensitivity, and cytopenias), coronary artery disease, and recurrent deep venous thrombosis presented with a rash within days of resuming several medications.

This was not the first occurrence of rash in this patient. Three years before our initial encounter with this patient, she had an acute episode of hyperpigmented patches with dusky centers over her arms, trunk, face, and vaginal mucosa. Despite mucous membrane involvement, there were fewer than 8 total lesions, desquamation was not present, and Nikolsky sign was negative. Therefore, the rash was thought to be inconsistent with Stevens-Johnson syndrome. A biopsy found an interface lymphocyte- and neutrophil- mediated dermatitis with vacuolar basement membrane alteration, necrotic keratinocytes, and melanophages. The rash was thought to be most consistent with a generalized fixed drug eruption (FDE). At this time, the patient self-discontinued all of her medications, including mycophenolic acid, 720 mg twice daily, amlodipine, 10 mg daily, and rivaroxaban, 20 mg daily.

Three years later, at an initial visit to a new rheumatologist, the patient reported an acute constellation of symptoms, including eye pain and redness resembling previous episodes of uveitis, joint swelling, Raynaud's symptoms, and alopecia. Laboratory evaluation found newly positive antinuclear antibody along with proteinuria. At this time, it was recommended to resume the aforementioned (self-discontinued) medications with addition of prednisone, 15 mg daily. Days later, recurrence of the rash developed in the same locations (Fig 1).

Review of the medical record found that the only 2 medications the patient was taking during both episodes of the fixed eruption were amlodipine and mycophenolic acid, the bioavailable form of mycophenolate mofetil. Because amlodipine has been reported to cause cutaneous adverse reactions in 49.6 of every one million prescriptions,[2] it was presumed to be the culprit drug. She was

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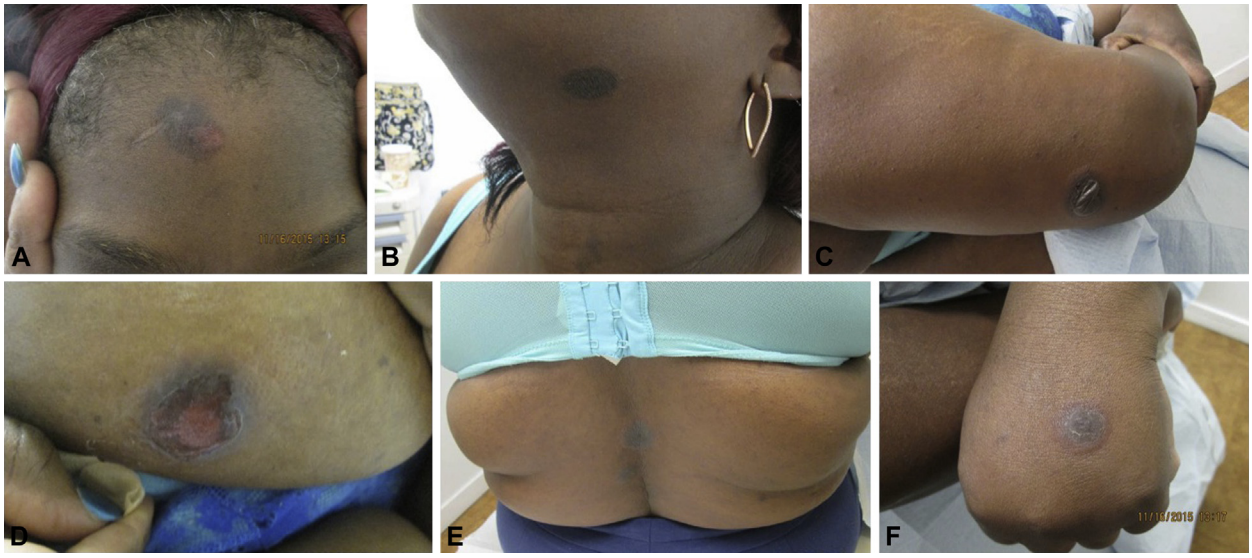

Fig 1. Generalized fixed drug eruption involving forehead (**A**), neck (**B**), right arm (**C**), left breast (**D**), back (**E**), and left dorsal hand (**F**).

encouraged to resume mycophenolic acid but not amlodipine. Within 1 day of resuming mycophenolic acid, a third occurrence of lesions developed in the same sites with the addition of a bullous component overlying the lesion on her right arm. Upon cessation of mycophenolate, her rash resolved over the ensuing week and has not recurred.

DISCUSSION

Fixed drug eruption is a common dermatologic adverse reaction to commonly prescribed drugs. Agents implicated in FDE include nonsteroidal anti-inflammatory drugs, tetracyclines, fluoroquinolones, trimethoprim, pseudoephedrine, cetirizine, and phenytoin.

Our patient had a generalized FDE in the same location on 3 separate occasions. During each of these, she was taking mycophenolate, and on the third occurrence this was in fact her only reported medication. Therefore, mycophenolic acid was identified as the likely culprit of her recurrent FDE.

On review of the available literature, FDE is uncommon in patients on immunosuppressive therapies. FDE has been reported in 1 patient taking abatacept for rheumatoid arthritis,[3] 1 patient taking azathioprine,[4] 1 patient taking doxorubicin for breast cancer,[5] and 2 patients taking paclitaxel (1 patient for ovarian cancer[6] and the other, who presented with bullous FDE, for breast cancer[7]). Although not consistent with a fixed drug reaction, the development of a psoriasiform skin eruption after the introduction of mycophenolate mofetil in a 32-year-old man with myasthenia gravis has been described previously.[8]

Fixed drug eruption can be alarming for patients and providers, especially when mucous membrane involvement or blistering is present. Fixed drug eruptions may even be misidentified as Stevens-Johnson syndrome. Because resolution of a fixed eruption is often uncomplicated with prompt cessation of the offending agent, it is important that physicians recognize this entity. Furthermore, dermatologic and medical providers should keep robust documentation of drugs capable of inciting fixed eruption, and mycophenolate mofetil should be added to our current database.

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