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Erythema multiforme during anti–tumor necrosis factor treatment for plaque psoriasis

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Tumor necrosis factor alpha (TNF-α) inhibitors constitute a class of biologic treatments utilized in the management of psoriasis. We report a case of a patient treated for chronic plaque psoriasis with the anti-TNF-α monoclonal antibody adalimumab, who developed erythema multiforme (EM). The patient had previously developed EM on two occasions while taking the TNF-α inhibitor etanercept. EM has previously been reported in connection with other TNF-α inhibitors, including etanercept and infliximab. To our knowledge, this is the first case reported in the literature documenting EM occurring subsequent to adalimumab treatment for psoriasis. The recurrent development of EM in our patient while being treated with distinct TNF-α inhibitors may suggest that EM is the consequence of a class effect with TNF-α inhibitors. (J Am Acad Dermatol 2010;62:874-9.)

Key words: adalimumab; erythema multiforme; psoriasis; TNF-α inhibitor

INTRODUCTION

As a potent stimulator of the inflammatory response associated with psoriasis, tumor necrosis factor-alpha (TNF-α) has been extensively studied as a potential target in the treatment of psoriasis. In recent years, several TNF-α inhibitors including adalimumab (Humira), etanercept (Enbrel), and infliximab (Remicade) have emerged as effective biologic treatments in the management of psoriasis. Etanercept was the first among this class of TNF-α inhibitors to receive US Food and Drug Administration (FDA) approval for the treatment of chronic, moderate to severe psoriasis in 2004, followed by infliximab in 2006, and adalimumab in 2008.[1] Common side effects of treatment with TNF-α inhibitors include injection site reactions, headache,

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Abbreviations used:

DIEM: drug-induced EM
EM: erythema multiforme
FDA: Food and Drug Administration
HAEM: herpes-associated EM
HSV: herpes simplex virus
IL: interleukin
TNF: tumor necrosis factor
VZV: varicella zoster virus

nasopharyngitis, increased triglycerides, dyspepsia, nausea, upper respiratory tract infection, pruritus, sinusitis, and fatigue.[2] Rare serious side effects reported with treatment include hypersensitivity reactions, demyelinating disease, deep fungal and tuberculosis infections, malignancy, lupus-like symptoms, and congestive heart failure exacerbation.[2] We report a case of a patient with plaque psoriasis who experienced two episodes of erythema multiforme (EM) while being treated with etanercept as well as one episode of EM while taking adalimumab.

CASE REPORT

A 67-year-old Korean American man with a 14-year history of chronic plaque psoriasis developed several vesicles and bullae on an erythematous base on his arms, legs, and trunk 11 days after receiving an 80-mg starting dose of subcutaneous adalimumab followed by a 40-mg dose 1 week later (Fig 1). The vesicles on his abdomen were grouped and occurred bilaterally at his medication injection sites (Fig 2). He also developed hemorrhagic vesicles on his palate and lower lips, which progressed to become large ulcers over the next week (Fig 3). During this same time, the vesicular lesions on his trunk and extremities evolved into targetoid, erythematous plaques with a dusky violaceous center (Fig 4). Swabs of unroofed vesicles were negative for herpes simplex virus (HSV) and varicella zoster virus (VZV) by use of direct fluorescent antigen testing and viral culture. Serology for HSV IgM was negative, but the patient displayed positive IgG titers against HSV-1, HSV-2, and VZV. Of note, on the same day he started adalimumab, he had begun a course of valacyclovir for an eruption of HSV-2 on his right buttock. To explore the possibility of a sensitivity to rubber latex contained within the adalimumab syringe, the patient had patch testing with a standard tray containing a black rubber mix as well as a radioallergosorbent test for IgE against natural latex, both of which were negative.

Biopsy of a vesicular lesion demonstrated a subepidermal bulla containing eosinophils, lymphocytes, and fibrin with necrotic cells along the basal layer of the epidermis adjacent to the bulla (Fig 5). There was also a superficial perivascular and interstitial mixed infiltrate composed of lymphocytes, eosinophils, and neutrophils. Perilesional direct and indirect immunofluorescence examinations were negative.

The patient's medical history was remarkable for non-insulin-dependent diabetes mellitus, hypertension, coronary artery disease, recurrent HSV-2 for which he has taken valacyclovir in the past without incident, and a positive tuberculin skin test for latent tuberculosis with a chest radiograph that was negative for pulmonary tuberculosis. His medications included metformin, sitagliptin, benazepril, metoprolol, amlodipine, doxazosin, aspirin, clopidogrel, folic acid, pyridoxine, adalimumab,

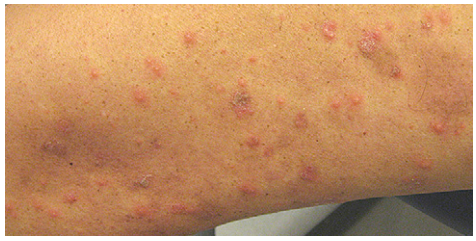

Fig 1. Vesicles on an erythematous base admixed with psoriatic plaques on right inner thigh.

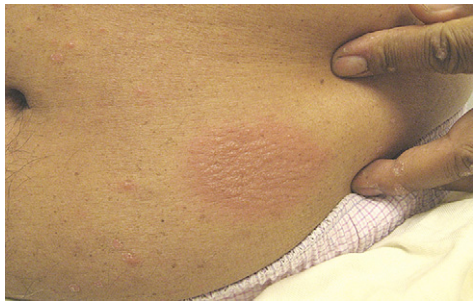

Fig 2. Grouped vesicles on left side of abdomen at site of adalimumab injection.

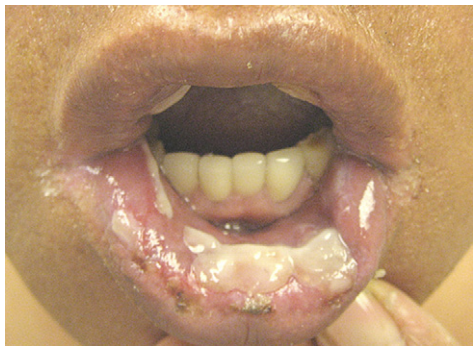

Fig 3. Ulcers on lip mucosa.