

Severe delayed erythema multiforme to vancomycin in a woman on regular hemodialysis

M.-Y. Lai*, C.-C. Lin, W.-C. Yang, Y.-Y. Ng, S.-D. Lee

Key words: adverse drug reaction; drug allergy; erythema multiforme; skin rash; vancomycin.

A 47-year-old woman, without history of allergy, presented to our emergency department with a progressive generalized itching skin eruption for 3 days. She was a Buddhist nun and had been on vegetarian diet for more than 10 years. She had been diagnosed as a hepatitis B carrier for decades and hypertension was also noted for 7 years, which was controlled by irbesartan and amlodipine in recent 4 years. She did not take any other medicines. For end-stage IgA nephropathy, she had been on regular hemodialysis via the native arteriovenous fistula (AVF) in her left forearm for 5 years. However, redness with mild local heat of the AVF was noticed at a local hemodialysis center about 2 months ago. For a suspicious infection of the AVF, intravenous vancomycin 750 mg was administered weekly there for 4 weeks. Because of limited effect, the dose of vancomycin was titrated to 500 mg three times a week for another 2 weeks. The redness of the AVF was partially resolved, but it got worse with progressive itching skin eruption over the whole body since 3 days before this hospitalization. She was referred to our hospital because the

A case of severe delayed erythema multiforme to vancomycin without other systemic symptoms.

skin eruption was resistant to oral and intravenous antihistamine therapy. On physical examination, diffuse pink-red plaques and target lesions (Fig. 1) on the trunk and four limbs with sparing of palmoplantar surface and scalp were noted. The patient claimed that the plaques resulted from confluent target lesions. The skin rashes were painless, but severely pruritic. There was no fever, blister, mucosal erosion, nor enlarged lymph node. The laboratory studies including bacterial cultures, viral serology tests and serum level of vancomycin were unremarkable. Delayed erythema multiforme to vancomycin was highly suspected. Vancomycin was thus discontinued on admission. Oral prednisolone 10 mg t.i.d. (for 1 week) and antihistamines were administered. Topical steroid and Calamine lotion for relieving pruritus were also prescribed. The progression of the skin rashes was stopped on the third day of oral prednisolone therapy. Of note, the original pink-red plaques regressed to multiple dusky target lesions 4–6 days after the prednisolone therapy. The dose of prednisolone was tapered to

5 mg t.i.d. for the second week, and then 5 mg b.i.d. for the third week. The skin eruptions completely subsided without sequelae in 3 weeks. The clinical diagnosis of erythema multiforme was confirmed by skin biopsy that showed a moderate perivascular mononuclear cell dermal infiltrate. There was no recurrence of skin rash in 1-year follow-up thereafter.

Erythema multiforme is an acute, self-limited and sometimes recurring skin condition considered to be a hypersensitivity reaction associated with certain infections (e.g. herpes simplex virus, *Mycoplasma pneumoniae*, fungal infection, varicella zoster virus, hepatitis C, cytomegalovirus and human immunodeficiency virus etc.) and medications [e.g. barbiturates, hydantoins, nonsteroidal anti-inflammatory drugs, penicillins, phenothiazines, sulfonamides, candesartan cilexetil (Atacand), rofecoxib (Vioxx), metformin (Glucophage), adalimumab (Humira), bupropion (Wellbutrin) and ciprofloxacin (Cipro) etc.] (1, 2). However, it has never been associated with vancomycin. Vancomycin-induced



Figure 1. Multiple pink-red plaques (resulted from confluent target lesions) and diffuse target lesions on left forearm, in which an engorged native arteriovenous fistula was created.

hypersensitivity syndrome (i.e. drug rash with eosinophilia and systemic symptoms) with cutaneous manifestation mimicking erythema multiforme (3), 'erythema multiforme major' (now revised as Stevens-Johnson syndrome) (4, 5), and toxic epidermal necrolysis have been reported (5). To our best knowledge, however, isolated erythema multiforme to vancomycin without other systemic symptoms, as our case, has never been reported in the literatures. Clinicians should be alerted that vancomycin might induce severe delayed erythema multiforme, even after its administration for a long period up to 6 weeks. The time delay between vancomycin administration and clinical symptoms in this patient is really unusual, which may be related to immune dysregulation in uremia and dialysis patients.

*Ming-Yu Lai, MD
Division of Nephrology
Taipei Veterans General Hospital
No. 201, Sec. 2, Shih-Pai Road
Taipei 11217
Taiwan
Tel: 886 2 28757501
Fax: 886 2 28219581
E-mail: mylai@vghtpe.gov.tw;
mylai1973@yahoo.com.tw

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