Bullous Erythema Multiforme following Herpes Zoster

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Erythema multiforme is a self-limited, usually mild and relapsing exanthematic intolerance reaction of the skin that is etiologically most often related to recurrent herpes simplex virus infection. Until now, despite its increasing incidence, varicella zoster virus has rarely been considered as an etiologic agent. We herein report a case of erythema multiforme following herpes zoster.

A 52-year-old man complained of multiple targetoid lesions with central bullae which developed 1 day ago and were progressively spreading to his whole body. He had suffered from the thoracic herpes zoster along the right T11-, and T12- dermatomes for 10 days. He had no history of HSV infection. He had been intermittently taking analgesics such as acetaminophen for 1 year because of low back pain, but had no history of drug eruption due to analgesics. Histopathologic examination showed subepidermal bulla with necrotic keratinocytes and vacuolization of the basal layer. Based on the clinical morphology and the histopathologic findings, our case could be presumptively diagnosed as a bullous erythema multiforme following herpes zoster. (Ann Dermatol 15(3) 116~118, 2003).

Key Words : Erythema multiforme, Herpes zoster

Erythema multiforme (EM) is an acute, self-limited syndrome with distinctive skin lesions with or without mucosal lesions[1]. It is usually associated with herpes simplex virus (HSV) infection, some drugs, and radiation therapy. Varicella zoster virus (VZV) has been rarely considered an etiologic agent. The pathogenic mechanism of EM is a cell-mediated immune reaction in which cytotoxic effector T cells destroy the keratinocytes expressing HSV-antigen or viral polymerase. HSV and VZV are the same members of herpes virus family. Considering the structural similarities between these viruses, we could assume that VZV could also be an etiologic agent of EM. Furthermore, there have been several reports in which VZV is a causative agent of EM[2-4]. We present a case of herpes zoster-associated bullous EM, where widely spreading targetoid skin lesions began to appear 10 days after the preexisting thoracic herpes zoster had developed.

Received January 4, 2003
Accepted for publication May 9, 2003
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CASE REPORT

A 52-year-old man presented with multiple targetoid skin lesions with a central bulla, which began to develop 1 day before being referred to us and were spreading over the whole body. He had suffered from the thoracic herpes zoster along the right T11-, and T12- dermatomes, 10 days before the onset of these targetoid lesions and had initially been treated with oral acyclovir for 3 days at a local clinic. The newly developed lesions were outside the affected dermatomes (Fig. 1A). When he was admitted to our hospital, he began to be treated with intravenous acyclovir because of the possibility of disseminated herpes zoster. However, during intra-

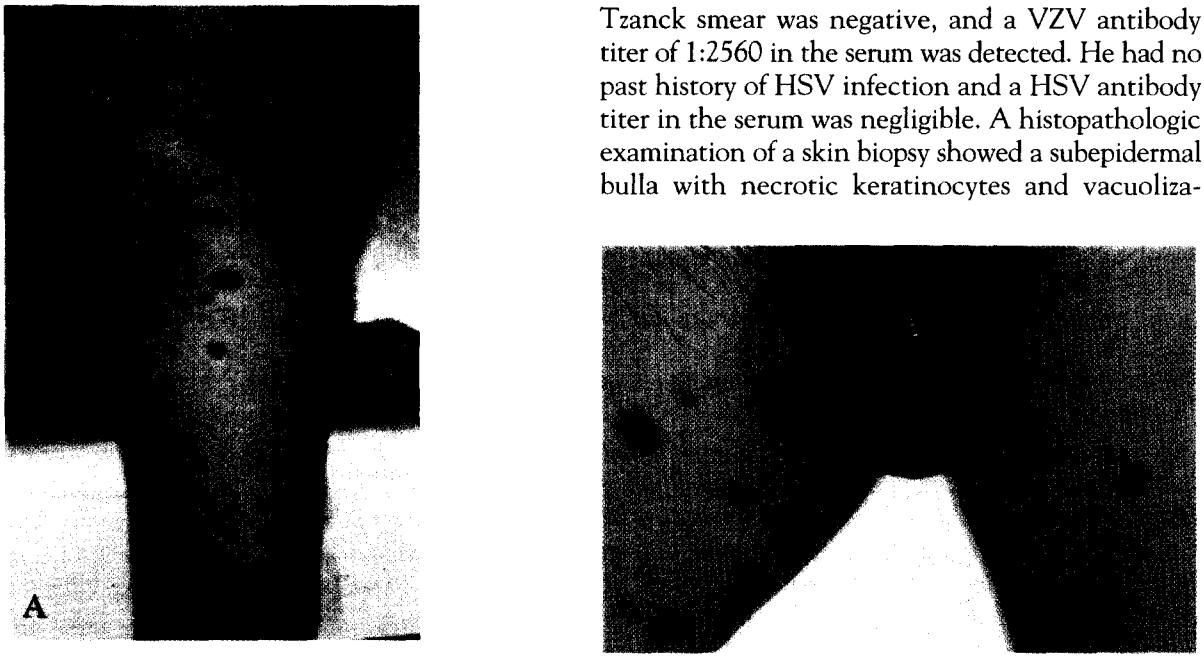

Fig. 1. Multiple erythematous papulo-vesicular lesions sparing the right T11- and T12- dermatomes affected by herpes zoster (A), symmetrically distributed, multiple, targetoid bullae on both thighs and diffuse scrotal erosions (B).

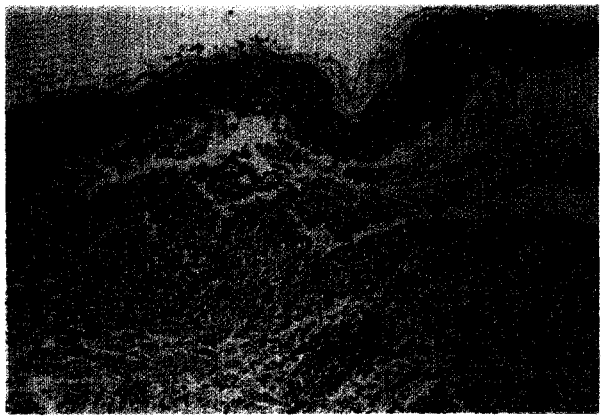

Fig. 2. The histopathologic examination showing a subepidermal bulla with necrotic keratinocytes and vacuolization of the basal layer. (H&E, ×200).

venous acyclovir treatment, the lesions continued to spread from the face to the trunk, to the extremities, with their symmetrical distribution and even to the oral mucosa, and the scrotum (Fig. 1B). The bullae were easily ruptured. To exclude the possibility of drug-induced bullous eruption, he was instructed to withdraw all medications including the intravenous acyclovir and the oral acetaminophen. However, the lesions were still spreading. The Tzanck smear was negative, and a VZV antibody titer of 1:2560 in the serum was detected. He had no past history of HSV infection and a HSV antibody titer in the serum was negligible. A histopathologic examination of a skin biopsy showed a subepidermal bulla with necrotic keratinocytes and vacuolization of the basal layer (Fig. 2). Based on the clinical morphology and the histopathologic findings, our case was considered as a bullous EM following herpes zoster, although we could not totally exclude the possibility of drug-induced EM. Systemic steroid was administered to reduce the progressive inflammation. The patient received oral prednisolone 40mg daily for 3 days, and then 20mg daily for 5 days. EM lesions were resolved over the next 2 weeks. We recommended the scratch/patch test or provocation by acyclovir and acetaminophen, but they were not performed because of patient's refusal. There has been no recurrence of similar skin lesions during the 3-month follow-up period.

DISCUSSION

EM is a disease spectrum that comprises a group of acute self-limited, cell-mediated immune reactions. Although a vast number of factors have been reported to cause EM, only three causative agents have been reasonably well documented; HSV, mycoplasma, and drugs[1]. HSV-1 and HSV-2 are closely related to EM, but VZV has rarely been considered as an etiologic agent, despite its in-

creasing incidence. In a few reported cases[2-4], VZV has triggered EM clinically following varicella in a child and herpes zoster in an adult, and they were almost all treated with acyclovir. Herpes zoster appears to play a role similar to that of herpes simplex infection in triggering EM, 1 to 2 weeks after the viral infection or reactivation[3]. Our patient presented with bullous EM, which was preceded by thoracic herpes zoster. HSV- or mycoplasma-associated EM could be excluded because there was neither clinical nor serological evidence of HSV or any other infection such as mycoplasma pneumonia. In this case, the possibility of drug-associated EM was not favored because there was no causal relationship between the clinical outcome and the used drugs (acetaminophen and acyclovir). It is strongly supported by the fact that the targetoid skin lesions were progressively and severely spreading despite the withdrawal of all medications. Furthermore, it is unlikely that acetaminophen was the causative drug because our patient had been already intermittently taking it for 1 year. Also we could not find any case reports of erythema multiforme or Stevens-Johnson syndrome induced by acyclovir in the literature. As in other previous reports, our patient showed an increased serum VZV antibody level. Based on these findings, this case could be diagnosed as bullous EM following herpes zoster. Our case is unique in that our patient was not responsive to acyclovir, but was responsive to systemic steroid. Along with other reports, this case suggests that VZV be included in the possible causative agents of EM.

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