

LETTER TO THE EDITOR

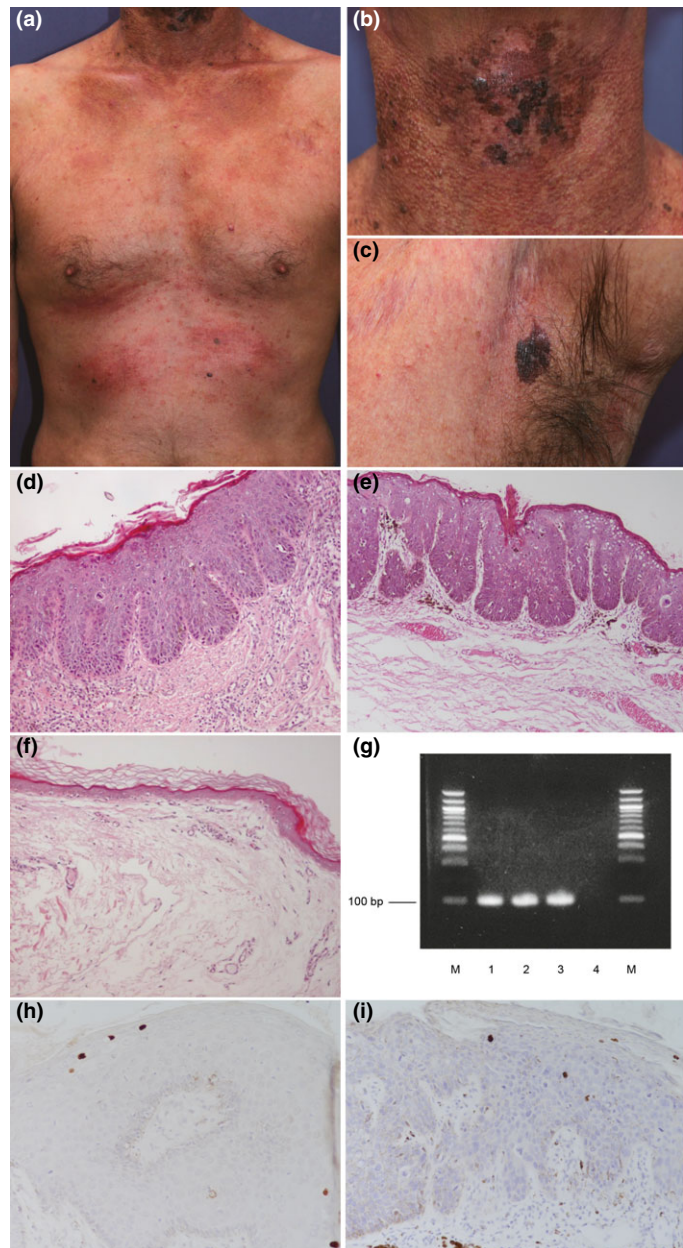
Case of multiple Bowen diseases associated with human papillomavirus type 16 in a patient with atopic dermatitis

Dear Editor,

Genital Bowen disease (BD) is known to be associated with high-risk types of human papillomavirus (HPV) infection, and

HPV may also be associated with extragenital BD.¹ Here, we report a case in which a patient with atopic dermatitis (AD) developed multiple HPV type 16-associated extragenital BD

Figure 1. (a) Eczematous lesions were seen on the patient's trunk and arm. (b) Multiple, brown, slightly raised plaques were present on the patient's neck. (c) A brown plaque developed on the patient's axilla. (d,e) Histological findings. In the (d) neck and (e) axillary lesions, atypical keratinocytes were irregularly distributed throughout the epidermis, and single cell keratinization, hyperchromatic nuclei and the clumping of nuclear chromatin were also seen. There were many melanophages within the dermis. No koilocytosis was observed (hematoxylin–eosin [HE], original magnification $\times 100$). (f) The normal skin adjacent to the Bowen disease (BD) lesions exhibited marked atrophication (HE, $\times 100$). (g) Agarose gel electrophoresis of the PCR products with a pair of primers specific for human papillomavirus (HPV) type 16. M, 100-bp ladder marker; 1, positive control; 2, DNA isolated from the BD lesion on the patient's neck; 3, DNA isolated from the BD lesion on the axilla; 4, negative control. A positive band of 96 bp was detected in lanes 2 and 3 as well as in the positive control. (h,i) Immunohistochemical examination with a mouse monoclonal anti-HPV antibody (clone K1H8, DAKO, Kyoto, Japan). Several positive cells with nuclear staining were observed in the upper malpighian layer in the (h) neck and (i) axillary lesions ($\times 200$).



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lesions. The lesions developed on the patient's atrophic skin, which itself was caused by long-term topical steroid therapy for AD.

A 47-year-old Japanese man was referred to our department to have his neck and axillary lesions examined. He had a more than 30-year history of AD and had mainly been treated with topical steroid ointments. He had no other diseases. A physical examination showed diffuse eczematous AD lesions on his trunk, extremities and face (Fig. 1a). In addition, multiple, brown, slightly raised plaques were noted on his neck and left axilla (Fig. 1b,c). The surrounding skin was markedly atrophic and telangiectatic. There was no similar plaque on his hands and genitalia. A histopathological examination of the neck and axillary lesions revealed that atypical keratinocytes were irregularly distributed throughout the epidermis, and the clumping cells were also seen (Fig. 1d,e). The normal skin adjacent to the BD lesions exhibited marked atrophication (Fig. 1f). Thus, a diagnosis of BD was made. There was no suspicious history of arsenic exposure. We did not test for HIV. The tumors were excised, and the resultant wounds were covered by skin grafts. No recurrence has been observed for 18 months.

The polymerase chain reaction (PCR) was performed using the GP5⁺/6⁺ primer sets to test for HPV DNA, as described previously.^{1,2} The amplified PCR products from the lesions yielded positive bands, which demonstrated a partial sequence match with HPV type 16. We confirmed this result by performing PCR with a HPV type 16-specific primer set, as described previously (Fig. 1g).³ We did not detect any β -papillomavirus DNA in BD lesions and normal skin of our patient. Immunohistochemical analysis showed positive staining for HPV in several cell nuclei at the upper malpighian layer (Fig. 1h,i).

Our case is peculiar in that HPV-associated BD lesions developed on the neck and axilla, where the skin was atrophic because of long-term topical steroid therapy. To infect the skin, HPV needs to gain access to basal keratinocytes.⁴ In many cases, it is considered that this is facilitated by exogenous microtraumas or other localized breaks in the epithelial

barrier. In our case, scratching precipitated by pruritus might have caused numerous minor traumas. Furthermore, the patient's atrophic epidermis might have allowed HPV to reach the basal layer more easily. Even if HPV reaches the basal layer, it needs to escape the host immune system to maintain an infection. However, AD patients are more susceptible to pathogens because of abnormalities in their innate immune systems, for example, they have reduced levels of antimicrobial peptides and exhibit diminished recruitment of innate immune cells to the skin and Toll-like receptor 2 defects.⁵ We consider that all of these factors contributed to the HPV infection in our case.

CONFLICT OF INTEREST: None declared.

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