Acta Derm Venereol 2014; 94: 482–483

SHORT COMMUNICATION

Detection of Human Papillomavirus Type 56 in Giant Condyloma Acuminatum

Takahiro Ishibuchi, Akira Shimizu*, Madoka Kato, Yuko Takeuchi, Kumi Aoyama, Masahito Yasuda, Ayumi Takahashi, Etsuko Okada, Sei-ichiro Motegi, Hiroo Amano and Osamu Ishikawa

*Department of Dermatology, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan. *E-mail: ashimizu@med.gunma-u.ac.jp*

Accepted Sep 3, 2013; Epub ahead of print Nov 28, 2013

Giant condyloma acuminatum (GCA) is a cauliflower-like condyloma acuminatum. Low-risk human papillomavirus (HPV) infection, such as that of HPV types 6 or 11, is associated with the disease (1). HPV type 56 is a high-risk HPV type that is sometimes detected in skin tumours (2). In particular, nail Bowen's disease presenting with longitudinal melanonychia has been reported to be frequently associated with HPV type 56 (2–4). We herein report a case of multiple giant condylomata acuminata in the groin and scrotum caused by high-risk HPV type 56 infection.

CASE REPORT

A 54-year-old man noted a small nodule on the right groin 6 years previously that had slowly increased in both size and number. The patient had neither a significant past medical history nor a significant family history. A physical examination revealed multiple cauliflower-like nodules in his right groin and scrotum. We suspected GCA and performed a skin biopsy. A histopathological examination revealed marked hyperkeratosis, parakeratosis and papillomatosis. Koilocytosis was seen in some areas without nuclear atypia. Routine laboratory tests revealed no abnormalities. Antibodies against HIV, HCV and HBV were negative. The patient was diagnosed as having GCA. Some of the tumours were surgically excised, while the others were resected using carbon dioxide laser ablation under general anaesthesia.

Formalin-fixed and paraffin-embedded tissue samples were cut into 10-μm sections. After obtaining informed consent, DNA was extracted from the sections using Dexpat® (Takara, Kyoto, Japan). The method and PCR conditions used have been previously described (2). HPV PCR was performed with the $GP5^+/GP6^+$ consensus primers (5). The PCR products were purified and cloned into a pGEM®-T Easy vector (Promega, Madison, WI, U.S.A.) and transfected into *Escherichia coli*. The PCR products cloned into the vectors were sequenced with an automated sequencer. DNA extracted from bowenoid papulosis of another patient was used as a control, in which HPV type 16 was detected (2).

The amplified PCR products were electrophoresed on 2% agarose gel, and a PCR band was seen at the expected position of 140 bp. DNA sequencing revealed that the sequences corresponded to the L1 gene of HPV 56 (GenBank: X74483.1) (data not shown).

HPV-56-positive cells with nuclear staining were observed in the upper epidermis and stratum corneum of the lesion on *in situ* hybridisation (Fig. 1a). Furthermore, HPV immunohistochemistry revealed that the viral proteins were localised in the upper epidermis and stratum corneum (Fig. 1b).

DISCUSSION

HPV type 56 was reported as a new type of HPV in 1989 and belongs to the high-risk group (6). HPV type 56 is sometimes found in invasive cancers of the cervix and cervical intraepithelial neoplasia. Recently, we demonstrated a relatively high prevalence of HPV type 56 infection in patients with Bowen's disease and a close association between HPV type 56 and Bowen's disease with longitudinal melanonychia (2, 4). We also previously reported a case of an HPV type 56-positive lesion in the groin that exhibited deeply pigmented keratotic plaques (4). There have been several reports

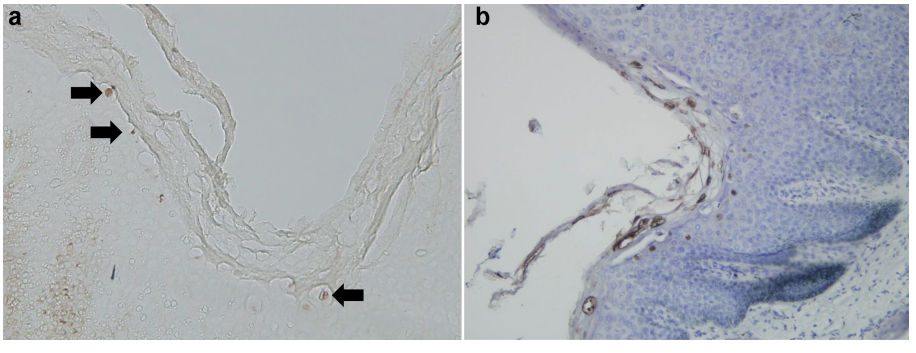

Fig. 1. Demonstration of human papillomavirus (HPV) in the lesion. (a) HPV DNA was detected in the nuclei of the epithelium on *in situ* hybridisation (⬆). The catalysed signal amplification method (GenPoint System; Dako, Kyoto, Japan) was used. The probe was a biotinylated high-risk HPV probe cocktail (GenPoint HPV; Dako) that contained type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 HPV DNA. (b) Immunohistochemistry using an anti-HPV antibody (K1H8; Dako) demonstrated HPV capsid proteins in the epithelium. Original magnification × 100.

 doi: 10.2340/00015555-1755
 ISSN 0001-5555

of skin lesions in which HPV type 56 was detected; however, all of these cases involved Bowen's disease (3, 7–9). Low-risk HPVs such as HPV types 6 and 11 are usually detected in patients with condyloma acuminatum. However, other HPVs, including intermediate- and high-risk HPVs such as HPV types 2, 16, 18, 30–33, 35, 39, 41–45, 51–56 and 59, have been detected in patients with condyloma acuminatum (1). To the best of our knowledge, this is the first case of GCA caused by HPV type 56.

GCA is also called GCA of Buschke and Löwenstein and is recognised to be one type of verrucous carcinoma, along with verrucous carcinoma of the oral cavity and plantar verrucous carcinoma (10). Our case did not show the clear downward proliferation characteristic of GCA of Buschke and Löwenstein. Therefore, we did not diagnose the patient with GCA of Buschke and Löwenstein, but rather with multiple giant condylomata acuminata.

Condyloma acuminatum usually manifests as multiple exophytic papillomatous lesions; however, several unusual clinical manifestations have been reported, i.e. condylomata acuminata with pigmented papular lesions (11), pigmented plaque-type condyloma acuminatum (12) and GCA of Buschke and Löwenstein. Why our patient developed multiple giant tumours is unclear; however, infection with high-risk HPV type 56 may partly account for this phenomenon.

REFERENCES

1. Grayson W. Infectious diseases of the skin. In: Calonje E, Brenn T, Lazar A, Mckee P, editors. Mckee's skin pathology with clinical correlations. 4th ed. Tront: Elsevier; 2012. p. 760–895.
2. Shimizu A, Tamura A, Abe M, Motegi S, Nagai Y, Ishikawa O, et al. Detection of human papillomavirus type 56 in Bowen's disease involving the nail matrix. Br J Dermatol 2008; 158: 1273–1279.
3. Lambiase MC, Gardner TL, Altman CE, Albertini JG. Bowen disease of the nail bed presenting as longitudinal melanonychia: detection of human papillomavirus type 56 DNA. Cutis 2003; 72: 305–309.
4. Shimizu A, Tamura A, Abe M, Amano H, Motegi S, Nakatani Y, et al. Human papillomavirus type 56-associated Bowen's disease. Br J Dermatol 2012; 167: 1161–1164.
5. de Roda Husman AM, Walboomers JM, van den Brule AJ, Meijer CJ, Snijders PJ. The use of general primers GP5 and GP6 elongated at their 3' ends with adjacent highly conserved sequences improves human papillomavirus detection by PCR. J Gen Virol 1995; 76: 1057–1062.
6. Lorincz AT, Quinn AP, Goldsborough MD, McAllister P, Temple GF. Human papillomavirus type 56: a new virus detected in cervical cancers. J Gen Virol 1989; 70: 3099–3104.
7. Inokuma D, Aoyagi S, Saito N, Iitani MM, Homma E, Hamasaka K, et al. Bowen's disease of the nail matrix presenting as melanonychia: detection of human papillomavirus type 56. Acta Derm Venereol 2009; 89: 638–639.
8. Ohishi K, Nakamura Y, Ohishi Y, Yokomizo E, Ohara K, Takasaki M, et al. Bowen's disease of the nail apparatus and association with various high-risk human papillomavirus types. J Dermatol Sci 2011; 63: 69–72.
9. Uezato H, Hagiwara K, Maruno M, Ramuzi ST, Khaskhely NM, Oshiro M, et al. Detection of human papilloma virus type 58 in a case of a perianal Bowen's disease coexistent with adult T-cell leukemia. J Dermatol 1999; 26: 168–173.
10. Xiaowei Xu EL, Chen L, Elder DE Lever's histopathology of the skin. 10th ed. Elder DE ER, Bernett L, Johnson J, Murphy GF, Xiaowei Xu, editors. Philadelphia: Lippincott Williams & Wilkins; 2005.
11. Kimura S. Condylomata acuminata with pigmented papular lesions. Dermatologica 1980; 160: 390–397.
12. Shimizu A, Tamura A, Nakatani Y, Shimizu N, Hoshino H, Ishikawa O. Pigmented plaque-type condyloma acuminatum associated with human papillomavirus type 6. J Dermatol 2012; 39: 860–861.