

RESEARCH NOTE

Unusual HPV Types in Cutaneous Warts in Association with Immunological Deficiency

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There are now at least 70 known types of human papillomaviruses (HPV). Historically they have been grouped according to the location of the lesions, thus the terminology mucosal types (including HPV infecting the genital and the respiratory tracts) and cutaneous types (including HPV causing cutaneous warts and epidermodysplasia verruciformis - EDV). The different HPV types present diverse oncogenic potential and data have accumulated to support a role for mucosal HPV in cervical cancer. Genital HPV 16, 18, 31, 33 and 35 represent the high risk viruses associated to malignancy while HPV 6 and 11 have been predominantly found in benign genital lesions. In cutaneous lesions, HPV 1 and 2 are related to common warts while HPV 5 and 8 are associated to EDV (EM de Villiers 1994 *Curr Topics Microbiol Immunol* 186: 1-12). Thus, HPV typing predicts partially the site of the infection, the pathological features and the clinical course of the infection.

This study was undertaken to determine the HPV types infecting cutaneous warts of two immunodeficient patients attended at Hospital Santa Casa de Misericórdia, Rio de Janeiro, Brazil. Patients presenting multicentric cutaneous and genital warts were biopsied. Both cases were clinically and histologically diagnosed as typical HPV-induced verrucae. Samples were analyzed by using non-isotopic *in situ* hybridization (NISH) kit from

Createch Diagnosis (Holland) to detect HPV types 1, 2, 6, 11, 16, 18, 31, 33 and 35, which is described in detail by SMB Cavalcanti et al. (1994 *Mem Inst Oswaldo Cruz* 89: 575-580). The kit included HPV positive and negative tissue biopsies that were used as controls in every experiment. Positive tissues for HPV1 (skin verrucae), HPV 6 and HPV 16 (cervical condyloma) were also used as controls.

Patient 1 was a 30 years old man, presenting one-year long verrucous lesions extending from right hand to pubis and anal region. NISH revealed HPV types 31, 33 and 35 in five tested biopsies (two from the right hand, one from the pubis and two from the anal region). HPV 6 and 11 were detected in the anal biopsies. Neither HPV 1 nor HPV 2 were detected. This patient was infected by HIV and presented AIDS-related complex.

Patient 2 was a 39 years old man, presenting four-year long cutaneous warts in hands and feet, where lesions were both dorsal and plantar. Genital lesions were not detected. Three samples (right hand and dorsal/plantar left foot) were analyzed by NISH. High risk HPV 16 and 18 were detected in all the samples. HPV 6 and 11 were also demonstrated in the left foot plantar wart. HPV 1 and 2 were not found. This patient presented T-cell inherited cellular immunodeficiency characterized by a partial suppression of these cells, revealed by flow cytometry.

Immunological restriction in healthy patients seems to represent an important condition to the maintenance of specific HPV types in different body sites and to the spontaneous regression of HPV-induced lesions. The appearance of HPV types usually associated to genital infection and cancer in cutaneous warts may reflect the immunological failure of the body defense system, leading to persistent lesions. Genital HPV types have only exceptionally been reported in extragenital locations: invasive carcinoma of the fingers (RL Moy et al. 1989 *JAMA* 261: 2669-2673), Bowen's disease of the foot (MS Stone et al. 1987 *Arch Dermatol* 123: 1517-1520) and Bowenoid Papulosis of the face (JJ Grob et al. 1991 *Genitourin Med* 67: 18-20).

Since an epidemiological study was not performed, the source of the infection was not determined. The presence of associated genital lesions in patient 1 suggests sexual transmission and spread but for patient 2 the absence of genital lesions makes this possibility unlikely. The risk of malignant progression of the lesions detected in both patients can not be excluded since oncogenic HPV types have been detected. Besides, the immunodeficiency condition related may cooperate to neoplastic transformation of the skin. As described by

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GYF Ho et al. (1994 *Int J Cancer* 56: 788-792), the depression of cell-mediated immunity described for renal transplant recipients and HIV-infected patients are important risk factors for the development of HPV-related malignant carcinomas.

Our study describes the occurrence of HPV infection of the skin caused by genital types in-

stead of the usual skin HPVs 1 and 2. It is interesting to note that the HPV types detected by NISH are related to persistence and progression to cancer. These unusual infections may be attributed to immunological impairment and have to be considered in the management of immunodeficient patients, due to its oncogenic potential.