Human papillomavirus type 59 identified in a verrucous cyst of the flank

The verrucous cyst is a non-plantar epidermoid cyst with histopathological features of human papillomavirus (HPV) infection, including papillomatosis and hypergranulosis of the cyst lining. We report the first case of a verrucous cyst demonstrating not only the histopathological and immunohistochemical features of HPV infection, but also homology with HPV type 59 on HPV genotyping. A 28-year-old male developed a palpable mass in his right flank. Histological examination revealed an intradermal cyst lined by an acanthotic and papillomatous squamous epithelium with prominent keratohyaline granules and squamous eddies. The keratinocyte nuclei were positive for papillomavirus antigens on immunohistochemistry and HPV genotyping demonstrated a homology to HPV type 59, a high-risk genital type. Although we only experienced a single case with such a finding, we suggest that it may be necessary to subject patients with verrucous cysts to a closer follow up for better characterization of their clinical behavior.

Key words: epidermoid cyst, human papillomavirus 59, verrucous cyst
minutes on ice. The samples were mixed with a hybridization solution made of 6X SSPE (saline-sodium phosphate-EDTA buffer; Sigma Chemical Co, St Louis, MO, USA) and 0.2% sodium dodecylsulfate, and applied to the DNA chip. Hybridization was performed at 40°C for 2 hours and then washed with 3X SSPE for 2 minutes, 1X SSPE for 2 minutes, and air-dried at room temperature. Hybridized HPV DNA was visualized using a DNA Chip Scanner (Scanarray lite; GSI Lumonics, Ottawa, Canada). Of the 22 types of mucocutaneous HPV tested, the type 59 probe hybridized with the fragment amplified from our specimen (figure 2).

Discussion

HPV has been detected in a wide spectrum of mucocutaneous lesions, ranging from benign lesions such as verruca vulgaris to malignancies such as squamous cell carcinoma [7]. The number of diseases for which a role of HPV has been implicated is growing, and with the development of typing techniques such as in situ hybridization and polymerase chain reaction, specific HPV are being identified for
each HPV-related disease entity. Epidermoid cysts arising in the palms and soles have also been shown to harbor HPV by immunohistochemistry and molecular studies, specifically types 57 and 60 [8-13], and HPV type 60 has been identified in an epidermoid cyst of non-palmoplantar location [14]. Furthermore, HPV has been demonstrated by PCR in verrucous cysts [1, 4], a rare entity first described by Meyer et al. in 1991; however, no specific types of HPV have been identified in such cysts. Verrucous cysts differ from epidermoid cysts in the appearance of the cyst linings: acanthosis, papillomatosis, hypergranulosis with prominent keratohyaline granules, and hyperkeratosis, all being features reminiscent of HPV infection. Koilocytic changes have also been sometimes reported, although they were not seen in our case. A striking feature in our case was the presence of squamous eddies in the cyst wall, resembling those seen in typical irritated seborrheic keratoses. Interestingly, five ‘epidermoid cysts with seborrheic verruca-like cyst walls’ have been previously reported [15] and described as showing acanthotic and papillomatous cyst linings, however, neither the presence of squamous eddies nor any relation to HPV were mentioned. Clinically, they are solitary lesions resembling epidermoid cysts and appearing most commonly on the face and back. They usually occur in adult patients, in contrast to common warts which are more prevalent in children or adolescents.

The verrucous cyst seen in our case showed histopathological features of HPV infection and also positivity for HPV capsid antigens by immunohistochemistry. However, this case is unique in that HPV genotyping demonstrated a homology to HPV type 59, a finding not previously mentioned. HPV type 59 is known to be a high-risk genital type, frequently detected in anogenital lesions such as cervical intraepithelial neoplasia and condylomata acuminata [16, 17]. HPV type 59 was initially cloned from a vulvar intraepithelial neoplasia and condylomata acuminata [16, 17]. HPV type 59 was initially cloned from a vulvar intraepithelial neoplasia and has been reported to show homology with HPV types 18, 45 and 39, which are also types associated with high-risk epithelial dysplasia. The detection of HPV type 59 in condylomata acuminata has been associated with immunosuppression [18]; however, our patient had no history or laboratory findings suggestive of immunosuppression.

Other than HPV-associated verrucous cysts and plantar epidermoid cysts, HPV has also been demonstrated in a verrucous trichilemmal cyst [6], and there are a few reports of papillomavirus occurring in epidermoid cysts in the literature [19, 20]. The pathogenesis of cutaneous cysts associated with viral infection still remains obscure, however, it is postulated that the cysts may be induced by the virus de novo, or that the virus may infect pre-existing cysts [3-6]. Mechanical inclusion of HPV-containing epithelium into the dermis of weight-bearing areas has been suggested as a possible explanation for plantar epidermoid cysts [8, 9, 13], but this seems less likely to be the mechanism for cysts arising in non-plantar locations. Localization of the virus in the follicular ostia with subsequent obstruction and cyst formation, and epidermoid metaplasia of HPV-infected eccrine ducts have also been proposed as possible mechanisms for palmoplantar epidermoid cyst formation [21].

More than 10 years have elapsed since the verrucous cyst was first described in the literature [1], and although this may be an underreported entity, there have been no reports up to date implicating an aggressive behavior for these cysts, despite the proliferative features in the cyst walls which may appear alarming. However, as HPV type 59 is known to fall into the high-risk group in anogenital lesions, and as persistent infections of the skin with high-risk genital HPV types have been reported to represent a risk factor for non-melanoma skin cancer in non-immunosuppressed individuals [22], we suggest that it may be necessary to educate these patients about self-examination and to perform thorough in-office physical examinations on a regular basis for a better characterization of its clinical behavior.

References


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The European Union of Medical Specialists (Union Européenne Médecins Spécialistes = UEMS) / Section of Dermato-Venerology and Section of Pathology will organize under the auspices of the International Committee for Dermatopathology the 4th International Board Certifying Examination in Dermatopathology (Diploma in Dermatopathology) in Frankfurt/Main, Germany, on December 2, 2006.

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For further information about this examination, please contact:
Helmut KERL, M.D. or Lorenzo CERRONI, M.D.
Department of Dermatology
Medical University of Graz
Auenbruggerplatz 8
A-8036 Graz / Austria
Ph.: + 43-316-385-2538
Fax: + 43-316-385-3424
e-mail: helmut.kerl@meduni-graz.at

or

Lorenzo CERRONI, M.D.
Department of Dermatology
Medical University of Graz
Auenbruggerplatz 8
A-8036 Graz / Austria
Ph.: + 43-316-385-2423
Fax: + 43-316-385-2466
e-mail: lorenzo.cerroni@meduni-graz.at