HPV 16-Positive Bowenoid Papulosis and Squamous-Cell Carcinoma of the Anus in an HIV-Positive Man

RENE RÜDLINGER, M.D., PETER BUCHMANN, M.D.


A homosexual man in stage IV of HIV infection, who suffers from HPV 16-positive Bowenoid papulosis of the anal region, is described. In one area the patient developed an HPV 16-positive squamous-cell carcinoma of the anus. Bowenoid papulosis represents a squamous-cell carcinoma in situ, and usually follows a benign clinical course. The possibility exists that immunocompromised individuals are at higher risk to develop cancer on the basis of Bowenoid papulosis.

[Key words: Bowenoid papulosis; Anal cancer; Human papilloma viruses; HIV infection]

Bowenoid papulosis is a recently recognized disease of the anogenital area of young men and women, which includes a wide spectrum of clinical features, including lichenoid pink or reddish brown papules and macular erythematous or leukoplakialike lesions. Bowenoid papulosis is usually a multifocal disease. Histologically, it is indistinguishable from Bowen’s disease. Bowenoid papulosis has been shown to be associated with various HPV types (HPV 16, 18, 34, 39). HPV 16 being the most common.

The natural history of Bowenoid papulosis is not entirely clear. Our experience is that persistence and new lesion formation over many years is a common feature in women (unpublished results). Spontaneous regression has been noticed occasionally and was seen in four of six of our male patients. Development into invasive cancer has been reported rarely and only so in women. Epidemiologic and virologic studies have established that Bowenoid papulosis and other anogenital HPV infections can be sexually transmitted. We report the case of a 34-year-old HIV positive homosexual man with HPV 16-positive Bowenoid papulosis of the anal region with concurrent HPV 16-positive squamous-cell carcinoma of the anus.

Materials and Methods

Patient History: This 34-year-old homosexual man, a heavy smoker (1 pack per day), was diagnosed as HIV-positive two years ago. When first seen for his anal problem, he was in stage IV of HIV infection (Kaposi’s sarcoma). The patient complained of pain and the frequent unanswerable urge to defecate and had noticed nodules in the perianal region. Examination revealed multiple flat papules and circular brown-blackish pigmentation of the perianal and anal regions, which was reminiscent of Bowenoid papulosis. One area raised suspicion of invasive growth on clinical grounds already (Fig. 1). The lesions were removed by scissor excision and biopsy specimens were bisected; half underwent histologic examination and half virologic analysis. Four months later a recurrence was removed surgically.

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Address reprint requests to Dr. Rüdlinger: Dermatologie USZ, CH 8091 Zürich, Switzerland.
FIG. 1. Bowenoid papulosis, clinical: multiple, mostly pigmented, some whitish papular and macular lesions of the perianal area. Arrow indicates squamous-cell carcinoma.

**Histology:** Biopsies were routinely fixed in formalin, in embedded paraffin, and stained with hematoxylin and eosin. Immunohistochemical staining for papillomavirus group specific common antigen was performed according to the manufacturer's specifications (Dako, Glostrup, Denmark).

**Virology:** In brief, total cellular DNA was extracted from snap frozen unfixed biopsies by proteinase K digestion (Boehringer), followed by phenol chloroform extraction. Five to 10 μg of total cellular DNA were RNAase treated, Pst 1 digested, and underwent electrophoresis on a 1% horizontal agarose gel. DNA was denatured, capillary blotted, and sequentially hybridized at Tm −35°C to 32PdCTP labeled, cloned HPV 6/11, 16, 18, 31, 33, 34, and 35 DNA,7,16−22 washed under low stringent conditions (Tm −35°C), exposed to radiographic film, then rewashed under conditions of high stringency (Tm −15°C) and exposed again.

**Results**

**Histologic:** The specimens taken from 7 and 12 o'clock displayed the classic features of Bowen's disease with acanthosis of the epidermis, due to elongation and thickening of the rete ridges, focal parakeratosis, and atypical squamous cells throughout the whole thickness of the epithelium (Figs. 2 and 3). In addition to changes of Bowen's disease, koilocytosis was present in some areas. The specimen from 4 o'clock displayed multiple polycyclic masses in the dermis, which were composed of typical as well as numerous atypical squamous cells. Here, the diagnosis of squamous-cell carcinoma was made (Fig. 3) Staining for papillomavirus common antigen was negative in all three specimens.

**Virologic:** Southern blot analysis of Pst 1 digested total cellular DNA revealed the presence of HPV 16 DNA in all three specimens (Fig. 4).

**Discussion**

Epidemiologic and virologic data have established a firm association between genital cancer and the presence of the DNA of specific papillomavirus types, mainly HPV 16 and 18.23,24 It is recognized, however, that the presence of certain HPV types such as HPV 16 alone does not suffice for an epithelium to become malignant. This has been demonstrated for HPV-positive cervical intraepithelial neoplasia, which does not necessarily progress into carcinoma.25 The question therefore arises: What factors other than HPV infection influence the course of HPV-associated disease? Among other causes, cigarette smoking has been discussed in this respect. Disorders of the (cellular) immune system lead to an increased susceptibility to papillomavirus-induced tumors and epithelial cancer. This is well known for immunocompromised renal transplant recipients26−30 and recently has been shown for cervical HPV infection in renal allograft women.31 The natural history of anal, as opposed to genital,