Human Papillomavirus Type 16-associated Periungual Squamous Cell Carcinoma in a Patient with Acquired Immunodeficiency Syndrome

Sir,

In the last few years, human papillomavirus (HPV) type 16 has been detected in numerous cases of Bowen's disease and squamous cell carcinoma (SCC) of the periungual region in immunocompetent individuals (1). This suggests an important role of HPV-16 in the development of SCC at this site. In all these cases the molecular hybridization techniques for the detection of HPV-DNA were used, but only twice on polymerase chain reaction (PCR)-amplified material (1, 2).

We here report the case of a young patient with AIDS who developed a periungual SCC. A PCR assay made it possible for us to detect the presence of HPV-16 DNA on paraffin-embedded tissue specimens of the tumour.

CASE REPORT

A 28-year-old white man with multiple relapsing periungual warts, which had been present for about 2 years, was referred to us because in the last few months a lesion on his right thumb had gradually enlarged and spread to involve the subungual region. The history revealed that the patient, who was a drug addict, had been discovered to be seropositive for HIV-1 in 1985. In 1990 he had spent 3 weeks in an infectious disease unit for a pneumonic infection due to *Pneumocystis carinii*. Since that time he had been taking zidovudine. At the time of our examination the laboratory data included a very low blood cell count: leucocytes $3.1 \times 10^3/mm^3$, erythrocytes $3.73 \times 10^6/mm^3$ and platelets $187 \times 10^3/mm^3$. There was a depletion of CD4 (25%) and a relative increase of CD8 (58%) T-lymphocytes with a CD4/CD8 ratio of 0.43. Total T-lymphocytes numbered $890/mm^3$.

Physical examination revealed a verrucous growth involving the ulnar portion of the right thumb. The tumour, which extended from the proximal and lateral nail fold to the distal portion of the nail bed, had destroyed the overlying nail plate. The proximal nail fold showed mild erythema and swelling. Multiple periungual warts were evident on the proximal and lateral nail folds of the 1st, 2nd, 3rd and 4th finger of both hands (Fig. 1). The patient had no clinical evidence or history of genital warts. A roentgenography of the finger was normal.

A skin biopsy from the right thumb revealed an early invasive SCC. A skin biopsy from the lateral nail fold of the 2nd right finger confirmed the diagnosis of a wart. The tumour was widely excised, and the defect was repaired with a split-skin graft. There was no follow-up, as we lost communication with the patient.

Histologic examination showed a squamous keratinocyte proliferation characterized by irregular acanthosis and elongation of the rete ridges associated with marked keratinocyte atypia and plemorphism. Dyskeratotic cells and numerous mitoses were scattered throughout the entire thickness of the neoplasm (Fig. 2). In some areas, features resembling a verruca vulgaris were also detectable, namely clumped coarse keratohyalin granules, vacuolated cells, multiple vertical layers of parakeratotic cells and prominent dilated capillaries. The dermis showed prominent papillomatosis of the papillary dermis and a sparse lympho-histiocytic infiltrate. The pathological picture was consistent with an early invasive SCC involving the nail bed and the lateral nail fold. Sections (10 μm) of the paraffin-embedded tissue block from the periungual SCC were analyzed for the presence of HPV-DNA sequences with PCR amplification. Amplification products were analyzed by dot blot hybridizations with digoxigenin-labelled internal probes specific for HPV types 6, 11, 16, 18, 31, 33 (3). A positive result was found for HPV type 16 (Figs. 3, 4).

DISCUSSION

Our patient developed the tumour from a pre-existing wart, and multiple warts were also present at the nail folds of all the other fingers. Immunocompetent patients with periungual SCCs frequently have a history of pre-existing warts at the site of the developing tumour. However, the presence of HPV-16 DNA in most subungual SCCs suggests that infection with this particular type of HPV may have, as in the genital tract, a fundamental role in the development of malignancies in the periungual region. A possible transmission of HPV-16 from the anogenital region to the fingers has also been postulated by several authors (4, 5).

According to Daniel III and colleagues an SCC of the nail bed in a young adult raise the suspicion of HIV infection (6). The reasons that make HIV-positive patients susceptible to the de-

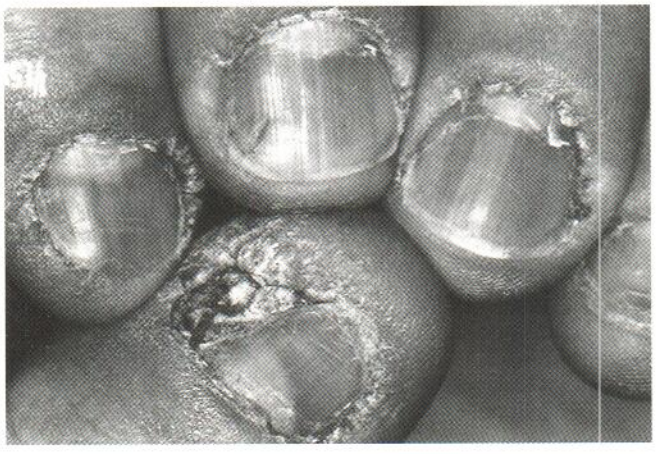

Fig. 1. Brown verrucous growth covering the lateral nail fold and nail bed of the right thumb. Small periungual warts are present on the proximal and lateral nail folds of all the fingers on the right hand.

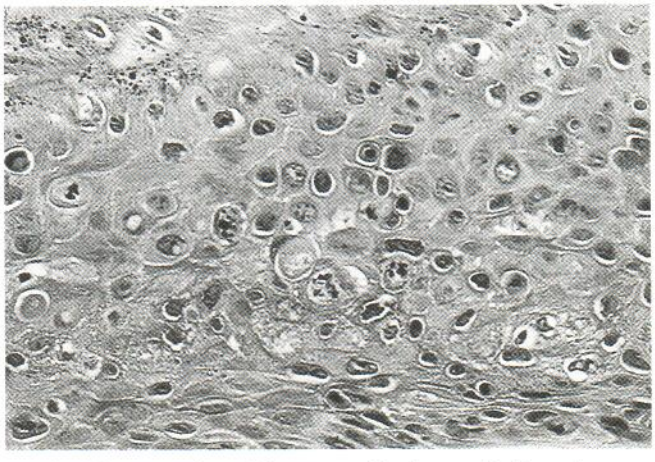

Fig. 2. High-power view of the tumour showing atypical keratinocytes, dyskeratotic cells and numerous mitoses involving the entire thickness of the neoplasm H&E: original magnification ×250).

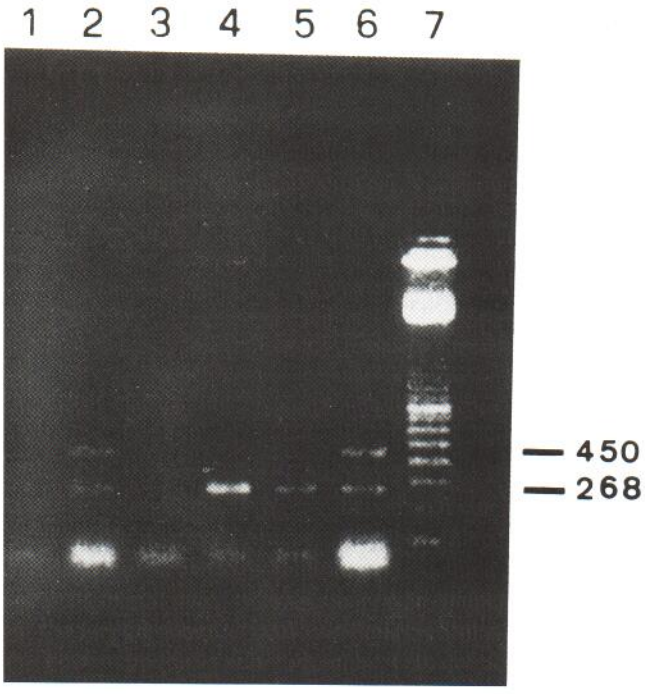

Fig. 3. Agarose gel electrophoresis of the PCR products on subungual carcinoma DNA and controls. *Lanes 1 and 3*: negative controls (distilled water). *Lane 2*: subungual carcinoma DNA. *Lane 4*: fibroblast DNA. *Lane 5*: normal skin biopsy DNA. *Lane 6*: HeLa cells DNA. *Lane 7*: DNA molecular weight markers.

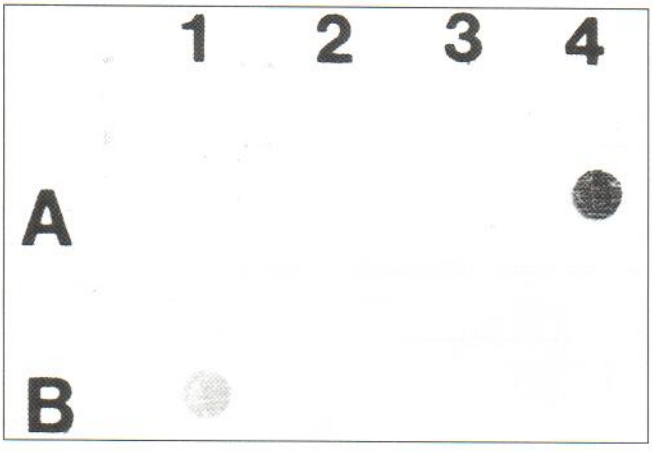

Fig. 4. Dot blot hybridization for HPV typing. *Line 1*: PCR products of subungual carcinoma DNA. *Line 2*: PCR products of fibroblast DNA. *Line 3*: PCR products of normal skin biopsy DNA. *Line 4*: PCR products of HeLa cells. *Row A*: hybridization with HPV 18 oligonucleotide probe. *Row B*: hybridization with HPV 16 oligonucleotide probe.

velopment of HPV-associated SCCs are still unclear. The possibility that SCC due to human papillomavirus may show more aggressive clinical manifestations in HIV-infected patients than in immunocompetent individuals is also under discussion (7). Immunosuppression increases the risk of developing malignancies, and AIDS with its associated immunosuppression seems to exacerbate HPV-mediated cytologic abnormalities (8, 9). An increased susceptibility to infection with HPV, together with the enhanced ability of this virus to induce malignant conversion, may therefore explain the high prevalence of HPV-associated malignancies in AIDS.

Periungual SCC should be included in the spectrum of HPV-induced tumours that frequently occur in HIV infection.

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