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Intralesional Interferon Alpha-2b Therapy for Buschke-Loewenstein Tumour

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A patient with a Buschke-Loewenstein tumour associated with human papillomavirus type 6/11 is reported. He was intralesionally treated with human recombinant alpha-2b interferon (9×10^6 IU/day) three times weekly. The tumour completely disappeared within 5 months of continuous treatment which was well tolerated. Sixteen months after completion of therapy the patient remains well and free of disease. ***Key words: condyloma acuminatum; human papillomavirus; squamous cell carcinoma; koilocytes.***

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Buschke-Loewenstein tumour is a term used to describe a rare maximal variant of condyloma acuminatum, mostly localized in the anogenital region, which has a locally aggressive course (1). Despite the originally described histological benignity of this human papillomavirus (HPV)-induced tumour, several cases with malignant transformation to frankly invasive squamous cell carcinoma have been reported (2–6).

Conventional topical therapy is ineffective, while laser treatment cannot easily reach the depth of the tumour (7, 8). Radical and often mutilating surgery is in most cases necessary; however, it is associated with a high recurrence rate (9) due to the persistence of HPV in the apparently normal surrounding skin. Thus, Buschke-Loewenstein tumour represents a frustrating therapeutic problem.

In view of the recently reported favourable therapeutic results of various forms of systemic recombinant interferon therapy in the management of resistant condylomata acuminata (10–12), we found it of interest to investigate the efficacy and safety of intralesional recombinant interferon alpha-2b in a case of Buschke-Loewenstein tumour.

CASE REPORT

A 39-year-old HIV-negative man presented at our Department with a 10-year history of a slowly growing exophytic tumour, which had been previously unsuccessfully treated with podophyllin. Physical examination was remarkable for a $8.7 \times 7.3 \times 5.6$ cm verrucous, multinodular, foul-smelling soft tumour at the left cruro-inguinal fold (Fig. 1A). Histological examination of multiple biopsy specimens obtained from various sites of the tumour revealed an excessive papillomatous proliferation of the hyper- and parakeratotic squamous epithelium (Fig. 2A). There was a focal occurrence of koilocytes at the upper epidermal layers, with no evidence of cellular atypia or stromal invasion. A mild inflammatory lymphohistiocytic infiltrate was seen in the upper corium. In situ hybridization performed on routinely formalin-fixed and paraffin-embedded specimens, using commercially available HPV-DNA probes, disclosed the presence of HPV types 6/11 (Fig. 2B). All results of routine laboratory investigations were within normal limits. X-ray, computer tomography, ultrasound, cardiological and ophthalmological investigations revealed no abnormalities.

The patient refused any form of surgical therapy. We decided then to start an intralesional interferon therapy. A written consent was obtained from the patient subsequent to a thorough explanation of the possible therapeutic effects and side-effects of the treatment. He was injected intralesionally with 9×10^6 IU human recombinant interferon alpha-2b (Intron A, Schering-Plough, Greece) three times a week. After 4 weeks of treatment, the tumour started shrinking and within 5 months a complete remission took place (Fig. 1B).

Interferon administration was generally well tolerated by the patient, who experienced occasional fever, myalgias and chills subsequent to the injection of the drug. None of these side-effects interfered substantially with the patient's daily activities. Interestingly, all laboratory variables remained unaltered during interferon administration. Sixteen months after completion of therapy the patient remains well and reveals no evidence of relapse.

DISCUSSION

Numerous therapeutic approaches have been employed over the years for the management of resistant condylomata acuminata but the optimal treatment modality has not yet been established. The pathogenesis of these HPV-induced lesions (13) makes interferon a logical therapeutic approach since this compound is capable of reducing viral replication and epithelial growth and of exerting immunomodulatory effects (14). Indeed, in recent studies systemic treatment of condylomata acuminata with interferon alpha resulted in favourable therapeutic responses ranging between 50% and 80% (15–17). In contrast to these promising findings, in a double-blind clinical trial systemic interferon alpha-2a was found to be ineffective in the treatment of recurrent condylomata acuminata (18); however, the doses applied in this investigation were low (1.5×10^6 IU three times a week) and the duration of therapy was very short (4 weeks).

To our knowledge, this is the first report of a complete remission of a Buschke-Loewenstein tumour subsequent to interferon monotherapy. Another study has demonstrated the reduction of this tumour to several pin-size lesions in response to a 6-month systemic administration of recombinant interferon alpha-2a alone (1.8×10^6 IU 5 days a week) (19), while disappointing therapeutic results of recombinant interferon alpha-2b were observed after 3 weeks of intralesional application to a patient with a Buschke-Loewenstein tumour (20). This compound has also been applied as an adjuvant therapy following CO_2 laser resection of a Buschke-Loewenstein tumour (21); however, whether the observed prevention of recurrences during the first 6 post-operative months may be ascribed to interferon action or not remains to be elucidated.

Our findings, together with the previously reported poor therapeutic response of this tumour to short-term therapy with interferon alpha-2b (20), suggest that long-term intralesional application of high doses of this compound represents an effective

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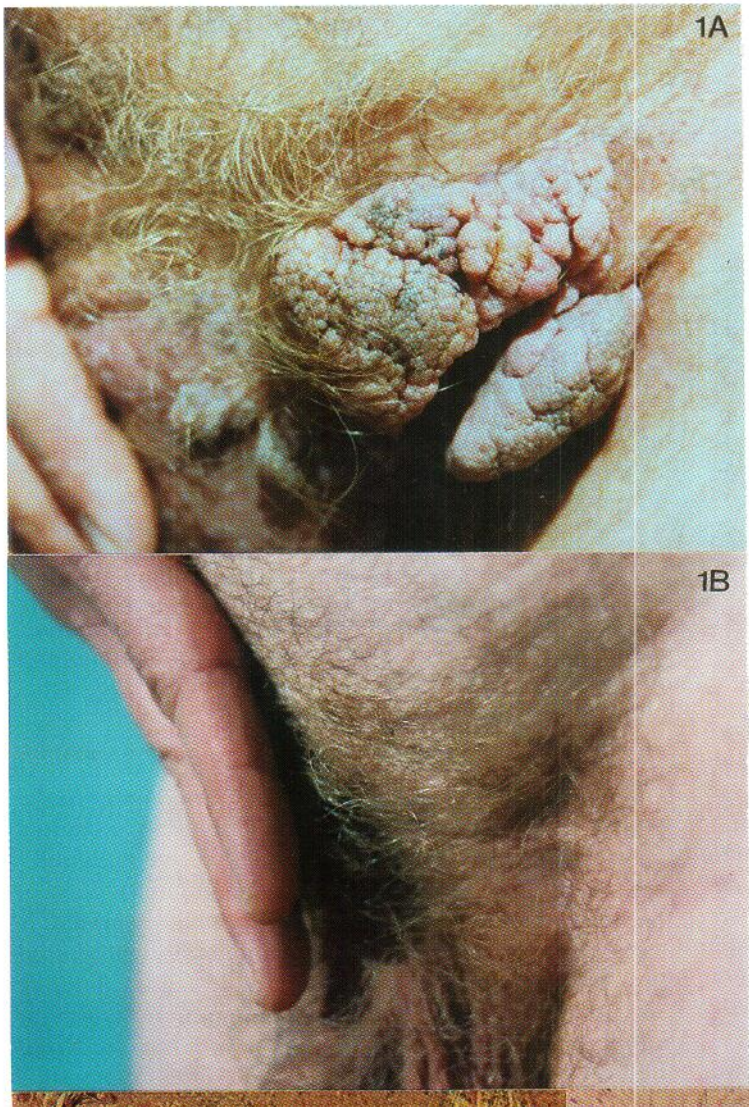

Fig. 1. Clinical presentation of Buschke-Loewenstein tumour before (A), and 5 months after (B) start of intralesional administration of recombinant interferon alpha-2b.

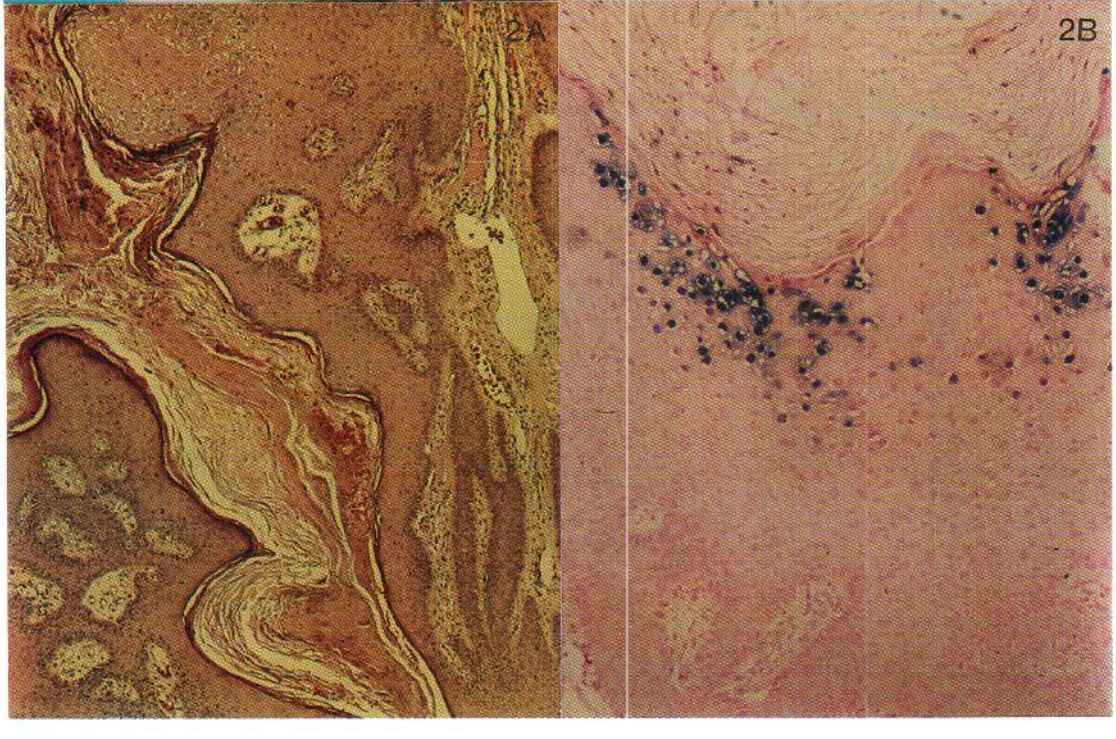

Fig. 2. A: Papillomatous proliferation, hyper- and parakeratosis of epidermis without any evidence of cellular atypia, focal occurrence of koilocytes (haematoxylin and eosin, ×30); B: In situ hybridization analysis for HPV in the Buschke-Loewenstein tumour. Detection of viral DNA by means of a biotin-labelled HPV-6/11 probe (alkaline phosphatase and counterstaining with neutral fast red, ×60).

alternative therapeutic modality for the management of Buschke-Loewenstein tumours with no malignant transformation.

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