

Immunosuppressive Drug therapy as a Potentiator of Anal Carcinoma in a Patient with Relapsing Lymphoma

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Introduction

Anal carcinoma represents 5% of the anorectal cancers, Its aetiology is linked to a number of different predisposing factors, among which the most recent and widely accepted is the Human Papilloma Virus (HPV). The multifactorial aetiology suggests that development of tumour depends on the synergy between this virus, carcinogens and the immunological status of the patient. We report a case that illustrates these points.

Case Report

A 35 year old man presented with multiple perianal skin tags for which an excision biopsy was performed. Subsequent histology revealed the presence of wide spread dysplastic change of Bowen's disease with areas of well differentiated keratinising squamous cell carcinoma. The immunoperoxidase staining for HPV was strongly positive. He was HIV negative and had stage IIa Hodgkin's disease in 1983, which was treated with upper mantle radiotherapy. Five years later he relapsed with recurrence in the liver and spleen, which was treated initially with Epirubicin, Vinblastine and Bleomycin, but due to pyrexial reactions it was changed after two courses to Chiorambucil, Procarbazine, Vincristine and Prednisolone. Seven such courses were given achieving complete remission. He had a further relapse : ear later in the middle zone of his right lung, with no evidence of disease elsewhere and received 3 courses of intensive multidrug regime chemotherapy which included Etoposide, Vinbiastine, Chiorambucil and Procarbazine, with which he again achieved complete remission. This treatment was followed by autologous marrow transplant, conditioned with a single dose of Etoposide and Meiphelan. Two years later he relapsed for the third time in the same pulmonary area and on this occasion was treated with 10 fractions megavoltage radiotherapy to the lung field followed by 5 courses of CCNU and Vindesine achieving remission.

Discussion

Anal carcinoma is rare, being 20-30 times less common than colonic cancer and represents only 5% of anorectal cancers¹. It occurs throughout the world but is particularly common in Brazil and India where the incidence of anal cancer is closely related to that of carcinoma of cervix, penis and vulva, suggesting a common aetiological factor².

The aetiology of anal cancer is not well understood, but is presumed to be multifactorial, representing an interaction between genetic and environmental factors³. Several predisposing factors are related to anogenital carcinoma like smoking, sexual orientation, viral warts, human papilloma virus infection, immune status and tumor suppresser genes^{3,4}. The case discussed illustrates the interaction of these factors in the development of anal carcinoma.

There is evidence that Hodgkin's disease predisposes the patient to HPV infection and that about 6% of such patients acquire it. HPV infection alone is insufficient to cause malignant transformation and only a small proportion of patients with HPV eventually develop tumours⁴. It has therefore been hypothesised that HPV may act as promoter in synergy with carcinogenic initiators, such as cigarette

smoking or exposure to radiation⁴. The expression and detection of HPV is modulated by the immune status of the host and an increased prevalence of HPV is known to occur during the mild and transient immune deficiency of pregnancy⁶. Similar trends have been seen with iatrogenic immune suppression in patients with renal transplant⁷ cardiac allograft recipients, patients after chemotherapy^{7,8} and in homosexual men with human immunodeficiency virus infection^{9,10}. Secondary neoplasms have been reported by Lokich¹¹ in patients who received chemotherapy for Hodgkin's disease, but these patients were not infected with HPV. We suspect that immunosuppression in our patient after multiple courses of chemotherapy caused expression of HPV which he acquired during the course of his Hodgkin's disease. HPV in synergy with radiotherapy resulted in the development of anal carcinoma. He was later treated with radical radiotherapy and there has been no evidence of recurrence of his anal carcinoma to date.

It is therefore recommended that special attention should be paid to the anogenital area of such immunosuppressed patients during follow-up. Any papillomata in the area should be regarded as carcinoma until proved otherwise by biopsies.

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