Severe anal condylomata acuminata following high-dose chemotherapy and autologous hematopoietic stem cell transplantation : A case report

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Abstract

We report the case of a 37 years old male patient who developed severe anal condylomata acuminata after high-dose chemotherapy and autologous hematopoietic stem cell transplantation for follicular non-Hodgkin's lymphoma. Anal warts were particularly disabling, refractory to the treatment and finally imposed diversion colostomy. The role of cellular immunodeficiency observed after high-dose chemotherapy and autologous hematopoietic stem cell transplantation as etiology of anal condylomata is discussed. (Acta gastroenterol. belg., **1996**, 59, **254-255**).

Key words : condylomata acuminata, hematopoietic stem cell transplantation, non-Hodgkin's lymphoma.

Introduction

Cellular immunodeficiency is well documented following autologous hematopoietic stem cells (HSC) transplantation (1), resulting both from impaired T-cell activation, and defective production of the principal T-cell growth factor : IL-2. There is no evidence that peripheral blood HSC may be superior to bone marrow HSC in accelerating immune reconstitution (2). Viral infection or reactivation may be related to this cellular immunodeficiency including herpes simplex, cytomegalovirus, herpes 6 (3,4). We describe here a case of severe anal warts, a viral infection rarely reported after autologous HSC transplantation, probably related to cellular immunodeficiency following high-dose chemotherapy (HDC) and autologous transplantation.

Case report

A 37 years old male patient was referred in February 1994 for the treatment of low grade follicular non Hodgkin's lymphoma (NHL) classified as B according to the Working Formulation. Past medical history was negative, except for previous anal warts ten years ago. Clinical stage was IVA ; serum LDH and β2 microglobulin were elevated ; CD4+ lymphocytes level was normal : 710/μl representing 49% of the total lymphocyte count. HIV serology was negative. The patient was treated according to the GELF (Groupe d'étude des lymphomes folliculaires) 1994 protocol arm B group 2 consisting of four courses of standard CHOP (cyclophosphamide, adriamycine, vincristine, prednisone) chemotherapy, followed by cyclophosphamide and VP16 plus filgrastim (Neupogen® Amgen-Roche) for collecting HSC in peripheral blood. In June 1994, high-dose cyclophosphamide and VP16 were administered, combined with fractionated total body irradiation. Autologous peripheral blood HSC were infused and filgrastim was started on day 1. During the period of aplasia, the patient was placed in isolation room. On day three, he developed Streptococcus pneumoniae septicemia and required intravenous antibiotherapy. Hematologic recovery was uneventful : 13 days to obtain a level of 500 neutrophils/μl and 19 days to reach 20,000 platelets/μl. On day 17, anal discomfort appeared, associated with small perianal warts. Local treatment with YAG laser and podophyllotoxin was begun. Prophylactic intravenous gammaglobulin was administered weekly over three months. Despite the treatment, the anal lesions progressed and became disabling. Concurrently, pancytopenia developed. Three months following grafting, hemoglobin was 7.9 g/dl (normal : 12-17), platelets 61,000/mm^3 (normal : 150-350,000) and leukocytes 1,310/mm^3. There was a important lymphopenia : 280/mm^3 with abnormal CD4/CD8 ratio : 0.2. CD4 cells represented only 7% and CD8 cells were 36%. Viral serologies remained negative (cytomegalovirus, herpes simplex, herpes zoster, herpes 6, Epstein Barr virus and B19 parvovirus), HTLV1 determination was not performed. Both cytologic and cytogenetic bone marrow examinations including PCR for rearrangement of bcl-2 gene excluded recurrence of the NHL but displayed marrow hypoplasia. In October 1994, extensive surgical removal of the anal lesions was performed under general anesthesia. Histological examination confirmed typical tuberous condylomas. After surgery hematologic parameters progressively resolved.

rh-Interferon α2A (Intron A® Schering-Plough) 3 × 10^6 units three times a week was begun in December 1994 for both NHL and anal warts. Intron A® is still administered. Condylomata recurred 4 months later. This was disabling and for patient's comfort a diversion colostomy was performed in March 1995. Twenty months after transplantation, the patient is free of NHL

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and condylomata but remains with a colostomy in place.

Discussion

Anal warts, due to human papillomavirus (HPV) infection, is a well described entity in the setting of cellular immunodeficiency. The asssociation between condylomata and HIV infection is well known particularly in male homosexuals (5). Interetingly in autologous HSC transplantation for neoplasia, which can be followed by a profound cellular immunodeficiency, anal warts were rarely reported, while cases of condylomata acuminata after kidney and cardiac transplantation have been described (6,7,8). Significantly in immunodeficient patients, HPV infection may be a predisposing factor for anal carcinoma, and primarily involves type 16 HPV (9). HPV DNA can be detected in genital warts and ano-rectal carcinomas. In our patient cellular immunodeficiency was severe with a CD4+ cell count extremely low. In HIV patients, a statistically significant relationship exists between levels of CD4+ lymphocytes and the detection of epithelial HPV DNA, suggesting a direct relation between incidence of HPV infection and the degree of cellular immunosuppression (10).

In our case, both local treatment and large surgical resection failed and the patient required a diversion colostomy. Relapse of condylomata acuminata in immunodeficient patients seems more frequent but is rare after radical surgery (5). The role of interferon as maintenance therapy after surgery remains controversial (11). Interestingly, the genital warts developed concomittantly with marrow hypoplasia. The origin of this pancytopenia was never precised and resolved progressively after surgical treatment of condylomata acuminata.

In conclusion, we describe severe and morbid anal warts occurring after autologous peripheral blood HSC transplantation for follicular NHL. These viral lesions appear to be related to cellular immunodeficiency and may predispose to anal neoplasia. The treatment is difficult and often disappointing.

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