Should HIV patients be considered a high risk group for the development of prostate cancer?

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ABSTRACT

INTRODUCTION Only very few case reports exist regarding the incidence of prostate cancer in younger HIV-infected patients.

PATIENTS AND METHODS Two incidences of HIV-infected men diagnosed with prostate cancer, from a cohort of about 200 men treated at St George's Hospital aged 40 years or more are reported.

DISCUSSION On the basis of the evidence presented in both case reports and from the literature, clinicians should be aware that men with HIV infection should be considered a high-risk group for prostate cancer, and consider early PSA screening.

KEYWORDS

HIV – Prostate cancer

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The era of highly active antiretroviral therapy (HAART) has led to an increase in age of the HIV-infected population. Kaposi's sarcoma and non-Hodgkin's lymphoma are recognised as AIDS-related malignancies, but other cancers are not yet associated with HIV infection. However, case reports exist that suggest a positive association between prostate cancer and HIV infection. To illustrate this point, we discuss two incidences of HIV-infected men diagnosed with prostate cancer, from a cohort of about 200 men treated at St George's Hospital aged 40 years or more.

Case report 1

A 64-year-old man was diagnosed with HIV in 1987 and treated for 6 years with antiretroviral (Zidovudine) monotherapy. His CD4 count varied between 280 and 400 cells/ml over this time. In 1998, he presented with haematuria and was found to have a PSA of 4.6 ng/ml but declined to have any further PSA testing until April 2001 when he re-presented with lower urinary tract symptoms and a PSA of 9.5 ng/ml. Prostatic biopsy revealed a Gleason 3+2 adenocarcinoma in 1 of 8 tissue cores, and CT and bone scans confirmed disease to be organ-confined. He initially declined treatment and chose to have his PSA monitored. HIV status at the time of diagnosis showed a CD4 count of 356 cells/ml and a viral load of 1242 copies/ml. Following serial rises in PSA, treatment for prostate cancer commenced in February 2002, initially with neoadjuvant hormones, and subsequent radical radiotherapy to the

prostate. In August 2002, the CD4 count fell to 160 cells/ml and viral load increased to 3999 copies/ml. He started HAART, in a clinical trial of a combination of didanosine, nevirapine, efavirenz and lamivudine. His PSA remains stable at 1.1 ng/ml. Despite the antiretroviral therapy fully suppressing the viral load, he has had a poor immunological response to treatment, with the CD4 count staying below 200 cells/ml. He had a cerebrovascular accident causing a right hemiparesis in September 2003.

Case report 2

A 58-year-old man was diagnosed with HIV in 1997. His baseline CD4 count was 380 cells/ml. He commenced an antiretroviral combination of stavudine, didanosine and nevirapine, which fully suppressed the viral load. The CD4 count rose to 950 cells/ml by June 2000 when he chose to have a treatment interruption because he had developed moderately severe lipodystrophy. He was diagnosed with prostate cancer in October 2002, with a CD4 count of 485 cells/ml during a hospital admission with infective myositis of the left iliacus muscle, when he was found to have a PSA of 5638 ng/ml. Bone scan confirmed the presence of metastatic disease throughout the axial skeleton. The patient was treated initially with bicalutamide monotherapy, and this was converted to maximal androgen blockade (bicalutamide and leuporelin) in June 2003, after prophylactic breast bud irradiation and on the commencement of tamoxifen for breast tenderness. His PSA had fallen dramatically to 25

ng/ml at this stage, but by December 2003, it had risen to 113 ng/ml. HIV status at this time showed stable disease, with a CD4 count of 415 cells/ml and a viral load of 20,757 copies/ml. However, he was recommenced on HAART (Kaletra, Tenofovir, Lamivudine) in the hope that this may boost his immunity and help control the spread of prostate cancer. The bicalutamide was stopped in October 2003 but he continued on leuporelin. His PSA has continued to rise and he also complains of severe hip pain for which he is being treated with local radiotherapy and strontium, but he is unsuitable for any chemotherapy due to his increased susceptibility for opportunistic infections.

Discussion

Only very few case reports exist regarding the incidence of prostate cancer in HIV-infected patients, some as young as 40 years.¹ This seems to suggest a possible link between HIV and more aggressive cancer, supported by case report 2 where the father too suffers with prostate cancer but has been well for the past 10 years.² HIV infection is associated with reduced cell-mediated immunity, and humoral responses predominate in these patients, which are thought to be pro-angiogenic. The chronic immune activation associated with a high viral load has been shown to lead to the release of factors such as macrophage inflammatory protein (MIP-1) which inhibit apoptosis via p53 suppression, and these factors provide an environment in which cancer cells may flourish.³ Further work has demonstrated homology with the HIV gene for gp41 and DNA fragments isolated from prostate cancer tissue samples,⁴ which raises the possibility of a causal link between HIV and prostate cancer.

There have been suggestions in the past that the increased risk of prostate cancer in HIV-positive patients

may be an adverse effect of antiretroviral therapy.¹ The two cases presented above both developed prostate cancer in the absence of concurrent antiretroviral therapy. Whether the treatment interruption undertaken by the second patient, and subsequent immune deterioration precipitated his acute presentation with disseminated cancer can only be speculated upon.

The debate regarding national PSA screening is ongoing, but it is widely accepted that men at higher risk of prostate cancer (*i.e.* those with a family history) should undergo early PSA testing. It seems clear from the literature that men with HIV infection should be considered a high-risk group; we suggest, on the basis of the evidence presented in both case reports and from the scientific community, that clinicians be aware of this fact when treating seropositive male patients, and consider early PSA screening.

Although these cases use prostate cancer as an illustration, it seems likely that as the HIV-positive population ages, they will become vulnerable to other tumours not traditionally associated with the disease, and possibly be at greater risk of aggressive forms. It seems likely that awareness will have to extend across the surgical specialties such that the diagnosis is not overlooked in these patients.

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