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Fatal Bladder Carcinoma in Woman with Human Immunodeficiency Virus: A Case Report

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ABSTRACT

Background: Chronic human immunodeficiency virus (HIV) infection is associated with an increased incidence of Non-Acquired Immunodeficiency Syndrome (non-AIDS) defining cancers. To date, only a limited number of cases of bladder cancer have been linked with HIV infection in women. We sought to describe the clinical characteristics of HIV-associated bladder cancer.

Methods: A 54-year-old female patient presented with symptoms of an occlusive syndrome. Medical examination was followed by a CT scan. The imaging revealed a significant finding. There was a noticeable process within the bladder. Further evaluation and management were recommended.

Results: Spontaneous urinary cytology revealed the presence of malignant cells. An endoscopy was performed under spinal anesthesia, uncovering a large sessile tumor with necrotic areas located on the ventral aspect and dome of the bladder. Due to the severity of the condition, a palliative resection was carried out. Subsequent histological examination identified the tumor as a high-grade urothelial carcinoma, with evidence of muscle invasion. This diagnosis confirmed the aggressive nature of the disease, highlighting the necessity for further medical management and intervention.

Conclusion: Bladder cancers in HIV-infected patients are rare but can occur in relatively young individuals with a low nadir CD4 cell count. These cancers often exhibit aggressive pathological features and can be fatal.

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Introduction

Due to the long-term efficacy of antiretroviral therapy (ART) and the associated increase in life-expectancy of HIV-infected patients, cancers now represent up to one third of all causes of deaths among HIV-infected patients [1].

AIDS-related malignancies in HIV-infected patients are mainly related to current immunodeficiency and viral infections, but other factors such as a low nadir CD4 count may also be involved [2–3]. Also, non-AIDS-related malignancies are an increasing cause of death, up to 22%, among HIV-infected patients in France [1].

While bladder cancer is one of the most common malignancies worldwide, very few cases of bladder cancer in HIV-infected patients have been reported in the literature [4–5].

Bladder cancer has been reported in association with HIV infection in a limited number (six) of published case reports [6-7]. Large epidemiologic studies conflict on whether there is an increased incidence of bladder cancer in the HIV-infected population. In a study from Zambia (1980-1989), involving 7836 cases of neoplasia, bladder carcinoma (6.3%) was the third leading malignancy reported, after carcinoma of the cervix (19.6%) and Kaposi's sarcoma (7%) [8]. However, a review of the cancer registry of Uganda for incidence rates from 1989 to 1991 showed a decline in the incidence of bladder cancer with the emergence of AIDS-related Kaposi sarcoma [9]. Linked population-based AIDS and cancer registry data (1978-1996) from the United States, including 302,834 adults with HIV/AIDS, identified 48 people with HIV associated bladder cancer with a relative risk of approximately 0.6 in this group compared to the general population [10]. A 2007 meta-analysis of several studies involving 444,172 individuals with HIV/AIDS did not demonstrate an increased incidence of bladder cancer in the HIV population compared to the general population [11]. Most recently, a 2008 epidemiologic study using HIV/AIDS Cancer Match Study data reported a lower incidence of bladder cancer in the HIV population as compared to the general population with a standardized incidence ratio of 0.7 [12].

To date, there have been no published series that specifically address the association and management issues related to bladder cancer in the setting of HIV-infection. Therefore, the aim of this study was to investigate a series of HIV-associated bladder cancer cases, together with cases previously published in the literature, and to identify particular risk factors, clinical findings, pathologic features, management issues, and/or response to therapy in this group of immunocompromised patients.

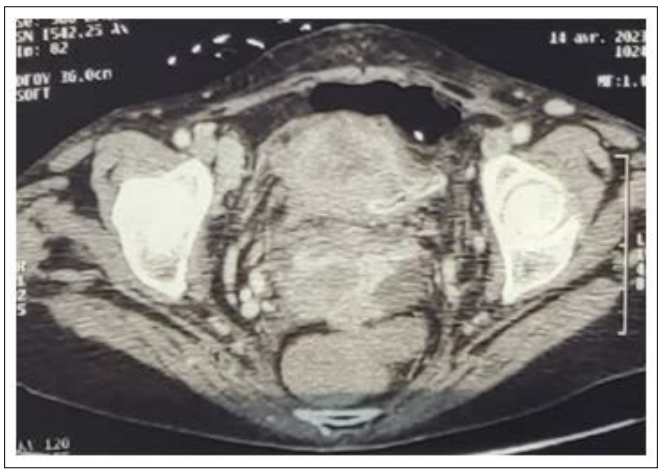
Observation

A 54-year-old female smoker and alcoholic who had weaned herself off the habit 12 years ago, had been treated for HIV since 1990 and was well controlled on lopinavir/ritonavir with an undetectable viral load. She had an Escherichia coli and group D Streptococcus urinary tract infection treated with C3G, and had been gas and matter-free for 20 days with fecal vomiting and pelvic pain.

The CT scan showed mechanical occlusion of the bowel, with distension of the small intestines measuring 60 mm in maximum diameter, with visualization of a transitional level at the hypogastric level producing the beak sign. There was also distension of the stomach and duodenal frame measuring 44 mm in maximum diameter at the D3 level, which were probably the site of stercoral contents.

The Patient Underwent an Emergency Discharge Colostomy

The CT scan revealed the presence of a fairly well-defined, regularly contoured, endoluminal, heterodense, budding PDC in the right lateral bladder wall and at the level of the bladder dome. It measures 52 mm in anterosuperior diameter, 58 mm in transverse diameter and 27 mm in height. Laterally, this process infiltrates the peri-bladder fat and comes into contact with some of the small intestines.



Secondary Liver and Lymph Node Involvement

Spontaneous urinary cytology showed malignant cells. Endoscopy under spinal anesthetic revealed a huge sessile tumor with necrotic areas, in the ventral aspect and dome of the bladder.

A palliative resection was performed. Histological examination disclosed a high-grade urothelial carcinoma invading the muscle.

palliative radiotherapy was planned, but it had to be discontinued in the second cycle because of severe leucopenia, thrombopenia. 5 months later the patient died.

Discussion

The etiology of bladder pathology in patients with HIV is mainly either infectious or neurological [13]. Bladder carcinoma constitutes an exceptional finding in this population. The diagnosis in young adults of a rare and aggressive neoplasm, although it is not an indicator of AIDS, could indicate HIV infection [14]; epidemiological data may provide more information about this concern. In contrast to the opinion of some authors [15] who doubt the value of having such patients evaluated urologically, we emphasize that possible bladder carcinoma must not be overlooked in the presence of hematuria or irritative persistent symptoms in a young adult with HIV.

Indeed, in the general population bladder cancers usually occur at a median age of 77 years in females, much older that the median age of most cohorts of HIV infected individuals [16].

Our study shows that bladder cancer can occur in patients with HIV-infection although it remains a rare event seen in only 0.2% in Paris. When accounting for the different age and sex structure of cohort and of the French general population however, the global SMR was estimated at 3.44 (95% CI: 0.89–7.65), suggesting that we have observed more cases of bladder cancers than expected. The prevalence of bladder cancer in HIV-infected patients remains however much lower than that of other malignancies in this population, with prevalence rates of Kaposi sarcoma and non-Hodgkin lymphomas reported to be ten-fold higher, and prevalence rates of anal and lung cancers reported to be 5-fold higher on average in 2006 in France [17]. Indeed, bladder cancers have been rarely reported in the literature among HIV infected patients, with a few case-reports. Recent epidemiologic studies have also reported a low prevalence of bladder cancer in HIV-infected patients, similar or even lower than in the general population, but these studies have been performed in patients with AIDS and might therefore have overlooked the real prevalence of bladder cancer today in the HIV population on ART [18]

Smoking is a well-known risk factor for bladder cancer and cigarette smoke is responsible for approximately one-half of cases of urothelial cancer in both men and women. The proportion of smokers in HIV-infected patients is usually higher than in the general population putting them therefore at higher risk for bladder cancer. In nationwide study in Denmark, 76% of the HIV-infected patients were current smokers as compared to only 39% of the control population. Smoking-related cancers accounted for 23% of cancers in the HIV-infected population and the risk of these cancers was increased by 2.8-fold as compared to the control cohort [19]. This is the case was reported in our study. These data altogether suggest that smoking cessation should be emphasized in HIV-infected patients especially as patients are getting older.

Our study and literature review showed that bladder cancers in HIV-infected patients share common characteristics with bladder cancers in non-HIV-infected individuals, a high proportion of smokers, painless hematuria as the main presenting symptom, and histopathology yielding mainly urothelial (transitional cells) carcinomas which account for 90% of all bladder cancers [20].

There are however distinct features of bladders cancers in HIV-infected patients that may suggest a potential increase in the incidence of this cancer in the near future in this population [20].

Interestingly, the median age of patients with bladder cancer both in our case and in the literature appears to be at least 10 years younger on average than in the general population suggesting that, according to the increasing life-expectancy of HIV-infected patients with ART today, our patients may experience even more bladder cancers in the future [20].

Indeed, the proportion of bladder cancers in a recent study increased by at least 5-fold in HIV infected patients above 50 years old as compared to those between 40 and 49 [18].

Case	Age	Gender	CD4 count (cells/ mm3)	HIV load (copies/ mL)	HAART	Clinical Presentation	Pathology	TNM (stage) at diagnosis	Therapy	Outcome
Wolf4 2001	37	Female	318	NR	NO	Hematuria, LAP	TCC HG	T1N0M0 (stage I)	TURBT Radiation	Alive
Case1	67	Female	445	<50	Yes	Hematuria, LAP	TCC HG	T4N0M0 (stage IV)	Palliative radiation Embolization of one vesical artery	NR
Our case	54	Female	440	NR	Yes	Frequency, Dysuria, LAP, Weight loss	TCC HG	T3N2M1	Palliative radiation	Died within 5 months

NR = not reported; LAP = lower abdominal pain; TCC=Transitional cell carcinoma; HG= High grade; HAART= highly active antiretroviral therapy; TURB=transurethral resection of bladder tumor.

The role of immune suppression in the development of AIDS-related and non-AIDS related malignancies has been well established especially for virally-induced cancers such as EBVH-HV-8, HBV/HCV and HPV-related cancers [2–3]. In our case patient has no severe immune deficiency with a median CD4 cell counts above 500 cells/mm3, however a low nadir of CD4 cell count can been associated with an increased risk of non-AIDS related cancers such as HPV-related anal cancers [3].

A relationship between HPV infection and urothelial bladder cancer has also been suggested by a number of studies and HPV can infect the epithelia of the bladder. Condyloma acuminatum, characteristic of HPV infection has been reported in the bladder. A recent meta-analysis found that the prevalence of HPV among cases of bladder cancers could be as high as 17% [21]. In our case HPV was not detected by PCR in the tumor biopsy, but a sizable proportion of patients had HPV-related lesions at the time of cancer diagnosis [20], suggesting that HPV infection might be associated with bladder cancer especially among HIV infected patients. More studies should be performed to assess the prevalence of HPV in bladder cancers in the HIV-infected population and its role in the pathogenesis of urothelial cancers.

Another unique feature of these bladder cancers in HIV-infected patients was the high rate of aggressive tumors with muscle invasion in 46% and high-grade histology in 73%, which can explain the poor outcome of our patients with a case-fatality rate of 27%, much higher than in the general population.

Physicians in charge of HIV-infected patients should be aware that their patients, as they become older, face an increased risk of bladder cancer, especially those with a low nadir CD4 cell count, who smoke, and also potentially those with HPV infection. Also, because bladder cancers in HIV-infected patients seem to be more aggressive, this diagnosis should be suspected in any patient with hematuria or dysuria and should prompt rapid urologic examination.

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