Background

HIV-infected patients have a higher risk of developing malignancies than general population, especially virus-associated cancers. The advent of the combined antiretroviral therapy (ART) led to a strong reduction of the incidence of AIDS-defining cancers (ADCs) and raised life expectancy among people living with HIV/AIDS. As the same time, new issues have emerged: chronic degenerative diseases and non-AIDS-defining cancers (NADCs) have increased. Currently, malignant neoplasms are the leading cause of death for PLWH in Western countries. For this reason, in recent years, international guidelines for the management of PLWH have highlighted the importance of oncological screening interventions, both those shared with the general population and those specific for PLWH. The aim of this study was to define from an epidemiological and prognostic point of view the neoplastic pathologies in PLWH.

Material and Methods

This retrospective, observational cohort study has been carried out at the Infectious Diseases Department, University Hospital of Padova, Italy. We enrolled PLWH with a cancer diagnosis occurred between January 1996 and March 2018 who met the following inclusion criteria: 1) Age over 18 years; 2) Diagnosis of primary malignant neoplasia concomitant or subsequent to the diagnosis of HIV; 3) Histological, cytological or radiological diagnosis of primary malignant tumor according to diagnostic criteria of each cancer (metastatic or concurrent, coexistence of primary tumors, in situ carcinomas and tumor recurrences were excluded). 4) At least two follow-up visits after the diagnosis of cancer. This study was approved by the local Ethical Committee.

Results

188 patient were enrolled, for a total of 204 cancer diagnoses; 15 patients had two or more tumors in the observation period. Second and third diagnosis of cancer in the same patient were excluded in order to avoid bias in the survival analysis; therefore, statistical analysis was performed on 188 patients with 188 different cancers. They were equally distributed in the two observation periods (94 cases in each period), with median age at the diagnosis of malignancies of 46.5 years (IQR 38.75-54).

The 188 patients were female and 9% of foreign nationality; these percentages didn’t change significantly between the two observation periods. 105 patients had an ADC and 85 patients had a NADC, respectively 67 and 27 in the period 1996-2006 and 36 and 58 in the period 2007-2018. The most frequent neoplasms were NHL (27.7%), KS (27.7%) and hepatocellular carcinoma (9.5%), as shown in Table 1.

Regarding NADCs, patients with undetectable viral load and CD4+ lymphocytes T cells >500 cells/μl at tumor detection were 18.5% and 7.4% respectively in the first observation period and 70.7% and 44.8% in the second, with a statistically significant difference (Table 2). The median age at the NADC finding increased significantly from 42 years to 55.5 years (Table 3).

Analysis survival of the entire population is shown in figure 2 and divided for cancer type in figure 3. Survival differed significantly with the type of tumor: KS was associated with an excellent survival (85.4% at 10 years), while NHL and HCC were associated with an increased risk of mortality, with similar survival in the first two years of follow-up (52.8% and 52.1% respectively) and a significant increase in mortality for HCC from the second to the fifth year of follow-up.

Conclusions

In our series, according to the literature data, the neoplastic disease still represents a major cause of morbidity and mortality. The study showed a significant reduction in the diagnosis of ADCs from the first to the second observation period. ADCs, however, continue to occur primarily in a context of severe immunosuppression and high viral load. Even in the second period, a considerable proportion of ADCs occurs in patients not in antiretroviral treatment, who become aware of their neoplasticity simultaneously with the diagnosis of cancer (late presenters). On the other hand, we have highlighted a significant increase in NADCs over time. These tumors are not strictly related to the state of immunosuppression, in fact the risk of onset persists despite immune reconstitution and optimal control of HIV viremia, probably because the risk is linked to the aging of PLWH, to the chronic inflammation and to the immunosenescence. Finally, the survival of patients with HIV infection and malignancy is predominantly influenced by the type of cancer diagnosed. Being in ART at the time of the diagnosis of neoplasms has been shown to reduce the risk of mortality, as well as a high value of CD4+ lymphocytes at nadir.

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In addition, highest CD4+ nadir values, taking cART at the time of tumor diagnosis and, obviously, the complete remission of cancer correlate all with a better survival (Table 4). In multivariate analysis, the CD4+ value at nadir and the diagnosis of KS were found to reduce mortality, while the diagnosis of hepatocellular carcinoma was found to increase the risk of mortality by about 3 and a half times (Table 5).

Table 1. Characteristics of cancers at diagnosis, for ADCs and NADCs and for the period of observation.

Table 2. Immunovirological parameter determined by NADL and NADC and by observation period.

Table 3. Characteristics of women at diagnosis, for ADCs and NADCs and for the period of observation.

Table 4. Results of multivariate model. The Hazard Ratio is a coefficient that multiplies the basic risk, expressing the effect exerted by the coexisting factor.

Table 5. Characteristics of patients at diagnosis, for ADCs and NADCs and for the period of observation.

References


Figure 1. Kaplan-Meier survival probability over time, expressed in months, over the whole cohort.