



Original article

A case-control study of non-AIDS-defining cancers in a prospective cohort of HIV-infected patients[☆]

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ABSTRACT

Introduction: We present a case-control study of non-AIDS-defining cancers (NADCs) in a cohort of HIV-infected patients where we value the incidence, survival and prognostic factors of mortality.

Methods: All NADCs diagnosis conducted from 2007 to 2011 in 7 hospitals were collected prospectively, with a subsequent follow up until December 2013. A control group of 221 HIV patients without a diagnosis of cancer was randomly selected.

Results: Two hundred and twenty-one NADCs were diagnosed in an initial cohort of 7067 HIV-infected patients. The most common were: hepatocellular carcinoma 20.5%, lung 18.7%, head and neck 11.9% and anal 10.5%. The incidence rate of NADCs development was 7.84/1000 people-year. In addition to ageing and smoking, time on ART (OR 1.11; 95% CI 1.05–1.17) and PI use (OR 1.72; 95% CI 1.0–2.96) increased the risk of developing a NADC. During follow-up 53.42% died, with a median survival time of 199.5 days. In the analysis of the prognostic factors of mortality the low values of CD4 at tumour diagnosis (OR 0.99; 95% CI 0.99–1.0; $p=0.033$), and the previous diagnosis of AIDS (OR 2.06; 95% CI 1.08–3.92) were associated with higher mortality.

Conclusions: Predictors of NADCs in our cohort were age, smoking, CD4 lymphocytes and time on ART. Mortality is high, with NADC risk factors being low CD4 count and previous diagnosis of AIDS.

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Estudio caso-control de tumores no defintorios de sida en una cohorte prospectiva de pacientes infectados por el VIH

R E S U M E N

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Cáncer de pulmón
Cáncer anal
Cáncer de cabeza y cuello
Cáncer de piel
Linfoma de Hodgkin
Tratamiento antirretroviral

Introducción: Presentamos un estudio caso-control de tumores no defintorios de sida (TNDS) en una cohorte de pacientes infectados por el VIH en la que valoramos las tasas de incidencia, supervivencia y factores pronósticos de mortalidad.

Métodos: Se recogieron de forma prospectiva en 7 hospitales, los diagnósticos de TNDS realizados de 2007 a 2011, con seguimiento posterior hasta diciembre de 2013. Se seleccionaron de forma aleatoria un grupo control de 221 pacientes VIH sin diagnóstico de cáncer.

Resultados: Se diagnosticaron 221 TNDS en una cohorte inicial de 7.067 pacientes VIH. Los más frecuentes: hepatocarcinoma 20,5%, pulmón 18,7%, cabeza y cuello 11,9% y anal 10,5%. La tasa de incidencia de desarrollo de TNDS fue de 7,84/1.000 pacientes-año. Además de la edad y el tabaco, el tiempo en TAR (OR 1,11; IC 95% 1,05-1,17) y el uso de IP (OR 1,72; IC 95% 1,0-2,96) aumentaron el riesgo de desarrollar un TNDS. Durante el seguimiento fallecieron el 53,42%, con una mediana de supervivencia de 199,5 días. En el análisis de los factores pronósticos de mortalidad, los valores bajos de CD4 en el momento del diagnóstico del tumor (OR 0,99; IC 95% 0,99-1,0; p = 0,033) y el diagnóstico previo de sida (OR 2,06; IC 95% 1,08-3,92) se asociaron con una mayor mortalidad.

Conclusiones: Los predictores de TNDS en nuestra cohorte fueron la edad, el consumo de tabaco, los linfocitos CD4 y el mayor tiempo en TAR. La mortalidad es alta, siendo factores de riesgo los CD4 bajos en el momento del diagnóstico del TNDS y el diagnóstico previo de sida.

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Introduction

Since the beginning of the AIDS epidemic, the risk of developing neoplasms has been higher in patients infected with the human immunodeficiency virus (HIV) than the general population. Before the introduction of antiretroviral treatment (ART), the so-called AIDS-defining cancers (ADCs) – non-Hodgkin's lymphoma, Kaposi's sarcoma and invasive cervical cancer – constituted more than 85% of the neoplasms; these ADCs have been associated with a viral aetiology and, in general, are directly associated with the patient's immunosuppression.¹

With the increase in survival and ageing of the HIV-infected population since the introduction of ART, the spectrum of diseases associated with HIV infection has changed dramatically; other ailments such as non-AIDS-defining cancers (NADCs) have made an appearance.²⁻⁴ Cancer databases and registers show a significant decrease in ADCs and a rapid increase in NADCs, which have become the most common cause of neoplasm in HIV-infected patients.^{1,5-8} These NADCs, which do not always have a viral origin, tend to behave more aggressively and the diagnosis is usually made at a more advanced stage of the disease than in non-HIV infected patients, so they have a worse prognosis, currently being one of the main causes of mortality in HIV-infected patients.⁹⁻¹²

The most studied NADCs are Hodgkin lymphoma (HL)¹³ and anal cancer.^{14,15} Other cancers, also described in these patients, with a behaviour different from that observed in the general population, are: lung carcinoma,^{16,17} liver cancer,¹⁸ testicular cancers, squamous cell carcinoma of the conjunctiva, multiple myeloma and leiomyosarcoma in paediatric patients.¹ Interestingly, a lower incidence of prostate, breast and bladder carcinomas has been described in some series.¹

The objective of this study is to analyse the incidence and risk factors of developing NADCs in a prospective cohort of HIV-infected patients, measuring survival and identifying their prognostic factors.

Material and methods

During a period of 5 years (from January 2007 to December 2011), all new diagnoses of NADCs were collected in an initial prospective cohort of 7067 HIV-infected patients in 7 hospitals in

northern Spain (SEINORTE group), with subsequent clinical follow-up until 31st December 2013. Likewise, a control group of 221 patients was randomly selected from the cohort. The criteria were that of being alive as of 1st January 2007 and not having been diagnosed with any neoplasm before the end of the case inclusion period. Data on the total follow-up time of each patient is available (since January 2007 or later if the patient started his follow-up afterwards until 31st December 2011 or earlier if the patient dies or is lost to follow-up).

Age, sex, date of HIV diagnosis, previous or concomitant AIDS diagnosis and its date, the HIV infection risk group, nadir of CD4 lymphocytes, CD4 lymphocytes at the time of cancer diagnosis, the use or not of ART with date of onset, the known time of HIV infection, co-infections of hepatitis viruses and the signs or symptoms of liver disease; the neoplasm's date of diagnosis and form of presentation; other predisposing factors for it (smoking, alcohol, sexual promiscuity, etc.).

Likewise, semi-annual follow-ups have been carried out, in which the patient's vital signs, current treatments, CD4 lymphocytes and HIV viral load are collected.

Given the diversity of neoplasms and the fact of wanting to get a better understanding of these patients' prognostic factors, survival and progression, in addition to the general assessment we have divided the NADCs into 3 large groups:

1. Infection-associated NADCs. In this group we have included HL and the Epstein-Barr virus; liver cancer and hepatitis B and C viruses (HBV and HCV); and NADCs of the vulva, vagina and penis, as well as the human papillomavirus (HPV).
2. Smoking-associated NADCs: lung neoplasms and head and neck cancers (tonsil, lip, tongue, larynx, pharynx and oesophagus) have been included in this group.
3. NADCs not associated with infections or smoking, which would include the rest of the neoplasms.

Although there is a growing literature that shows that some cancers of the head and neck, and less likely of the lung, may have a viral aetiology associated with HPV,¹⁹ given that the presence of this virus is not systematically determined in these specimens' biopsies, we preferred not to include them in the infection-related group.

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