Lung cancer and HIV infection. A case report and literature review

ANDRÉS REYES-CORCHO*
DIANELIS P. SIERRA MARTÍNEZ‡
TERESITA SABATÉS-LLERANDI§
FRANCISCO DELGADO-PINO‡
MAGALYS OLIVERT-CRUZII
NERY DÍAZ¶

* Former Member of the Division of Internal Medicine and Infectious Disease. Gustavo Aldereguía Lima Teaching Hospital, Cienfuegos, Cuba.
‡ Division of Internal Medicine and Infectious Disease. Gustavo Aldereguía Lima Teaching Hospital, Cienfuegos, Cuba.
§ Division of Onco-Hematology. Gustavo Aldereguía Lima Teaching Hospital, Cienfuegos, Cuba.
II Department of Pathology. Gustavo Aldereguía Lima Teaching Hospital, Cienfuegos, Cuba.
¶ Department of Radiology. Gustavo Aldereguía Lima Teaching Hospital, Cienfuegos, Cuba.

Trabajo recibido: 02-IV-2009; aceptado: 26-VI-2009

Conflicto de intereses: Ninguno

Key words: Human immunodeficiency virus-1, HIV, acquired immunodeficiency syndrome, AIDS, lung cancer.

ABSTRACT

Lung cancer (LC) is the third more frequent malignancy in human immunodeficiency virus-1 (HIV)-infected individuals. The first case of LC in a Cuban HIV-infected patient is presented. It was a squamous cell carcinoma at advanced stage (III-B) and the clinical evolution was unfavorable; however, the patient did not develop acquired immunodeficiency syndrome (AIDS)-related events. Most HIV-infected patients with LC are symptomatic at diagnosis, reflecting an advanced disease (stages III-B/IV) between 70 and 90% of cases. Adenocarcinoma is the most frequent histological type. LC represents a new challenge in HIV-infected population, so its prevention, early diagnosis, and management should be included in the long-term follow-up of this group of patients.

RESUMEN

El cáncer de pulmón (CP) es la tercera neoplasia más frecuente en individuos infectados por el virus de la inmunodeficiencia humana-1 (VIH). Se presenta el primer caso de CP en un paciente VIH-positivo en Cuba. Se trató de un carcinoma epidermoide en estadio avanzado (III-B) y la evolución clínica fue desfavorable; no obstante, el paciente no presentó alguna enfermedad relacionada con el síndrome de inmunodeficiencia adquirida (SIDA). La mayoría de los pacientes VIH-positivos con CP están sintomáticos en el momento del diagnóstico, reflejando una enfermedad avanzada o metastásica (estadios III-B/IV) entre el 70 y el 90% de los casos. El adenocarcinoma es el tipo histológico más frecuente. El CP representa un nuevo desafío en la población infectada por VIH, por lo que su prevención, el diagnóstico precoz y el abordaje terapéutico adecuado deben ser incluidos en el seguimiento a largo plazo en este grupo de pacientes.

Palabras clave: Virus de la inmunodeficiencia humana-1, VIH, síndrome de inmunodeficiencia adquirida, SIDA, cáncer de pulmón.
INTRODUCTION

Lung cancer (LC) is the third most common malignancy in human immunodeficiency virus-1 (HIV)-infected patients, only preceded by Kaposi sarcoma (KS) and non-Hodgkin lymphomas (NHL). The widespread use of highly active antiretroviral therapy (HAART) has been associated with a dramatic reduction in the incidence of acquired immunodeficiency syndrome (AIDS)-related events, particularly opportunistic infections. Prolonged life expectancy for HIV-infected population has changed the morbidities and causes of death, to included non-AIDS-defining cancer, and in this case LC as a challenge for the next decades.2,3

CLINICAL CASE

The patient was a 38-year-old male with sexually acquired HIV infection since 2001. He smoked one half-pack of cigarettes daily. The patient began HAART with lamivudine, stavudine, and nevirapine in 2005 for several CD4+ T-cell counts lower than 200 cells. He was admitted in the Department of Infectious Disease at Gustavo Alderegua Lima Teaching Hospital expressing moderate decay, decreased appetite and unintentional body weight loss of ten pounds for three months. He was found to have respiratory symptoms such as nonproductive cough, shortness of breath with middle efforts and right chest pain exacerbated by inspiration for the last 3 weeks. He denied fever, night sweats or hemoptysis. On physical examination he had mild skin and mucosal pallor, decreased breath sounds and localized wheezing at the middle third of right lung field. We identified bilateral neck lymphadenopathies without inflammatory signs.

At the time of admission the blood analysis showed moderate anemia (9 g/dL hemoglobin) and mild leukocytosis. There were no alterations in blood chemistry, and C-reactive protein was negative. His absolute CD4+ T-cell count and percent were 525 cells/mm³ and 21%. The patient’s plasma viral load (PVL) was undetectable (< 50 copies per milliliter) by nucleic acid amplification. Three months after the diagnosis of malignancy the patient’s CD4+ T-cell count and percent were 338 cells/mm³ and 18%. The chest radiograph performed on admission showed bilateral hilar thickening, more pronounced in the upper right branch. Few weeks later a homogenous rounded hilar opacity with tumoral appearance and non-homogeneous right pleural opacity were identified (Figure 1). The pulmonary functional test indicated normal spirometric parameters. Computerized tomography (CT) scan of chest showed a 40 x 36 mm hyperdense image suggestive of tumor, which occupied the anterior segment of upper lobe of the right lung, pleural thickening and a small nodular low density images above the tumor (Figure 2). Bronchoscopy revealed an occlusion of the 90% of anterior segment brochi by exophytic tumor. Bronchial cytology was positive for malignant cells and histological study confirmed the diagnosis of squamous cell carcinoma moderately differentiated (Figure 3).

On the basis of clinical presentation, histological and CT scan findings the patient was diagnosed as T2N0M0 (stage I-B) LC and surgical treatment was decided, but unfortunately the tumor was unresectable. After post-surgical histopathological reassessment the case was conclu-
ed in T4N1M0 (stage III-B). The patient had a favorable post-operative course and was discharged from the hospital after receiving three cycles of anti-tumoral chemotherapy with cisplatin and vinblastine. One month later he was re-admitted with new clinical data suggestive of mediastinal syndrome, mainly dyspnea, dysphagia, facial plethora, venous distension and edema in the neck and the upper chest and arms (Figure 4). The patient received palliative treatment and died two months later. Despite the torpid evolution, he never had AIDS-related morbidities after the diagnostic of cancer.

**DISCUSSION**

The first case of LC in an HIV-positive patient was reported in 1984. With independence of the studies design and the limited number of cases in some of them, the best evidence indicates that HIV-infected individuals have greater risk of LC respect to HIV-uninfected ones. This risk seems to be also superior in the era of HAART.10 Some studies had showed that HIV patients with LC are predominantly men and younger than patients without HIV infection. Nevertheless, recent epidemiological observations emphasized that the proportion of men among patients with LC tends to diminish as a result of the increasing number of smoking women in the general population, and the reduction of the relation men/women in the HIV-positive population.10,11 We presented a patient with an intense smoking habit, similarly to others cases reported in the literature. The well known association between tobacco and LC seems to be stronger in HIV-infected population, probably in correlation to the higher prevalence of the risk factor in this group of individuals.12

The ALIVE study indicated that HIV infection is a strong independent risk factor for LC.10 Also
the oncogenic potential of HIV has been described in vitro, particularly the effect of the tat protein gene up-regulation on the enlarged expression of the proto-oncogenes: c-myc, c-fos and the negative regulation of the suppressor gene p53. It is less well define if HIV-associated LC is the result of the immunodepression induced by the HIV, or represent a failure of the immunological surveillance as takes place in AIDS-defining malignancies. This case had an adequate immunological restoration and virological control when the diagnostic of malignancy was made. Several studies have suggested an association of severe immunodeficiency and progression to AIDS with the risk of LC. Other, did not show relation of the CD4+ T-cell count and the PVL with the occurrence of cancer.

Scarce evidences indicated that HIV infection can increase the carcinogenesis induced by tobacco and propitiates the imbalance between cell differentiation and proliferation as a consequence of genomic instability. At the same time, many antiretroviral drugs like zidovudine and lamividine may induce genomic toxicities and injuries to DNA, but the clinical significance of these observations has not been clarified.

The patient developed presumptive symptoms of malignancy several months before the hospitalization. Finally, he was classified as having a III-B stage tumor after the surgical-histopathological examination. Some studies have showed that the majority of HIV-infected patients with LC are symptomatic at the time of the diagnosis, reflecting an advanced or metastatic disease (III-B/IV stages) in the 70 to 90% of cases. Similar percentages can be found in HIV-negative individuals.

Another important aspect to take in consideration in the clinical evaluation of HIV-infected patient with suspicion of LC is the co-existence of other pulmonary diseases, such as tuberculosis, Pneumocystis jirovecii pneumonia (PCP), cytomegalovirus pneumonitis and pulmonary Kaposi sarcoma. Although the frequency of these AIDS-related morbidities has fortunately diminished after the introduction of HAART, they can motivate diagnostic difficulties that require the utilization of radiological and histological studies to confirm or rule out the diagnosis of cancer.

Few series have studied the radiological findings in HIV-positive patients with LC. The literature describes the typical existence of a medium diameter peripheral mass, frequently in upper lobes. Also several clinical series have reported the finding of mediastinal lymphadenopathies and pleural effusion even without knowing the primary locatong of the tumor. These observations are related to the predominantly peripheral location of the adenocarcinoma, the most frequent histological type in the general population and in this group of patients, paradoxically the one that less association had shown with smoking.

The patient had a squamous cell carcinoma with moderate differentiation. In developed countries squamous cell carcinoma was the most common type of LC until the end of the past century, but today only represents 29%. In the HIV-infected population this histological type groups between the 19 and the 52% of non small cell pulmonary cancers respect to the adenocarcinoma, whose frequency is estimated between 31 and 52%. The histological frequency of LC in HIV-positive individual has a similar pattern that in general population.

An issue of particular importance is the appropriate treatment according to the stage of LC, specially the surgical treatment. The protocols of surgical treatment do not vary in the presence of HIV infection, and it is well supported when the disease is localized and amenable to surgery, also in locally spread tumor, patients with adequate pulmonary function and good general state, regardless the immunological status. At present, results of anti-tumoral chemotherapy in these patients are scarce and inexact. A rate of progression of 50 to 70% has been reported after the first-line therapy.

Most available evidences suggest worst response to chemotherapy and radiotherapy in this group of patients. This might be explained by the pharmacological interactions and additive toxicity between anti-neoplasic drugs and some antiretroviral drug included in the HAART strategy, as well as by the increased risk of opportunistic infections related with anti-tumoral therapy.

The majority of studies have found smaller survival rate in HIV-positive as compared with HIV-
negative controls (4.5 vs. 10 months). One study showed that the 2 years survival did not change after the introduction of HAART (10%). The real impact of HAART on the incidence and survival of LC has not been observed as well as for other AIDS-related malignancies. Currently, LC is responsible for three times more cancer deaths than NHL, and it is responsible for 11 to 40% of all non-AIDS-defining cancer deaths.

Recently, data from two surveys on deaths in HIV patients conducted in France demonstrated the increasing prevalence of deaths attributable to non-AIDS-related cancers. Other observation from the Data Collection on Adverse Events of anti-HIV Drugs (D:A:D) indicated that long term HAART is associated with an increased risk of death related with non-AIDS-defining malignancies but not of death attributable to AIDS-defining malignancies. Likewise, this study demonstrated that severe immunodepression is a strong independent risk factor for death attributable not only to AIDS-defining but also to non-AIDS-defining cancers. In both studies, LC was the most common tumor among the different non-defining cancers.

Probably, the increased survival of HIV-infected patients secondary to the extension of HAART has resulted in long-term survival, and makes more probable the increasing of death rates attributable to non-HIV related diseases. In the case of malignancies, their occurrence might be mediated by the risk factors present in the general population, such as smoking for LC.

CONCLUSIONS

The available evidences indicate that in the presence of HIV infection LC occurs in younger individuals than in the general population, smoking is present in 80% of cases and adenocarcinoma is the most frequent histological type. The immunodepression has a controversial role in the risk of LC and it is still a matter of debate. Probably, HAART has not had a significant impact in the incidence of the disease, as it has occurred with AIDS-defining malignancies. There is a limited number of clinical observations about the efficacy and security of treatment protocols for LC in these patients. Thus, cancer prevention, screening, early diagnosis and improved management and surveillance should be included in routine long-term follow-up of HIV-infected individuals.

REFERENCES

Lung cancer and HIV infection


Correspondence:
Andrés Reyes-Corcho, MD, MSc, PhD.
Former Member of the Division of Internal Medicine and Infectious Disease. Gustavo Alderdegua Lima Teaching Hospital, Cienfuegos, Cuba.
E-mail: reycidalvaro@yahoo.es