



A RELAPSING CASE OF KAPOSÍ'S SARCOMA

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Abstract: *Kaposi's Sarcoma (KS) is one of the most common HIV-related malignancies. The incidence of KS has dramatically declined after the introduction of highly active anti-retroviral therapy (HAART). Some in vitro studies have reported direct antiangiogenic effects of protease inhibitors (PI). In some reports, tumour regression after starting a PI-based therapy has been described; however, non-randomized clinical trial have failed to confirm any significant difference between PI-based and non-nucleoside reverse transcriptase inhibitor-based regimens.*

Here we describe the case of a patient who experienced a relapse of KS after switching from a PI-based to a PI-sparing regimen.

KEY WORDS: *Kaposi's sarcoma, HIV, Oncology, Highly active antiretroviral therapy.*

INTRODUCTION

Kaposi's sarcoma (KS) is one of the most common HIV-related malignancies¹⁻³. KS is a multicentric angioproliferative cancer of endothelial origin⁴ affecting the skin, lymph nodes and visceral organs (lungs, gastrointestinal tract, liver and spleen)⁵. It is caused by the Human Herpesvirus-8 (HHV-8)⁶, which is also associated with multicentric Castleman's disease and Primary Effusion Lymphoma (PEL), a rare form of B-cell lymphoma⁷. KS is classified into four epidemiological types: classic form, affecting elderly men of Mediterranean or Eastern European Jewish ancestry; endemic form, often affecting children in Central and Eastern Africa; iatrogenic form, a typical form of immunosuppressed subjects; epidemic form or AIDS-KS⁴⁻⁸. KS is usually characterized by disseminated and pigmented skin lesions, involving the head and neck area, upper torso or extremities and evolving from a flat-stage (in which they are called "patch lesions") to a plaque-stage (in which

nodularity and oedema are more common)⁴⁻⁹. Immunodeficiency, including HIV infection, is a major risk factor for KS: in fact, although it can be diagnosed at any stage of HIV infection, KS occurs more commonly in the setting of severe immune suppression and elevated viral load¹⁻¹⁰. The primary goals of treatment of KS are lesion regression, palliation of symptoms and prevention of KS progression¹⁰. In this context, highly active antiretroviral therapy (HAART) represents an essential part of the treatment because of its multifactorial effects, including inhibition of HIV replication, diminished production of HIV-1 transactivating protein Tat, amelioration of immune response against HHV-8 and possibly direct antiangiogenic activity associated with PI administration^{4,10-12}.

We describe the case of a man with AIDS-related KS, who relapsed after switching from a PI-based to a PI-sparing regimen, when his CD4 T-cell count was more than 800 cells/ μ l and HIV viral load was below 1000 copies/ml.



Fig. 1. KS lesions extended quickly to the tibial region, ankles and feet bilaterally (2004, before treatment).

Case presentation

We present the case of a 46-year-old Caucasian man, who was diagnosed with HIV infection in 1994, after the appearance of KS skin lesions of the second toe of the left foot. CD4 T-cell count at baseline was 522 cells/ μ l.

In 1995 two new skin lesions appeared in the left foot and right ankle and they were surgically removed to perform an histological examination. Local relapses were observed until 1999 but no visceral lesions were reported.

In 1996, when the CD4 T-cell count was 451 cells/ μ l, antiretroviral therapy with didanosine (ddI) and zidovudine (ZDV) was started. In April 1998, antiretroviral therapy was changed to include a PI (saquinavir (SQV), stavudine (d4T) and lamivudine (3TC)). In November, when CD4 T-cell count was 675 cells/ μ l and HIVRNA 800 copies/ml, a new lesion was observed in the right arm. SQV was substituted with indinavir/ritonavir (IDV/RTV), obtaining a good viroimmunological response. KS was stable, with no characteristics of activity.

In April 2001, the patient experienced nephrolithiasis due to IDV as well as progressive lipodystrophy. As a consequence, HAART was modified, switching from a PI-based to a PI-sparing regimen with efavirenz (EFV). During the following months, CD4 T-cell count remained stable but HIV RNA was not completely suppressed.

In November 2003, there was a relapse of KS, with the appearance of new lesions involving the lateral margins of both feet. Therefore, HAART

was changed again, switching from efavirenz-tolopinavir/ritonavir (LPV/r).

Despite a good viroimmunological control, in March 2004 some new skin lesions appeared on the feet; in September, d4T was changed to tenofovir (TDF) and KS lesions extended quickly to the tibial region, ankles and feet bilaterally (Figure 1). No visceral lesions were found. Considering the rapid evolution of the disease, the patient was transferred to the National Cancer Institute of Aviano. He started two cycles of chemotherapy according to the CPT-11 protocol (Irinotecan), completing four more cycles at the Oncological Centre of the Garibaldi Nesima Hospital in Catania (March 2005). His HAART regimen included ZDV, 3TC, TDF and LPV/r. A complete response to treatment was observed, with progressive improvement of KS skin lesions, which are still in remission (Figure 2).

Currently, HAART regimen has been simplified and the patient is taking DRV/r and raltegravir (RAL), with a good viroimmunological response and complete clinical remission of KS.

Discussion

KS remains one of the most common tumours in HIV-infected individuals and is a significant cause of morbidity and mortality, particularly in sub-Saharan Africa¹³. Its clinical presentation is variable, ranging from small skin lesions in asymptomatic patients to invasive disease with visceral organ involvement¹⁰.



Fig. 2. Progressive improvement of KS lesions (2005, after treatment).

There are no standard therapy protocols. Treatment decision-making depends on the extent and rate of tumour growth, disease stage, HIV RNA viral load, CD4 T-cell count and patient's overall conditions⁴. Unfortunately, there is no eradicating treatment for KS, so durable remission may be a reasonable therapeutic goal^{4,10,14,15}. HAART is an essential part of the treatment of AIDS-KS¹⁶: effective antiretroviral regimens alone have been associated to both the reduction in the incidence of epidemic KS and the regression of the number and size of lesions. Indications for adding systemic chemotherapy to HAART include widespread skin involvement (>25 lesions), extensive cutaneous KS, symptomatic oedema, symptomatic visceral KS and immune reconstitution inflammatory syndrome (IRIS)¹⁰.

HAART has multifactorial effects on KS, including inhibition of HIV replication, amelioration of immune responses against HHV-8 and possible PIs antiangiogenic activity¹⁰: some data suggest that PIs may inhibit the activity and proliferation of endothelial cells and decrease the production of TNF- α , IL-6, IL-8 and VEGF¹³. However, several studies demonstrated that there is no difference between the use of PI-based and NNRTI-based regimens^{1,13,17}. In fact, HAART-induced immune

restoration seems to be implicated in the reduced incidence of KS, especially the visceral forms, independently of the antiretroviral class¹.

CONCLUSIONS

The advent of HAART has significantly reduced the incidence of KS in the HIV-infected individuals¹⁸. Though both PIs and NNRTIs are effective in inducing immune restoration, in our case switch to EFV was associated with suboptimal virological control and KS recurrence. Our case suggests that for patients with KS the use of a PI-based regimen may represent the most appropriate strategy, alone or in combination with systemic and local therapy.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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