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Hodgkin lymphoma in an HIV infected patient: relapses, poly-pathologies and complexity of the therapeutic management

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ABSTRACT:

Hodgkin lymphoma (HL) in patients with HIV/AIDS is a challenging task because of the lack of established treatment and the need of meticulous attention to drug-drug interactions between highly active antiretroviral agents (HAART) and standard multi-agent chemotherapy. We report a case of recurrent HL in a patient, affected by HIV/AIDS and HCV-infection. The complex therapeutic management has been described; integrase inhibitors have shown a favorable interaction profile, allowing the completion of the chemotherapy regimen.

Keywords: Antiretroviral therapy, HIV, Integrase inhibitors, Hodgkin lymphoma.

INTRODUCTION

Despite successful anti-retroviral therapy (ART) and the reduction of AIDS-related cancers, the Hodgkin lymphoma (HL) incidence, as well as the other non-AIDS-defining cancers, is increasing[1]. The clinical management of HL is complicated in the HIV population as it is usually diagnosed at an advanced stage of HIV disease, chemotherapy has multiple drug interactions with antiretrovirals (ART) drugs and current guidelines do not provide specific guidance on the most appropriate regimen. We describe the complexity in practical management of a patient and the need for multidisciplinary collaboration in therapeutic decisions.

CASE PRESENTATION

We report the case of a Caucasian man with a long history of HIV and HCV infection both acquired in 1984 for past intravenous drugs use. In 1996 he presented several AIDS-defining diseases, specifically cerebral toxoplasmosis and cytomegalovirus retinitis. On September 2001 the patient reached his CD4 lymphocytes nadir (one cell/mmc), and HIV viral load of 330,000 copies/ml. He had taken in the past several combinations of ART with low adherence because of a borderline personality disorder not properly diagnosed and treated. In July 2003, after entering a residential care facility and adequate treatment of his mental disorder, he began successful ART with atazanavir boosted by ritonavir, stavudine, tenofovir.

The choice of medicines was based on to the resistance profile to different anti transcriptase (RT gene mutations drugs: 74V 103R 184V 190A 179D 122E 123E 196E 123G 142v 178m 214L). Subsequently, the viremia was always undetectable and CD4 + lymphocytes showed a slow recovery (between 2004 and 2005, the CD4 range was between 100 and 200 cells/mmc). In 2005 he presented a febrile illness with fatigue anorexia, weight loss and sweating. He was treated unsuccessfully with intravenous antibiotics for a presumed bacterial infection. Then, he was properly diagnosed as Hodgkin's lymphoma (stage IV B with a deeper involvement of lymph nodes (above- sub-diaphragmatic) and bone marrow in the spine of the pelvis). For this reason, with the support and control of hematologists, the patient has been treated with the chemotherapy scheme of ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) for a total of 6 cycles but with doses reduced because of toxicity. The period of chemotherapy was not easy to handle for multiple complications, but ultimate-

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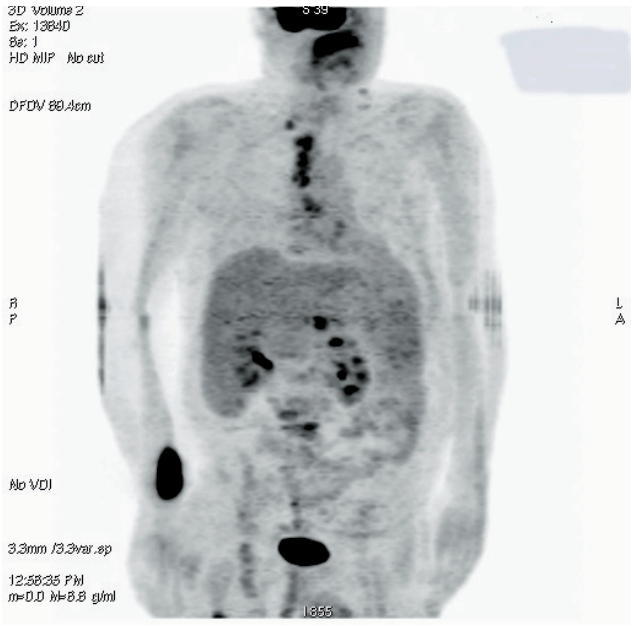

Figure 1. PET CT examination documents the lymphoma recurrence at the level of the mediastinal lymph nodes and in the lumbar spine.

ly the patient achieved a complete remission of the disease. ART was changed and the patient was treated with atazanavir/ritonavir, tenofovir, emtricitabine. In May 2007, CD4 + lymphocytes were 239/ml.

Two years after the date of lymphoma remission, the patient had a relapse, and then was treated again with a second-line salvage chemotherapy regimen consisting of four cycles of combined ifosfamide, gemcitabine, vinorelbine (IGEV). This regimen reached a new disease remission. The doses of chemotherapy were reduced for toxicity problems.

The patient was diagnosed with congestive heart failure at the end of the 4th cycle, which made impossible the goal of the autologous transplantation.

Figure 1 demonstrates the positron emission tomography/computed tomography (PET/CT) image documenting the recurrence of lymphoma. Arterial hypertension, metabolic syndrome, multifactorial heart disease with an episode of congestive heart failure, a chronic obstructive pulmonary disease (related to the cigarette smoking and chemotherapy) with type I respiratory failure was documented in this patient. He had to take many medications such as chlorpromazine, orphenadrine, risperidone, sertraline, diazepam, gabapentin, enalapril, furosemide, omeprazole; occasionally he took bronchodilators. The HL occurred again. The patient was treated for heart and lung problems during the 3rd and 4th relapse with a salvage chemotherapy including etoposide and procarbazine, judged by the hematologists as the most appropriate and least risky.

Patient's condition was better during the 5th HL relapse. New more aggressive salvage chemotherapy (DHAP – cisplatin, cytarabine, dexamethasone) was chosen to try again to consider the autologous program. The pharmacological management of patient has been particularly complicated during this period of disease remissions and relapses. ART was modified with ritonavir, darunavir, emtricitabine and raltegravir, considering the frequent use of proton pump inhibitors and the availability of new molecules with.

The chemotherapy-induced vomiting was managed by the suspension of Darunavir boosted ritonavir. The ART was continued with raltegravir-tenofovir-emtricitabine scheme allowing to give the full chemotherapy dose and to improve temporarily the patient's condition. The ART was effective throughout the long course of

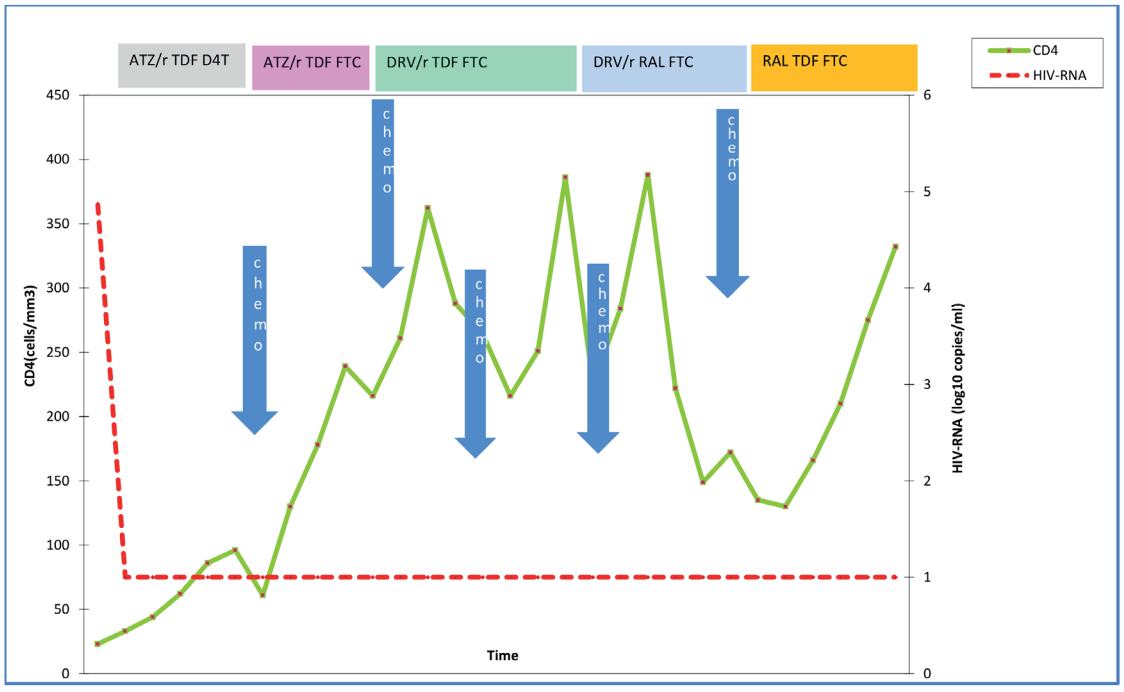

Figure 2. Patient's history of chemotherapy, CD4 cells count and HIV-RNA level. ATZ/r = atazanavir/ritonavir, TDF = tenofovir, D4T = stavudine, FTC = emtricitabine, DRV/r = Darunavir/ritonavir, RAL = raltegravir.

chemotherapy; the HIV viremia was always undetectable. The CD4 + cell count, HIV-RNA and chemotherapy are reported in Figure 2.

TREATMENT DECISIONS AND FOLLOW-UP

Multiple illnesses are identified in HIV-positive individuals. Careful thought and a continuous dialogue with specialists from other disciplines are extremely important. The patient's management requires different skills and approach to drug interactions, not always known. This clinical case was managed with a close collaboration with the hematologist, cardiologist and psychiatrist, whereas because of toxicity, the chemotherapy was reduced on several occasions. Considering co-morbidity and required pharmacological treatment the choice of ART becomes more limited. There are no specific recommendations for the management of patients treated with chemotherapy in the guidelines for antiretroviral therapy. Recent studies[2] have demonstrated the benefits of integrase inhibitors regimen. Italian Guidelines[3] released in 2013 suggest the use of integrase inhibitors, mainly for fewer drug interactions. A regimen with less interaction and toxicity allows to treat the patient better and to give full chemotherapy doses. Particularly, the interactions between antineoplastic[4] and antipsychotic drugs[5] arise since the PI and non-nucleoside reverse transcriptase inhibitors have both significant interactions with many of the antineoplastic drugs. Integrase inhibitor represents a very favorable profile of interactions, allowing a successful course of treatment in the presented case.

Conflict of Interests:

The Authors declare that they have no conflict of interests.

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