Case Reports

Primary non-Hodgkins lymphoma of the ovary in the background of human immunodeficiency virus (HIV): A bold and curative approach to treatment

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Summary

Non-Hodgkins lymphoma of the ovary is a rare disease and there is only one previously documented case arising in a patient with human immunodeficiency virus (HIV). In this report, the authors discuss the management of a case of non-Hodgkins Lymphoma of the ovary occurring in a patient with HIV and demonstrate that treatment regimens may be successfully implemented in this immunocompromised population without an increase in adverse effects.

Key words: Non-Hodgkins Lymphoma; Ovary; Human Immunodeficiency Virus.

Introduction

There were an estimated 39.5 million (34.1 million-47.1 million) people worldwide living with HIV at the end of 2006 according to the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organisation (WHO). Based on UNAIDS estimates, approximately 63% of people living with HIV in the world are from the sub-Saharan Africa region [1]. Just over 5,000,000 South Africans were HIV-positive in 2004, which constitutes 11% of the population [2].

There has been considerable improvement in access to antiretroviral therapy for adults in sub-Saharan Africa with an estimated 100,000 people receiving antiretroviral therapy in 2003, increasing to more than 1.3 million in 2006 [3]. In South Africa antiretroviral treatment is initiated once the CD4 count is below 200 cells/µl, in the absence of other AIDS-defining illnesses.

Inkosi Albert Luthuli Hospital based in Durban, South Africa, is a state-run facility privileged to have access to the latest chemotherapeutic and biologic therapies as well as a fluorodeoxyglucose (FDG)-positron emission tomography/computerised tomography (FDG-PET/CT) scan facility. This institution also has to contend with the raging HIV pandemic and HIV-associated malignancies. The lack of a cancer registry in South Africa is a major limiting factor towards performing an accurate assessment of the impact of HIV-associated malignancies in our health system [2].

We discuss the presentation and management of a rare case of HIV-associated primary non-Hodgkins lymphoma of the ovary.

Case Report

A 25-year-old para 1 woman presented with an eight-month history of right-sided iliac fossa pain. There was no associated weight loss or night sweats reported.

On enquiry into previous medical illnesses, we learned that she had been diagnosed with extrapulmonary tuberculosis, diagnosed on a positive acid fast bacilli (AFB) culture of the ascitic fluid in 2000. She was treated with a course of anti-TB treatment for 12 months. She was also diagnosed with HIV in 2005 and has been on antiretroviral treatment since diagnosis.

She was initially evaluated at her regional hospital. An ultrasound pelvis done showed a mixed echogenic mass with solid and cystic components noted superior to the uterus and extending into both adnexae measuring approximately 7.7 cm in diameter. A laparotomy was performed at the referral centre which revealed a large cystic right ovarian tumour measuring 16 cm x 17 cm x 10 cm. In view of her age and parity, only a right oopherectomy was performed. Histology revealed high-grade non-Hodgkins B cell lymphoma with CD20 immunopositivity. Positive staining for Ebstein-Barr virus was also demonstrated.

She was subsequently referred to our clinic. We requested a FDG-PET/CT scan (Figure 1) as a baseline staging investigation which revealed an FDG avid mass in the right adnexal region. Sub-centimetre paraaortic lymph nodes were noted on computed tomography (CT) scan with normal FDG uptake.

The patients' serum beta-2 microglobulin (beta 2M) level was 2.7 mg/l and serum lactate dehydrogenase (LDH) level was 305 U/l. The patient refused a bone marrow aspirate, and trephine biopsy. Her baseline CD4 count was 468 cells/µl.

She was subsequently started on a course of R-CHOP (Rituximab 375 mg/m^2 IV d1, Cyclophosphamide 750 mg/m^2 IV d1, Doxorubicin 50 mg/m^2 IV d1, Oncovin 1.4 mg/m^2 IV d1, Prednisone 100mg/day p.o D1-5). She received six cycles of this regimen. Her CD4 count was repeated thereafter and was found to be 369 cells/µl. The use of systemic chemotherapy and rituximab was well tolerated by the patient without haematological toxicities.

Response to treatment was evaluated with a repeat FDG-PET/CT scan (Figure 2).

She subsequently received involved field radiotherapy (IFRT) to a dose of 30 Gy in 2 Gy fractions to the right adnexal region. She did not experience any adverse effects to the radiotherapy. The patient remains alive and well to date.

Revised manuscript accepted for publication July 20, 2009

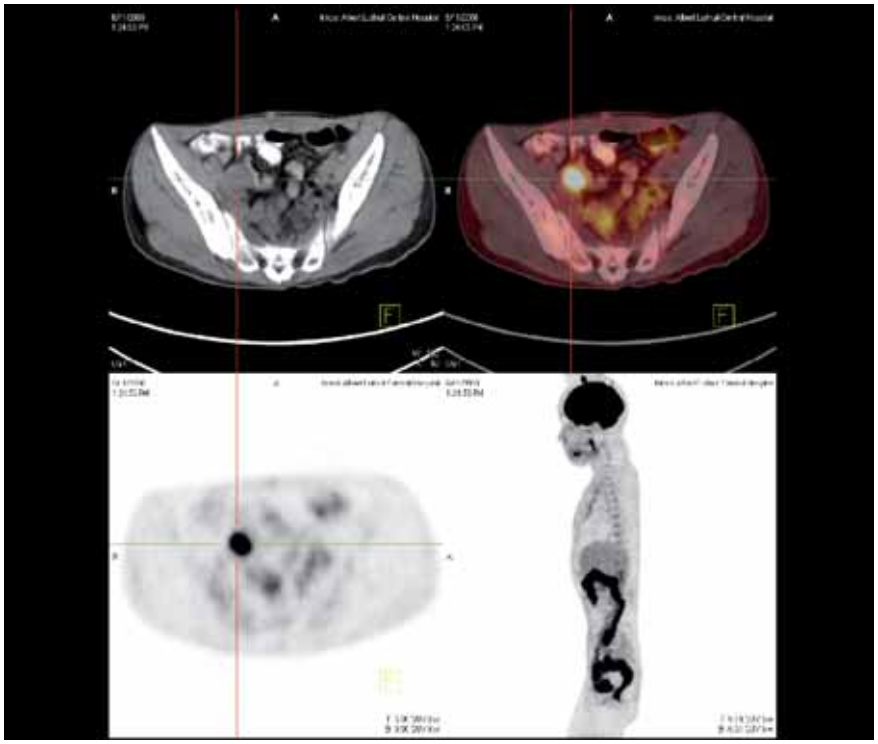
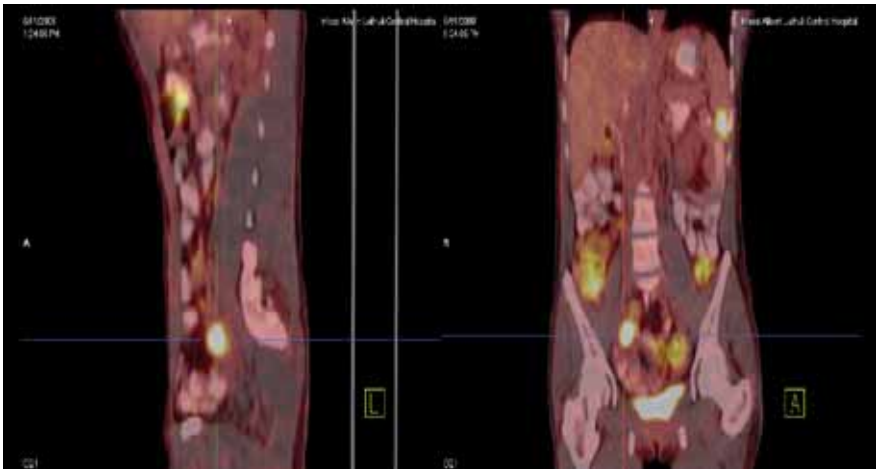
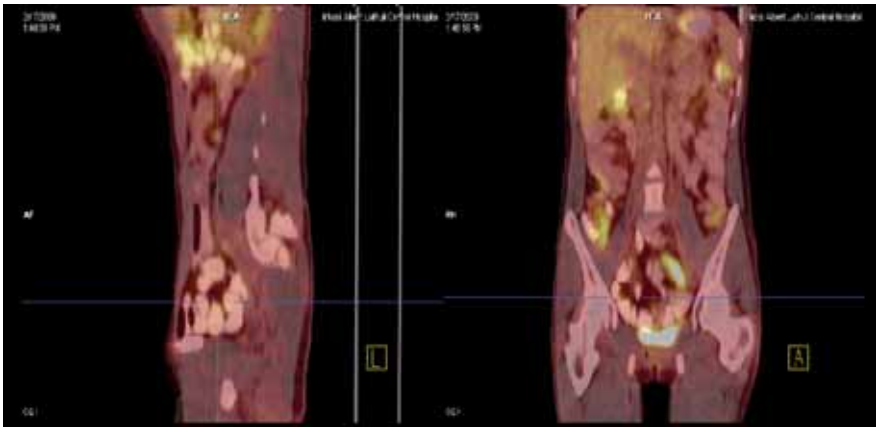


Figure 1. — FDG- PET/CT scan image on presentation with FDG uptake noted in the right adnexal region.



A. Pre-treatment



B. Post-treatment

Figure 2. — Comparison of FDG-PET scan images before and after treatment.

Discussion

Non-Hodgkins lymphoma (NHL) occurs 60-200 times more frequently in the HIV-infected population than in the general population [2]. Approximately 1-6% of HIV-positive patients develop lymphoma each year [4].

The incidence of NHL appears to be on the wane with the increasing use of highly active antiretroviral therapy (HAART) [4]. It is thought that immune reconstitution accompanying the use of HAART offers a protective effect on the development of AIDS-related lymphoma and may account for the declining incidence of NHL. A decline in CD4 counts has also been documented to increase the likelihood of developing lymphoma [5].

The vast majority of lymphomas observed in the HIV population are of B cell origin. The classification of HIV-associated lymphomas can be broadly divided into five main groups: polymorphic lymphoid proliferations (5% of all HIV-associated lymphomas), systemic NHL of various histological subtypes that are more commonly seen in the immunocompetent (80%), plasmablastic lymphoma of the oral cavity (3%), primary central nervous system lymphoma (15%), primary effusion lymphoma (4%), and Hodgkin's lymphoma. The latter is not an AIDS-defining illness [4].

Systemic NHL occurs more commonly in advanced HIV infection, with CD4 counts below 100 cells/µl. Most of these represent high-grade lymphomas with patients often presenting with advanced stage. The most frequent sites of involvement are the gastrointestinal tract, lung, liver, bone marrow and central nervous system [4].

Extranodal NHL accounts for 20-24% of all NHL. They most commonly arise from the gastrointestinal tract, lung, central nervous system and skin as well as the thyroid and salivary glands. While the female genital tract and particularly the ovary may be sites of metastatic involvement, primary genital tract lymphomas are rare neoplasms, accounting for less than 0.5% of all genital cancers and representing 1.5% of all non-Hodgkin's disease. The most common genital sites are the ovary, cervix and corpus of the uterus. Primary lymphomas of the vagina or vulva are uncommon. These tumours usually occur in the 5th decade of life, although the age at presentation is variable. The common presenting symptoms include intermittent vaginal bleeding, dyspareunia, vaginal discharge and pelvic pain [6].

The commonest histological subtype of primary ovarian NHL is diffuse large B-cell lymphoma. Genital lymphomas tend to have a less aggressive course than nodal NHL. It also has a low incidence of recurrence and is associated with a good prognosis. The 5-year survival rate is between 80-90% [6].

On account of the rarity of the disease, there is no established consensus on management. Based on the literature, the mainstay of treatment for primary genital lymphomas is radiotherapy alone or in combination with surgery and/or chemotherapy [6].

In the pre-HAART era, prognosis for patients with AIDS-related lymphomas was dismal with a median survival of five to eight months. Reduced-dose chemotherapy regimens were often used in these patients. Currently patients are treated with HAART and standard dose chemotherapy, which has resulted in response rates comparable to those seen in immunocompetent patients [2]. The introduction of HAART has resulted in an improvement in overall survival when compared to historical controls based on recent reports from a number of groups. The complete remission rate and overall survival with CHOP chemotherapy has improved with the addition of HAART to chemotherapy resulting in a shift in the treatment goal towards complete remission [5].

Adverse effects of chemotherapy include myelosuppression resulting in opportunistic infections as well as drug interactions between chemo-agents and antiretrovirals [2]. Prophylaxis against opportunistic infections remains a major consideration due to the anticipated decline in CD4 cell counts while on chemotherapy in both immunocompetent and immunocompromised patients. Established guidelines in the management of HIV infection suggest that prophylaxis against *Pneumocystis carinii* pneumonia should commence when the CD4 count falls below 200 cells/mm^3 and against mycobacterium avium complex when it falls below 50 cells/mm^3 [5].

HIV-associated systemic NHL has frequent expression of the CD20 receptor which has led to extensive investigations into the role of rituximab in combination with chemotherapy [4]. Rituximab in addition to chemotherapy has yielded improved response rates (70% complete response with a 59% 2-year survival) [5].

There is only one other reported case on HIV-associated primary NHL of ovary, although in that case the patient was unable to receive treatment due to financial constraints [7]. In countries such as South Africa, we are constantly challenged by the need to offer standard-of-care treatment protocols in the backdrop of the HIV/AIDS epidemic and its attendant morbidities. This case emphasises the need for an appropriate patient selection to ensure that HIV-positive patients may still be in a position to be treated with regimens utilised in immunocompetent patients.

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