A Rare Case of Good Outcome of Hodgkin Lymphoma in a Patient with HIV on Antiretroviral Therapy (ART)

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Patient: Male, 58-year-old
Final Diagnosis: Nodular lymphocyte-predominant Hodgkin lymphoma
Symptoms: Lymphadenopathy
Medication: —
Clinical Procedure: Lymph node biopsy
Specialty: Infectious Diseases • General and Internal Medicine • Oncology

Objective: Unusual clinical course
Background: Recent reports have shown an increased incidence of Hodgkin lymphoma (HL) in patients treated with antiretroviral therapy (ART) for human immunodeficiency virus (HIV) infection. This report is of a case of nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) with a good outcome in a 58-year-old Nigerian HIV-positive man who was being treated with ART.

Case Report: A 58-year-old HIV-positive man presented to a clinic for evaluation of a left axillary mass. He was diagnosed with HIV in 2005, which was well-controlled by ART. He reported intermittent swelling in the left axillary region for several years. Results of a physical examination were significant for mild tender left anterior axillary lymphadenopathy. He had a computed tomography (CT) scan of the chest and neck, which showed left axillary adenopathy, with the largest measuring 3.5×2.0 cm. A staging positron emission tomography-computed tomography (PET/CT) showed focal uptake in 2 left axillary lymph nodes with no other sites involved. He underwent excision of the left axillary lymph node. Histopathology was consistent with nodular lymphocyte-predominant-type Hodgkin’s lymphoma (NLHPL). He underwent radiation therapy with a total dose of 3600 centigray (cGy) according to National Comprehensive Cancer Network (NCCN) guidelines. The 5-month follow-up PET/CT scan showed no evidence of malignancy.

Conclusions: We present a case of HIV-associated NLHPL that had an indolent course and a good treatment outcome. This case highlights the importance of regular physical examination in HIV patients while on treatment with ART and accurate diagnosis of the cause of lymphadenopathy to prevent extra-nodal spread in cases of lymphoma.

Keywords: Antiretroviral Therapy, Highly Active • HIV • Hodgkin Disease

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Hodgkin lymphoma (HL) is the most common acquired immune deficiency syndrome (AIDS)-defining malignancy in human immunodeficiency virus (HIV)-infected patients, usually presenting at an advanced stage and in unusual locations in individuals with HIV/AIDS [1]. A literature review showed that the risk of developing Hodgkin lymphoma (HL) is about 10 times higher in HIV-positive patients compared to HIV-negative patients [2]. The mechanism involves an increased CD4+ T cell response providing antiapoptotic pathways and mechanisms for immune escape by tumor cells [3]. The incidence of Hodgkin’s Lymphoma has increased in patients with HIV following use of ART, with the most common histological type being mixed cellularity lymphoma [4]. HL in HIV patients usually presents aggressively with unfavorable subtype and poor therapeutic outcome compared with non-HIV patients [1]. This report is of a case of nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) with a good outcome in a 58-year-old HIV-positive man while treated with ART (Figures 1,2).

Case Report

A 58-year-old HIV-positive man presented to clinic for evaluation for mass in the left axilla region for several years. He was diagnosed with HIV in 2005, which was well-controlled on ART. He reported intermittent swelling in the left axillary region for several years. He denied fever, chills, night sweats, or weight loss. A physical examination at the time was unremarkable with the exception of mild tender left anterior axillary lymphadenopathy. Laboratory workup revealed a total leukocyte...
count of 7.1 K/uL, hemoglobin of 16.1 g/dl, and platelet count of 304 K/uL. Renal and liver function test results were within normal limits. CD4 count was 1262 cells/L and viral load was within the undetectable range. He underwent a computed tomography (CT) scan of chest and neck, which showed bilateral enlarged jugular chain lymph nodes and left axillary adenopathy, with the largest measuring 3.5×2.0 cm, suspicious for an underlying neoplastic process. He underwent a staging positron emission tomography-computed tomography (PET/CT), which showed focal uptake in 2 left axillary lymph nodes measuring 1.8×1.3 cm and 1.3×1.0 cm, with no other site involved. He underwent excision of the primary left axillary lymph node. Histopathology of the axillary lymph node showed nodular replacement of normal architecture with histiocytes, lymphocytes, and typical lymphocyte-predominant (LP) cells (‘popcorn’ cells), which expressed BCL-6, CD-20, and EMA, consistent with a diagnosis of NLPHL. He received site radiation therapy with a total dose of 3600 centigray (cGy) in 18 fractions at a daily dose of 200 cGy per fraction for 1 month duration according to National Comprehensive Cancer Network (NCCN) guidelines. He had a 5-month follow-up PET/CT scan, which showed no evidence of malignancy.

Discussion

Since the introduction of ARTs, the incidence of opportunistic infections and AIDS-defining cancers, such as Kaposi sarcoma, invasive cervical cancer, and aggressive B cell non-Hodgkin’s lymphoma (NHL), has decreased in HIV-infected individuals [5]. Compared to the dramatic decrease in incidence of NHL with the introduction of ART, the incidence of HL has increased in patients with HIV following use of ART [4,5]. The mechanism is believed to be immune restoration characterized

Figure 2. Photomicrographs of the immunostaining of the axillary lymph node for B cell lymphoma 6 (BCL6) protein and epithelial membrane antigen (EMA), which were consistent with a diagnosis of nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). (A) The expression of B cell lymphoma 6 (BCL6) protein. Magnification ×100. (B) The expression of EMA by the cell membrane of the scattered single lymphocyte-predominant (LP) cells (‘popcorn’ cells), which is characteristic of NLPHL. Magnification ×100.
by an increased CD4+ T cell response providing antiapoptotic pathways allowing immune escape by tumor cells [3]. Hodgkin lymphoma is the most common non-AIDS-defining malignancy in HIV patients, usually presenting at an advanced stage and in unusual locations in individuals with HIV/AIDS [1].

The World Health Organization (WHO) has classified HL into 2 pathological types – nodular lymphocyte-predominant HL and classical HL (cHL) – with cHL type mostly associated with HIV infection [6]. cHL can be further sub-grouped, with the most frequent among patients living with HIV being mixed cellularity, followed by nodular sclerosis and lymphocyte-depleted [7]. In a cohort study involving 104 patients with HL treated with ART, the predominant histologic subtype was mixed cellularity, with most patients presenting with “B” symptoms and extra-nodal involvements [8]. Our patient was diagnosed with nodular lymphocyte-predominant type (NLPHL).

NLPHL is an indolent subtype of HL [9] accounting for 5% of patients diagnosed with HL [9]. It is predominantly seen in males and African Americans [10]. The malignant cells seen in NLPHL are referred to as lymphocyte-predominant (LP) cells, which are derived from transformed germinal center B cells [11]. Most patients present with advanced-stage disease (Ann Arbor stage III-IV), although the incidence of early-stage disease appears to be increasing in the cART era, and most patients still present with systemic B symptoms and extra-nodal involvement [12,13]. Our patient presented with lymphadenopathy as the only clinical feature, with no B symptoms or extra-nodal involvement.

Regardless of HIV status, once HL is diagnosed, patients are expected to undergo pretreatment clinical evaluation, which involves detailed history, physical examination, laboratory evaluation such as complete blood cell count, chemistry tests, CD4 count, HIV viral load and viral serologies. Radiographic staging with positron emission tomography (PET)/computed tomography (CT) is also required to identify any extra-nodal involvement.

Diagnosis of HL is made based on tissue biopsy with immunophenotypic and morphological analysis [12]. In NLPHL, histology findings reveal neoplastic lymphocyte-predominant (LP) cells within the background of cells in nodular growth pattern. LP cells typically have immunophenotypic staining positive for CD20, BCL-6 (B cell lymphoma), and epithelial membrane antigen (EMA) and are negative for CD-15 and CD-30 [14]. Cells in the background nodular growth pattern can either be T or B lymphocytes, with immunophenotypic staining positive for CD3, CD4, CD57, CD21, and CD23 [14]. Our patient was noted to have atypical lymphoid cells positive for BCL-6, CD-20, and EMA.

Treatment is based on staging and several prognostic factors [12]. Most patients present with advanced-stage disease and are either treated with chemotherapy or radiation, or a combination of chemotherapy and radiation, along with ART in HIV-positive patients. Our patient had non-bulky early-stage IA NLPHL, which involved a single lymph node region, requiring radiation therapy based on National Comprehensive Cancer Network (NCCN) guidelines [15].

In terms of prognosis, several prognostic factors have been found to be associated with HIV-HL. Some of the adverse prognostic factors include histology subtype-MC, presence of systemic symptoms, and extra-nodal involvement, while good prognostic factors identified were CD4 count >100/UL and ART use [4]. Prior to the ART era, the prognosis of HIV-HL was poor; however, since the advent of ART, HIV-HL has had favorable outcomes and survival. A study that compared 83 patients with HIV-HL treated with ART and 21 patients with HIV-HL not on treatment found patients on ART had significantly better outcomes compared to patients not on ART [8]. Another study compared 159 HIV-positive patients with lymphoma with non-HIV patients with HL and found that even through high-risk features were associated with HIV-HL patients, the prognosis of these patients treated with cART and chemotherapy was markedly better and was similar to that of non-HIV-infected patients [13,16]. Our patient had LP histology, absence of B symptoms, extra-nodal involvement, and high CD4 count, favoring a good outcome.

Conclusions

This report has presented a case of HIV-associated NLHPL that had an indolent course and a good treatment outcome. This case highlights the importance of regular physical examination in HIV patients while on treatment with ART, and accurate diagnosis of the cause of lymphadenopathy to prevent extra-nodal spread from lymphoma.

Declaration of Figures’ Authenticity

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