



Case Report

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An Unusual Presentation of Nodular Lymphocyte-Predominant Hodgkin Lymphoma while on Antiretroviral Therapy - A Case Report

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Abstract

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 HIV-positive man who was on ART.

Case Presentation: A 58-year-old HIV positive male presented to clinic for evaluation for mass in the left axilla region for several years. He was diagnosed with HIV in 2005 and well-controlled on ART. Physical examination was remarkable for tender left anterior axillary lymphadenopathy. Laboratory workup were within normal limits. CD4 count was 1262 cells/L and viral load was undetectable. He underwent computed tomography (CT) scan of chest and neck which showed left axillary adenopathy as well as staging Positron emission tomography-computed tomography (PET/CT) that showed focal uptake in two left axillary lymph nodes. He underwent excision of the primary left axillary lymph node. Histopathology showed nodular replacement of normal architecture with histiocytes, lymphocytes, and typical lymphocyte-predominant (LP) cells, which expressed BCL-6, CD-20, and EMA, consistent with a diagnosis of NLPHL. Patient had site radiation therapy and had a 5-month follow-up PET/CT scan which showed no evidence of malignancy.

Conclusion: This report presents a case of HIV-associated NLHPL that had an indolent course and 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 lymphomas.

Keywords

Human Immunodeficiency Virus (HIV) infection, Antiretroviral Therapy (ART), Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)

Background

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 HIV/AIDS individuals [1]. A literature review showed that the risk of developing Hodgkin lymphoma (HL) is about 10 times higher in HIV patients compared to HIV-negative patients [2]. The Hypothesis is based on 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 usually presents aggressively with unfavorable subtype and poor therapeutic outcome, when 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.

Case Presentation

A 58-year-old HIV positive male presented to clinic for evaluation for mass in the left axilla region for several years. He was diagnosed with HIV in 2005 and 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. Physical examination at the time was unremarkable with 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 tests were within normal limits. CD4 count was 1262 cells/L and viral load was within undetectable range. He underwent computed tomography (CT) scan of chest and neck which showed bilateral enlarged jugular chain lymph nodes and left axillary adenopathy with largest measuring 3.5cm × 2.0cm suspicious for underlying neoplastic process. Patient had a staging Positron emission tomography-computed tomography (PET/CT) that showed focal uptake in two 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, or 'popcorn' cells, which expressed BCL-6, CD-20, and EMA, consistent with a diagnosis of NLPHL. Patient had site radiation therapy with 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 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

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of ART, the incidence of HL has increased in patients with HIV following use of ART [4,5]. The hypothesis behind this is believed to be due to immune restoration characterized by an increased CD4+ T cell response providing antiapoptotic pathways and mechanisms for immune escape by tumor cells [3]. Hodgkin Lymphoma is the most common non-AIDS defining malignancy in HIV patients presenting usually at an advanced stage and in unusual locations in HIV/AIDS individuals [1].

WHO has classified HL into two pathological types - nodular lymphocyte predominant HL and classical HL (cHL), with cHL type mostly associated with HIV infection [6]. cHL is further be 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, predominant histologic subtype was mixed cellularity, with most patients presenting with B symptoms and extra-nodal involvements [8]. In this case, our patient was diagnosed with Nodular Lymphocyte Predominant Type (NLPHL).

NLPHL is an indolent subtype of HL accounting for 5% of patients diagnosed with HL [9]. It is predominantly seen in male and African Americans [10]. The malignant cells seen in NLPHL are referred to as Lymphocyte-Predominant (LP) cells are derived from transformed germinal center B cells [11]. Most patients present with advanced-stage disease (Ann Arbor stage 3-4), though the incidence of early-stage disease appears to be increasing in the cART era, majority of 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 involvements.

Regardless of HIV status of patient, 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 involvements.

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 CD-20, BCL-6 (B-cell lymphoma), 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 usually 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 identified that is associated with HIV-HL. Some of the adverse prognostic factors include histology subtype-MC, presence of

systemic symptoms, extra-nodal involvement while good prognostic factors identified were CD4 count >100/UL, and ART use [4]. Prior to ART era, prognosis of HIV-HL was poor; however, since the advent of ART, HIV-HL has had favorable outcomes and survival. A study compared 83 patients with HIV-HL treated with ART and 21 patients with HIV-HL not on treatment and found patients on ART had significant 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 though high risk features were associated with HIV-HL patients, the prognosis of these patients, treated with cART and chemotherapy markedly improved and was like non-HIV-infected patients [13]. Our patient had LP histology, absence of B symptoms, extra-nodal involvement as well as high CD4 count favoring good outcome.

Conclusion

This report has presented a case of HIV-associated NLPHL 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.

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