CASE REPORT

Remission of a primary effusion lymphoma with initiation of highly active antiretroviral therapy and antiviral therapy in a previously untreated HIV-positive patient

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Abstract

Introduction: Primary effusion lymphoma (PEL) is a rare, high-grade large B-cell lymphoma characteristically associated with human herpes virus (HHV) 8 and often with coinfection by Epstein-Barr virus (EBV). Most patients present in the context of immunodeficiency, commonly with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). These lymphomas are often confined to the pleural, pericardial, or peritoneal spaces as lymphomatous effusions with no evidence of solid tumor. No standard line of treatment exists for patients with PEL and the prognosis remains poor.

Case description: We describe here the case of a 47-year-old man with a history of HIV managed with observation alone due to a low viral load and CD4 count of ~1000 cells/µl who presented with fatigue, dyspnea on exertion, and orthopnea discovered to be secondary to a new pericardial effusion. Cytology revealed an HHV-8 and EBV-associated primary effusion lymphoma. Given the new diagnosis, the patient started highly active antiretroviral therapy (HAART) and antiviral therapy and subsequently reached complete remission with no further treatment. Five years later, the patient remains with no evidence of disease.

Conclusions: Although the prognosis for PEL is usually poor, the remission of disease and lack of recurrent symptoms suggest that HAART and antiviral therapy alone in this patient was effective in controlling the lymphoma. After two years on antiviral therapy, the patient remains disease free.

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Key words: HIV/AIDS, HAART, primary effusion lymphoma.

Introduction

Primary effusion lymphoma (PEL) is a rare, high-grade large B-cell lymphoma [1]. PEL is characteristically associated with human herpesvirus 8 (HHV-8), and often with coinfection by Epstein-Barr virus (EBV) [2]. Most patients present in the context of immunodeficiency, commonly with a diagnosis of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). These lymphomas are largely confined to body cavities, such as the pleural, pericardial, and peritoneal spaces, as lymphomatous effusions without evidence of solid tumors. No standard line of treatment currently exists for patients with PEL and the prognosis remains poor with median survival of six months [1]. Here we describe a case of an HIV-positive patient who presented with stage IE pericardial PEL and reached remission on initiation of highly active antiretroviral therapy

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(HAART) and antiviral therapy alone. The patient continues to be followed and remains no evidence of disease (NED) five years after initial diagnosis.

Case description

A 47-year-old man presented in August 2013 with fatigue, dyspnea on exertion, and orthopnea. He had a prior history of HIV diagnosed in 2007, which was being managed with observation given a low viral load and a CD4 count of ~1000 cells/µl. Other significant past medical history included hepatitis B and C infection with positive antibodies and negative viral loads. An echocardiogram in August 2013 revealed a large, new pericardial effusion. Therapeutic pericardiocentesis resolved the symptoms and cytology showed large atypical cells consistent with primary effusion lymphoma. Immunohistochemistry was positive for CD30, CD45, CD138 and negative for CD20, CD79a, ALK-1, and T-cell markers. Molecular studies were positive for HHV-8, EBV, and immunoglobulin light chain gene rearrangement. The patient started antiviral therapy including antiretroviral therapy (dolutegravir, emtricitabine and tenofovir), valganciclovir and valacyclovir, all in standard doses immediately after diagnosis. Positron emission tomography/computed tomography (PET/CT) displayed diffuse, mildly fluorine-18 fluorodeoxyglucose (FDG)-avid nodes (standardized uptake value (SUV) study maximum 3.6 mg/dl, maximal diameter 1.3 cm). Bone marrow biopsy showed no evidence of disease. Mild lymphadenopathy seen on PET was attributed to active HIV infection.

The patient presented to our institution for the first time in October 2013. He was feeling well aside from anxiety regarding his diagnosis. Review of systems and physical examination were unremarkable. Review of his prior cytology confirmed primary effusion lymphoma. Repeat PET scan showed no current evidence of disease following one month of treatment with the above antivirals. Additionally, his HIV and EBV viral loads were undetectable and his HHV-8 viral load was 5,463 copies/ml.

A repeat chest X-ray and echocardiogram showed no evidence of disease, and management was continued with HAART, observation, and symptomatic treatment. At the last follow-up, the patient had been on HAART therapy and antiviral therapy for over five years and remained NED with no symptoms of pericardial effusion, normal CD4 cell count as well as undetectable HIV, EBV and HHV-8 viral loads.

Conclusions

The remission of disease and lack of recurrent symptoms suggest that antiviral therapy with HAART and valganciclovir is enough to control lymphoma in this patient. Although the prognosis for PEL is usually poor, after two further years on antiviral therapy, the patient remains disease free. As his CD4 count was in the normal range at lymphoma diagnosis, and as he received multiple agents, we cannot be certain whether antiviral therapy or qualitative immune reconstitution or both were at play.

Currently, no standard treatment for PEL exists. Intensive chemotherapy regimens (e.g. CHOP, EPOCH) are commonly used, though outcomes are still unfavorable with median survival under six months. HAART improves the prognosis of AIDS-related non-Hodgkin's lymphomas when combined with chemotherapy. Additionally, previous cases of PEL were reported with patients reaching complete, long-term remission on antiretrovirals alone [3–6]. Additionally, ganciclovir alone may have efficacy as noted both *in vitro* and in case reports [7, 8].

We must emphasize that antiviral therapy alone is not the standard of care and the true efficacy of this approach is unknown. As this is not efficacious in other types of lymphoma, antiviral therapy may be uniquely potent in PEL, which is heavily dependent on HIV and the co-virus HHV-8 for pathogenesis. Indeed, an antiviral approach based on pre-clinical apoptosis was successful in a single patient treated with interferon alpha (IFN-α) and azidothymidine (AZT) with complete resolution of malignant effusion in 5 days [9].

Currently, the AIDS Malignancy Consortium (AMC) is conducting a study to identify baseline clinical characteristics and effective treatment strategies that correlate with long-term survival in HIV-associated PEL. In addition, the study seeks to identify genomic markers that may provide prognostic information. With the results from the study, it might be possible to identify patients at the point of diagnosis for whom chemotherapy may be avoided and HAART and antiviral therapy alone may be enough.

Conflict of interest

The authors have no conflict of interest.

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