Promising Role of Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Human Immunodeficiency Virus Associated Non-Hodgkin's Lymphoma

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Abstract

This case report explores the potential role of FDG PET/CT in HIV -associated systemic non-Hodgkin's lymphoma (HIV-NHLs). In our locality, there are a cumulative total of 5523 reported HIV infections cases since 1984. We reported a case of HIV-related Burkitt's lymphoma (BL) and a case of diffuse large B-cell lymphoma (DLBCL) that underwent PET/CT examination in our PET centre. In HIV-NHLs patients, we must be reminded that not all hypermetabolic foci represent lymphomatous lesions. There is a close correlation between the pattern of lymphoid tissue activation in FDG PET/CT and HIV progression in patients without HIV-related malignancy. The unique patterns of lymphoid tissue activation observed in HIV-infected patients have great clinical implications. Secondly, HIV-infected patients are prone to suffer from opportunistic infections due to immunosuppression, particularly in those with high levels of HIV viral loads. FDG PET/CT cannot reliably differentiate metabolic active lymphoma from other benign diseases such as inflammation in the context of low CD4 count and high viral loads. In those cases, benign markedly hypermetabolic foci can be erroneously interpreted as lymphoma, particularly in those normal-sized lymph nodes. Furthermore, FDG PET/CT may be useful for assessing the efficacy of HAART in suppressing HIV replication and detecting its complication such as lipodystrophy. FDG PET/CT may play a potential useful role in staging and management of HIV -associated systemic non-Hodgkin's lymphoma. Plasma variables such as viral loads and CD4 count must be taken into account during image interpretation. FDG PET/CT as a potential useful tool for diagnosis, treatment response assessment and disease relapse detection in HIV -associated systemic non-Hodgkin's lymphoma worth to be further explored.

Keywords: Fluorodeoxyglucose positron emission tomography/computed tomography, highly active anti-retroviral therapy, human immunodeficiency virus-non-Hodgkin's lymphoma, lymphoma

Introduction

This case series reported two patients suffered from human immunodeficiency virus-associated non-Hodgkin's lymphoma (HIV-NHLs). Fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) can be useful in the staging, restaging and surveillance of HIV-NHLs patients. Its exact role in the clinical management of HIV-NHLs remains to be further explored.

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Case Reports

Case 1

A 54-year-old man presented with an enlarging mass in right parotid gland for 2 months. Fifteen years earlier, he was found to have HIV infection. He was treated with highly active anti-retroviral therapy (HAART) efavirenz, abacavir and lamivudine, and had returned to a satisfactory state of health since then. At that time,

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the patient's CD4 count was 274 cells/ul, and the HIV ribonucleic acid (RNA) level was 50,928 copies/ml (Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Test, v2.0). The high viral titer indicated suboptimal disease control as patient had poor drug compliance to HAART. Excisional biopsy of the right parotid mass revealed diffuse large B-cell lymphoma (DLBCL). The patient then underwent PET/CT for staging.

Positron emission tomography/computed tomography demonstrated hypermetabolic right parotid mass and segment VIII liver mass [Figures 1 and 2]. Patient was diagnosed to have stage IVE HIV-associated DLBCL of the right parotid gland with liver involvement. The international prognostic index was 1 (for stage IV disease), which was identified as the low risk group. The patient was treated with combination chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP), and rituximab was integrated from the second cycle onwards. During the treatment period, the CD4 count of the patient remained at 155-359 cells/ul, while the HIV RNA level came down from 50,928 at the beginning of treatment to 54 copies/ml when treatment ended. Follow-up PET/CT after six cycles of chemo showed metabolic remission of right parotid and liver lesions. The patient was deemed to be in complete remission according to the International Workshop Criteria (IWC) (Cheson 2007). Treatment was therefore stopped at six cycles and the patient remained well at the latest follow-up.

Case 2

A 45-year-old man presented with an enlarging tonsillar mass. Physical examination showed an enlarged left tonsil with irregular surface. There was a lymph node measuring 1 cm in maximal diameter on the left side of cervical region, which was rubbery and mobile. Baseline blood tests were normal. Biopsy of the tonsillar mass showed Burkitt lymphoma. Staging private PET/CT showed multiple hypermetabolic supra and infra-diaphragmatic lymph nodes with FDG avid foci at stomach and small bowel, suggestive of lymphoma involvement. The patient's serology test for HIV returned to be positive. The diagnosis of HIV was then confirmed by Western blot testing. He was started on tenofovir, lamivudine, and efavirenz. His baseline CD4 count and HIV RNA level were 105 cells/ul and 51,870 copies/ml (Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Test, v2.0) respectively. Patient was treated with immunochemotherapy with rituximab, cyclophosphamide, epirubicin, vincristine, and prednisolone. Prophylactic use of intrathecal methotrexate was given as part of the treatment protocol. During the treatment period, the CD4 count of the patient decreased from 105 cells/ul to a nadir of 54 cells/ul, and the HIV RNA came down from 51,780 copies/ml to <50 copies/ml at the end of treatment. He was treated with eight cycles of immunochemotherapy. Posttreatment follow-up PET/CT [Figure 3] showed that the patient achieved complete metabolic remission. The patient was deemed to be in complete remission according to the IWC. He remained well at the latest follow-up.

Discussions

According to the World Health Organization classification, HIV-NHLs include DLBCL, Burkitt's lymphoma, HIV-associated primary central nervous system lymphoma, primary effusion lymphoma and plasmablastic lymphoma of the oral cavity. Among the various histological subtypes, majority of them suffered from one of the three types of high grade B-cell

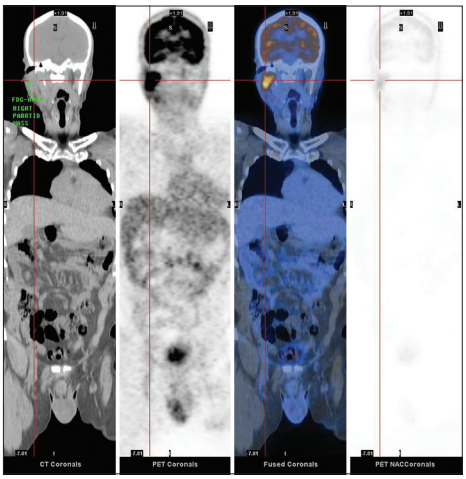

Figure 1: Stage IVE human immunodeficiency virus-associated diffuse large B-cell lymphoma with right parotid gland and liver involvement. Staging positron emission tomography/computed tomography showed markedly hypermetabolic right parotid mass with SUVmax of 9.9. It was consistent with biopsy proven diffuse large B-cell lymphoma

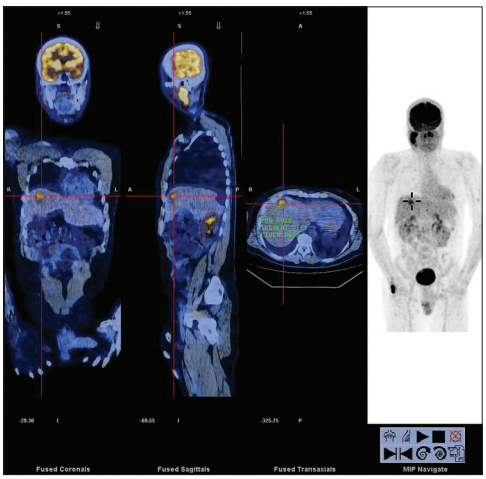

Figure 2: Hypermetabolic segment VIII liver mass was detected, SUVmax up to 5.3. It measured 23 mm × 29 mm in transaxial dimension. It resolved after six cycles of chemotherapy

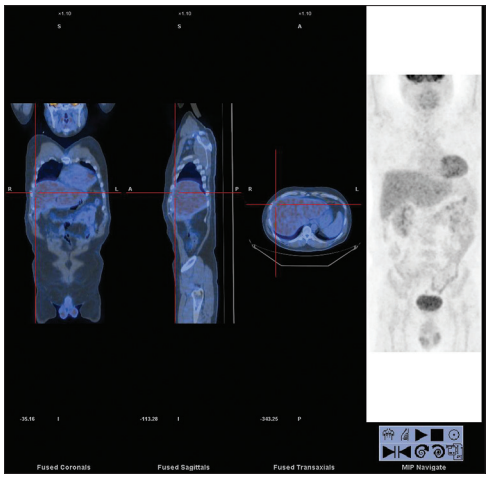

Figure 3: Stage IV human immunodeficiency virus-associated Burkitt lymphoma with involvement of lymph nodes, stomach and small intestine. Follow-up positron emission tomography/computed tomography showed disease remission of the supra and infra-diaphragmatic lymphomatous nodal deposits. No new hypermetabolic lymphomatous lesion is detected

lymphoma, namely the Burkitt's lymphoma, DLBCL with immunoblastic features or DLBCL with centroblastic features.[1] Patients with HIV-NHLs typically present with advanced-stage disease[2,3] and are more frequently associated with B symptoms including night sweats, fever and weight loss. Histological confirmation is required for the diagnosis of HIV-NHL. It is usually achieved through excisional biopsy, fine-needle aspiration or bone marrow biopsy. Staging is based on both clinical and radiological examinations. Biochemically, besides the routine blood counts, CD4 lymphocytes or HIV RNA viral load can reflect the disease activity and hence offers information of clinical significance.

Fluorodeoxyglucose PET/CT has assumed greater importance as one of the noninvasive tools for staging, restaging, and therapeutic surveillance for patients with DLBCL.[4] As a whole-body examination, it can effectively assess the extent of disease involvement in one single exam. It can also assess the chemotherapy response as illustrated in this case. Nevertheless, in HIV-related NHLs patients, we must be reminded that not all hypermetabolic foci necessarily represent lymphomatous lesions. Firstly, there is a close correlation between the pattern of lymphoid tissue activation in FDG PET/CT and HIV progression in patients without HIV-related malignancy. In acute phase, FDG uptake typically increases in the head and neck lymph nodes,[5,6] where hypermetabolic cervical, axillary, and inguinal lymph nodes are observed in mid stages. In late stage disease, increased colon and abdominal lymph nodes FDG uptake are detected.[5,6] The unique patterns of lymphoid tissue activation observed in HIV-infected patients have great clinical implications when FDG PET/CT is being used to detect nodal metastases.[6-8] Second, HIV-infected patients are prone to suffer from opportunistic infections due to immunosuppression, particularly in those with high levels of HIV viral loads. In one study,[8] two out of four patients with increased FDG lymph node activity with normal CT appearance were histologically proved to be benign. These patients had the lowest CD4 T-cell counts and the highest viral loads among the studied individuals. In another study,[9] five out of six hypermetabolic foci in the lungs in HIV-infected patients eventually turned out to be infection, with only one proved to be lymphoma. FDG PET/CT cannot reliably differentiate metabolic active lymphoma from other benign diseases such as inflammation in the context of low CD4 count and high viral loads. Hence, special caution should be exercised in FDG PET/CT interpretation in HIV-infected patients.

Traditionally, efficiency of HAART is assessed through measurements of variables in the plasma (such as viral loads), which may not accurately reflect the true level of immune activation or HIV replication in the lymphoid tissues. The fact that HAART can effectively reduce viral load carries diagnostic implications for FDG PET/CT in the evaluation of HIV-positive patients. It had been reported that HIV-infected patients with early and advanced HIV with no history of HAART showed increased FDG activity in peripheral lymph nodes, while patients on HAART showed no significant increased nodal FDG uptake.[10] Reappearance of increased nodal FDG uptake was detected upon interruption of HAART.[10] FDG PET/CT may be potentially useful for assessing the efficacy of HAART in suppressing HIV replication outside the plasma compartments.[7] Larger scale studies are required to further validate this phenomenon.

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