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Case Report

A Diffuse Large B cell Lymphoma (DLBCL) With Central Nervous System Involvement in a HIV Positive Patient

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Abstract

We present a case of a 18-year-old woman hospitalized in the Clinic of Hematology of Craiova (Romania) in September 2010 for a diffuse large B cell lymphoma-HIV associated, treated with intensive antiretroviral therapy (HAART) and eight cycles of rituximab-CHOP, with a good response (complete remission). After eighteen months, the patient relapsed in the central nervous system and develops a depressive syndrome. Central nervous system involvement is frequent in patients with secondary malignant lymphoma-HIV associated and may be expressed as neurological symptoms and psychiatric manifestations.

Keywords: DLBCL; HIV; Central nervous system involvement

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin's lymphoma. Hereditary immune deficiencies (ataxia teleangiectasia, Wiskott-Aldrich syndrome, severe combined immune deficiency) or acquired immune deficiencies (HIV-AIDS) represent risk factors for malignant lymphoma [1-3]. Malignant lymphoma in immunocompromised host (HIV-AIDS) has frequently a B phenotype, aggressive histology, frequent extra nodale localization, aggressive evolution, a bad prognosis and response to treatment. Treatment associated intensive antiretroviral therapy (HAART) and DLBCL specific therapy (rituximab-chemotherapy).

Patient, Methods and Results

A 18-year-old woman was evaluated in September 2010 in the Clinic of Hematology of Craiova (Romania) for fatigue, fever (38°C), weight loss and a left parasternal infiltrative tumor, 10/12 centimeter diameter. At the physical examination, the patient had no lymphadenopathies, hepatomegaly or splenomegaly. Laboratory results revealed mild anemia with a hemoglobin level = 10.6 g/dl, leukocyte count = 9210/mm^3 with 22% lymphocytes, platelet count =264.000/mm^3, erythrocytes sedimentation rate = 65/90 mm, fibrinogen = 420 mg%, serum lactate dehydrogenase (LDH) = 284 U/L. Hepatic and renal tests were normal. Bone marrow biopsy was normal. HIV test (ECLIA) was positive.

Nuclear magnetic resonance imaging (MRI) of the thoracic wall revealed multiple infiltrative lesions in the pectoral muscles.

The histopathological examination of the left thoracic tumour biopsy revealed a diffuse large B-cell non-Hodgkin's lymphoma. Immunohistochemistry showed that the malignant cells were positive for CD20 (B-cell marker), BCL2, Ki 67 (proliferation factor) and negative for vimentin, cromogranin, EMA.

The positive diagnosis of the patient was of diffuse large B-cell non-Hodgkin lymphoma stage IVB secondary to HIV infection.

The patient received antiretroviral therapy and eight cycles R-CHOP (rituximab + cyclophosphamide, doxorubicin, vincristine, prednisone). At the end of the eight cycles of R-CHOP, the patient was in complete remission that lasted for eighteen months. She continued antiretroviral therapy.

In November 2012, the patient returned in the Clinic with fatigue, weight loss, diplopia. Laboratory exams revealed mild anemia with a hemoglobin level = 10.8 g/dl, leukocyte count = 6250/mm^3 with 15% lymphocytes, platelet count = 295.000/mm^3, erythrocytes sedimentation rate = 85/mm, serum lactate dehydrogenase (LDH) = 284U/L. Hepatic and renal tests were normal.

Nuclear magnetic resonance imaging (MRI) of the cranium revealed a unique tumor of 1.3/2.1 cm in the left parietal region, between the precentral gyrus and supramarginal gyrus.

This tumor was surgically excided and the histopathological examination and immunohistochemistry revealed a central nervous system involvement of the DLBCL. The patient received radiotherapy in a total dose of 40Gy, CHOP regimen and antiretroviral treatment. After three months from the surgical intervention, the MRI revealed only a reactive fibrosis in the left parietal area, between the precentral gyrus and supramarginal gyrus (Figure 1 and Figure 2), but the patient developed a depressive syndrome associated with a low level of serum serotonin = 78µg/L.

Discussion

HIV-AIDS is the most common cause of acquired immune deficiency syndrome and the most important risk factor for the malignant lymphoma. The lower CD4 count is associated with a higher risk for malignant lymphoma. The highly active antiretroviral therapy (HAART) has significantly reduced the risk for development of malignant lymphoma [1]. On the other hand, HAART increased the overall survival and therefore may contribute to development of lymphoma. The majority of HIV-related lymphomas originate from germinal center B cells or postgerminal center B cells. The non-Hodgkin's lymphomas are five times more frequent in AIDS-patients which associated with Kaposi sarcoma [4-6]. Non Hodgkin's lymphoma associated with HIV-AIDS include diffuse large B cell lymphoma, Burkitt lymphoma, imunoblastic lymphoma and plasmablastic lymphoma [7,8]. The extranodale localizations are frequent [9-11]. Central nervous system lymphomas account for 15% of HIV-related lymphomas. In our patient, the extranodale localization was a very rare type of DLBCL developed in the pectoral muscles and central nervous system involvement occurred in relapse. The evolution of HIV-NHL is aggressive and has a bad prognosis. The therapy

associated HAART, rituximab + chemotherapy (CHOP) and radiotherapy in localization forms [12-14]. Our patient had a good response (complete remission) after eight cycles of R-CHOP but relapsed after eighteen months in the central nervous system. Because CNS relapse is atypical especially in HIV patients, we often think of CNS prophylaxis with MTX in such patients. In our case, the patient refused, however, the MTX therapy as prophylaxis for the central nervous system during the treatment and also after the relapse.

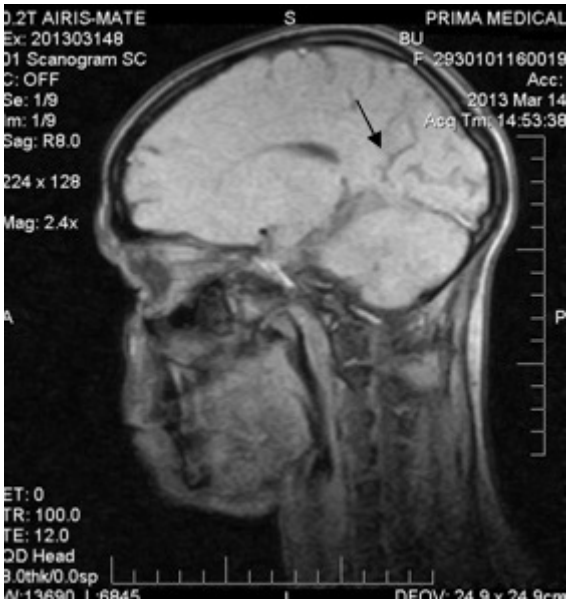

Figure 1: Reactive fibrosis left P (S)

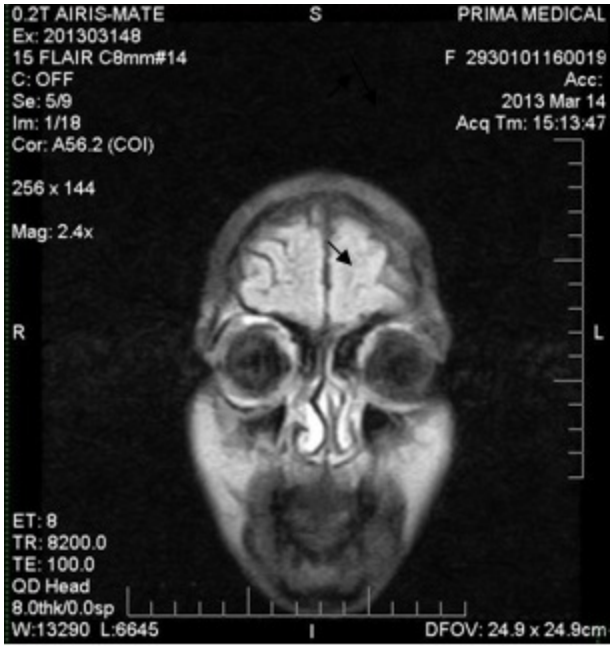

Figure 2: Reactive fibrosis left P (F)

The central nervous system involvement had a good evolution after surgical intervention and localized radiotherapy with a total dose of 40Gy. The depressive syndrome associated with a low level of serum serotonin might be induced by NHLs on a favorable genetic predisposition or by high dose of corticosteroids utilized in CHOP regimen. In the medical literature, some studies link co morbidities in NHL and depression in NHL survivors and other types of cancer [15-17].

Conclusion

Central nervous system determinations are frequent in patients with secondary malignant lymphoma-HIV associated and may be expressed as neurological symptoms and psychiatric manifestations.

References

1. Dal Maso L, Polesel J, Serraino D, Lise M, Piselli P, et al. (2009) Pattern of cancer risk in persons with AIDS in Italy in the HAART era. Br J Cancer 100: 840-847.
2. van Leeuwen MT, Vajdic CM, Middleton MG, McDonald AM, Law M, et al. (2009) Continuing declines in some but not all HIV-associated cancers in Australia after widespread use of antiretroviral therapy. AIDS 23: 2183-2190.
3. Dave SS (2010) Host factors for risk and survival in lymphoma. Hematology Am Soc Hematol Educ Program 2010: 255-258.
4. Gill PS, Levine AM, Krailo M, Rarick MU, Loureiro C, et al. (1987) AIDS-related malignant lymphoma: results of prospective treatment trials. J Clin Oncol 5: 1322-1328.
5. Knowles DM, Cesarman E (1997) The Kaposi's sarcoma-associated herpesvirus (human herpesvirus-8) in Kaposi's sarcoma, malignant lymphoma, and other diseases. Ann Oncol 8 Suppl 2: 123-129.
6. Knowles DM, Chamulak GA, Subar M, Burke JS, Dugan M, et al. (1988) Lymphoid neoplasia associated with the acquired immunodeficiency syndrome (AIDS). The New York University Medical Center experience with 105 patients (1981-1986). Ann Intern Med 108: 744-753.
7. Kaplan LD, Abrams DI, Feigal E (1989) AIDS-associated non-Hodgkin's in San Francisco. JAMA 261-271.
8. Shiramizu B, Herndier B, Meeker T, Kaplan L, McGrath M (1992) Molecular and immunophenotypic characterization of AIDS-associated, Epstein-Barr virus-negative, polyclonal lymphoma. J Clin Oncol 10: 383-389.
9. Friedman SL (1988) Gastrointestinal and hepatobiliary neoplasms in AIDS. Gastroenterol Clin North Am 17: 465-486.
10. MacMahon EM, Glass JD, Hayward SD, Mann RB, Becker PS, et al. (1991) Epstein-Barr virus in AIDS-related primary central nervous system lymphoma. Lancet 338: 969-973.
11. Kaplan LD, Kahn J, Jacobson M, Bottles K, Cello J (1989) Primary bile duct lymphoma in the acquired immunodeficiency syndrome (AIDS). Ann Intern Med 110: 161-162.
12. Ratner L, Redden D, Hamzeh F (1999) Chemotherapy for HIV-associated non-Hodgkin's lymphoma (HIV-NHL) in combination with highly active antiretroviral therapy (HAART) is nor associated with excessive toxicity. 3rd national AIDS Malignancy Conference, Bethesda 6-27.
13. Vose JM, Link BK, Grossbard ML, Czuczman M, Grillo-Lopez A, et al. (2001) Phase II study of rituximab in combination with

chop chemotherapy in patients with previously untreated, aggressive non-Hodgkin's lymphoma. J Clin Oncol 19: 389-397.

14. Sande MA, Gilbert DM (2000) The Stanford guide to HIV/AIDS therapy, 9th edn.
15. Smith SK, Zimmerman S, Williams CS, Preisser JS, Clipp EC (2008) Post-traumatic stress outcomes in non-Hodgkin's lymphoma survivors. J Clin Oncol 26: 934-941.
16. Golden-Kreutz DM, Andersen BL (2004) Depressive symptoms after breast cancer surgery: relationships with global, cancer-related, and life event stress. Psychooncology 13: 211-220.
17. Smith SK, Zimmerman S, Williams CS, Benecha H, Abernethy AP, et al. (2011) Post-traumatic stress symptoms in long-term non-Hodgkin's lymphoma survivors: does time heal? J Clin Oncol 29: 4526-4533.