Primary parotid B-cell lymphoma successfully treated with chemotherapy plus highly active antiretroviral therapy with prolonged survival and immune reconstitution in an acquired immunodeficiency syndrome patient: Case report and review of the literature

Marcelo Corti, Alicia Bistmans, Marina Narbaitz

Department of Internal Medicine, Infectious Diseases Orientation, Faculty of Medicine, Buenos Aires University, Oncology Unit, Hospital Ramos Mejía, Histopathology Laboratory, Academia Nacional de Medicina, Buenos Aires, Argentina

ABSTRACT

Non-Hodgkin’s lymphoma (NHL) is the second most common acquired immunodeficiency syndrome (AIDS)-defining cancer. In this population, up to 70-80% of cases may present as extranodal location as the primary clinical manifestation of the neoplasm disease. Gastrointestinal tract is the most frequent location of AIDS-associated NHL. However, salivary gland involvement, including the parotid gland is a rare complication in human immunodeficiency virus (HIV)-patients. Here, we describe a patient seropositive for the HIV, who developed a primary NHL of the parotid gland histologically classified as a high-grade diffuse large B-cell lymphoma. Patient was treated with a combination of chemotherapy plus highly active antiretroviral therapy with a good clinical, virological and immunological response and a prolonged survival, more than 5 years, without evidence of neoplasm relapse.

Key words: Acquired immunodeficiency syndrome, human immunodeficiency virus, non-Hodgkin lymphoma, parotid gland

INTRODUCTION

Patient infected with human immunodeficiency virus (HIV) have a higher risk to develop non-Hodgkin’s lymphoma (NHL) with extranodal involvement as a frequent clinical presentation of the neoplasm disease. NHL is the second most common neoplasm in this group and is usually of high-grade B-cell type.[1,2] The majority of extranodal lymphomas of the head and neck are NHL and only in 4-5% of the cases the parotid gland is involved.[3] Furthermore, the lymph nodes located within the salivary glands, especially the parotid glands, are rarely involvement in primary NHL.[4] Lymphoid infiltrates of the salivary glands in acquired immunodeficiency syndrome (AIDS) patients include a wide variety of pathological conditions, including autoimmune disorders and malignant lymphomas. In the general population, the majority of NHL involving the salivary glands are predominantly of low-grade or mucosa-associated lymphoid tissue type.[5,6] AIDS-associated B-cell lymphomas were commonly described to have atypical morphology, extranodal involvement as a primary manifestation and aggressive clinical course.

Here, we present a case of primary NHL of the parotid gland in an AIDS patient successfully treated with chemotherapy plus highly active antiretroviral therapy (HAART) with a prolonged survival and immune reconstitution free of neoplasm disease.

Address for correspondence: Prof. Marcelo Corti, Puán 381, 20 floor, C1406, Buenos Aires, Argentina. E-mail: marcelocorti@fibertel.com.ar
A 52-year-old man, infected with the HIV since 1991, was admitted in our Division of HIV/AIDS related illness with 1 month history of fever, night sweats and weight loss (5 kg in the last month). He was treated with HAART based on abacavir plus lamivudine plus atazanavir boosted with ritonavir (RTV) with a good immunological and virological response. At this moment, the CD4 T-cell count was 396 cell/µL and the plasma viral load was undetectable. Physical examination revealed a left-side parotid gland enlargement and swelling without regional lymphadenopathies. No symptoms or clinical signs of Sjögren’s syndrome or facial nerve palsy were detected. A chest X-ray was normal; relevant laboratory findings include: Red blood cells 3.6 × 10⁶/L, hemoglobin 14.60 g%, leucocytes count 6.6 × 10³/L, platelets 173 × 10³/L, erythrocyte sedimentation rate was more than 100 mm/1st and lactate dehydrogenase level of 1575 U/L (normal range up to 460 U/L). His liver and renal function tests were normal and the hepatitis B and C serology were negatives. Ultrasonography of the left parotid gland showed a parotid mass with hypoechoic areas. A computed tomography (CT) of the head and neck revealed a tumor lesion into the parotid gland with infiltration of the muscles and subcutaneous tissue with areas of necrosis. CT scan of thorax, abdomen, and pelvis were normal. A bone marrow biopsy did not show atypical cells. He underwent fine-needle aspiration under ultrasonographic guidance that was negative and a surgical biopsy was performed. Histopathological examination of biopsy smears showed a lymphoproliferative infiltrate composed of medium to large atypical lymphocytes with eosinophilic cytoplasm, hyperchromatic central nuclei and one to three nucleoli near the basal membrane [Figure 1]. Immunostaining with monoclonal antibodies showed that the atypical cells were positive for standard B-cell markers CD3, CD20, CD34 [Figure 2] with coexpression of Bcl-6, partial expression of Bcl-2 [Figure 3] and negative for MUM-1, VS38c and CD138. All antibodies were obtained from DAKO (Glostrup, Denmark). The Ki-67 (proliferative) index was 30% of the tumor cells [Figure 4]. Definitive histopathological diagnosis was diffuse large B-cell NHL primary of the parotid gland according to the World Health Organization classification. Epstein-Barr virus-encoded mRNAs were negative in tumor cells by in situ hybridization and polymerase chain reaction was negative to detect human herpesvirus-8 genome.

The patient given six cycles of chemotherapy based on rituximab, cyclophosphamide, vincristine, Adriamycin, and prednisone every 21 days and the same scheme of HAART with a subsequent improvement of his clinical condition.

After 5 years of this treatment, the lymphoma regressed completely and the patient is in a good clinical condition and without evidence of relapse or recurrence neoplasm disease. His last CD4 T-cell count was of 529 cell/µL (30%) and the plasma viral load remain undetectable.

**DISCUSSION**

The majority of HIV-related lymphomas are diffuse, large B-cell lymphomas (DLBCL). DLBCL are a heterogeneous group of NHL with distinct clinicopathological entities, including B-cell lymphomas with plasmablastic differentiation.\[^7\]

In contrast, all salivary glands NHL in HIV-infected patients are of high histopathological grade, arising the lymph nodes within the glands and expressed the B-cell phenotype.\[^4\]

Primary NHL arising the salivary glands, especially the parotid glands (70-80% of cases), are uncommon and include only the 1.5-5% of all salivary glands neoplasms and 4-5% of all extranodal lymphomas.\[^8,9\] Furthermore,
primary parotid NHL represent 1-4% of all parotid tumors; the frequent involvement of the parotid gland in comparison with the other salivary glands may be due to the presence of lymph nodes and lymphoid tissue within the gland.\footnote{10}

Dispenza et al.,\footnote{11} in a retrospective study of 346 patients underwent surgery due to parotid gland tumors assisted during 20 years, only detected 11 patients with diagnosis of the parotid gland NHL.

The definition of primary parotid gland lymphoma include some of the following criteria: (1) The parotid gland compromise should be the first clinical manifestation of the disease; (2) histologically, the disease should involve the gland parenchyma and (3) the presence of lymphoid malignant infiltrate.\footnote{5} We can demonstrate the three criteria in our patient.

The diagnosis of the parotid gland lymphomas is not easy due to the unspecific clinical presentation similar to other benign or malign parotid enlargement. This difficulty often results in unnecessary surgical interventions.\footnote{12,13} Early excision biopsy is necessary to confirm the diagnosis of these neoplasms and to determine the histopathological subtype.\footnote{2} The gold standard treatment of primary NHL of the parotid gland in HIV-seropositive patients is the combination of chemotherapy plus HAART as we can see in our patient. The impact of HAART on NHL response and survival has been well-demonstrated in several studies. Patients receiving HAART plus chemotherapy have a more significantly opportunity to achieve a complete remission.\footnote{12,13} Advanced neoplasm disease at presentation, bone marrow infiltration, prior diagnosis of AIDS and a poor performance status are associated with a shorter survival in HIV-patients associated NHL.\footnote{12,13}

Human immunodeficiency virus protease inhibitors (IP) may play a role in the treatment of patients with AIDS-related cancers. IP, especially RTV, can inhibit the metabolism of some anticancer drugs that are metabolized by the cytochrome P450 isoenzims. Combination of RTV and antineoplastic drugs can improve the treatment of HIV-AIDS patients with advanced and drugs resistant cancers.\footnote{14,15}

Improved survival in HIV-infected patients in the HAART era can increase the incidence of neoplasm diseases in this population. Primary NHL of the parotid gland is a rare complication of HIV/AIDS disease. Lymphoma should be included in the differential diagnosis of unilateral diffuse swellings of the parotid glands. Early diagnosis based on the histopathological and the immunohistochemical examination of biopsy smears following by the combination of chemotherapy plus HAART is necessary to improve the prognosis of this kind of patients.

REFERENCES


Cite this article as: Corti M, Bistmans A, Narbaitz M. Primary parotid B-cell lymphoma successfully treated with chemotherapy plus highly active antiretroviral therapy with prolonged survival and immune reconstitution in an acquired immunodeficiency syndrome patient: Case report and review of the literature. Clin Cancer Investig J 2014;3:401-4.

Source of Support: Nil, Conflict of Interest: None declared.