Plasmablastic lymphoma of the colon in HIV-positive patient

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ABSTRACT

Plasmablastic lymphoma (PBL) is a distinctive B-cell neoplasm which shows diffuse proliferation of large neoplastic cells, most of which resemble B-immunoblasts and have immunophenotype of plasma cells. PBL was originally described as a rare variant of diffuse large B-cell lymphoma (DLBCL) involving the oral cavity and occurring in the clinical setting of HIV[1] and latent Epstein-Barr virus (EBV) infection. We report a case of 49 year old HIV positive male with PBL involving the colon and rectum, who initially presented with constipation and rectal bleeding. A CT scan was performed which showed peri-colonic infiltration, rectal wall thickening and involvement of iliac, inguinal and mesenteric lymph nodes. A subsequent colonoscopy showed multiple lesions in the colon and rectum. Biopsy of these lesions showed monotonous proliferation of large lymphoid cells with immunoblastic features and immunohistochemical report was consistent with the PBL.

Keywords: Plasmablastic lymphoma, PBL, Immunohistology, Human immunodeficiency virus, HIV, AIDS, Epstein – Barr virus, EBV, Diffuse large B-cell lymphoma, DLBCL.

INTRODUCTION

In 1997, Delecluse et al reported 16 cases of diffuse large B cell lymphoma involving the oral cavity in HIV positive patients and designated them as Plasmablastic lymphoma (PBL).[1] Although the pathophysiological origin of PBL has not been fully characterized, the presence of Epstein-Barr virus (EBV) has often been documented in biopsy specimens, supporting a role for EBV in the pathogenesis of this lymphoma.[1] Most patients with PBL present with primary oral lesions.[1] This feature and its predilection for male gender and immunocompromised patients.[2] Below, we report a rare case of PBL involving the colon and rectum.

CASE REPORT

A 49 year old man with HIV (CD 4 count of 23 cells/ml), polysubstance abuse and postherpetic neuralgia presented to emergency room with progressively worsening constipation and intermittent blood in his stool for one month. He also reported mild diffuse abdominal pain for 3 months which was colicky in nature and unintentional weight loss of 20 pounds in the past 2 months. Patient also had complaint of fever and chills at the time of presentation.

On physical examination, the patient's abdomen was soft and non-tender. No masses or organomegal was found. There was no guarding or rigidity. A rectal mass was
palpated on rectal exam. A CT of the abdomen and pelvis was performed and shown in Figure 1.

A colonoscopy was performed which showed a large circumferential stricturing mass in the rectosigmoid colon and multiple other lesions involving the sigmoid, descending, transverse and ascending colon (Figure 2A to 2F).

Biopsy specimens of the lesions were taken and histopathology showed.

Histopathological examination revealed a monotonous proliferation of large lymphoid cells with immunoblastic features (abundant basophilic cytoplasm, open chromatin, prominent central nucleoli) as well as cohesive tumor cells resembling plasmablasts. In addition, mitosis and cell necrosis was seen. The cells had large rounded to oval somewhat eccentric nuclei, prominent nucleoli, and moderate to abundant amphophilic cytoplasm. Few lymphocytes and eosinophils were also seen. Tumor cells appeared to infiltrate in large cohesive masses with relatively well defined advancing edge mitotic figures, apoptotic cells, occasional tingible body macrophages, and cells with plasmacytic features.

**Immunohistochemical Report:** Following surface markers were found on the colonic malignant cells: CD 3, CD 4, CD 5, CD 7, CD 8, CD 20, CD 25, CD 30, CD 45, CD 79a, and CD 138. Malignant cells were also found to be positive for: EBV, EMA, Granzyme B, Pax-5.

Malignant cells were negative for: CD 10, Cyclin D1, Alk-1, HMB 45, Melan-A, Pancytokeratin, S-100, IgM.

**Flow Cytometry:** Population of CD 45 dimly positive B-lymphocytes with excess kappa light chain in association with a population of plasmacytoid cells with excess kappa light chains.

**Hematology Report:** Total Lymphocyte Count : 404 cells/ml, CD3+ (PanT): 262 cells/ml, CD4+/CD3+: 23 cells/ml, CD8+/CD3+: 223 cells/ml, CD4/CD8: 0.10, NK Cells (CD56+/CD3−): 28 cells/ml, CD19+ (PanB) : 76 cells/ml,
Hemoglobin-6.6 g/dL, Hematocrit-18.6%, Platelets-25000/µl, AST- 47 IU/L, ALT- 8 IU/L and Alkaline phosphatase-149 IU/L.

An abdominal sonogram was showed several enlarged lymph nodes in the upper abdomen and innumerable solid hyperechoic nodules scattered throughout all hepatic lobes. The liver was enlarged (18 cm). Ultrasound of Abdomen revealed Pelvic ultrasound showed maked thickening and hypervascularity of the rectal wall. A bone marrow biopsy revealed slightly hypercellular bone marrow with disruption of normal architecture, but orderly trilinear hematopoiesis was seen.

Our patient was already on Highly Active Antiretroviral Therapy (HAART), and after diagnosis of the PBL, patient underwent two cycles of the cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP regimen). In spite of HAART and chemotherapy, patient died in 6 months after the diagnosis of PBL.

**DISCUSSION**

Diffuse Large B-Cell Lymphoma (DLBCL) is the most common type of B-cell Non-Hodgkin’s Lymphoma (NHL). DLBCL is a heterogeneous group of tumors consisting of large, transformed B cells with a basophilic cytoplasm, prominent nucleoli, a diffuse growth pattern and a high (>40 percent) proliferation fraction.[9] Plasmablastic lymphomas are immunophenotypically distinct subtype comprising of late B cells expressing plasma cell markers (eg. CD 138, CD 38 and BLIMP1) instead of the pan-B cell markers found in typical DLBCL (eg. CD20 and CD79a). (Ref) PBL is also commonly divided into two major subtypes: PBL of the oral mucosa and PBL with plasmacytic differentiation. PBL is strongly associated with Epstein Barr Virus (EBV).[5] Other subtypes with plasmablastic or immunoblastic features include ALK-positive large B-cell lymphoma (LBCL), plasmablastic lymphoma (PBL), HHV-8 related primary effusion lymphoma and large B-cell lymphoma associated with multicentric Castleman’s disease.[8,9] Our patient was positive for CD 38, CD 138 and EMA which is consistent with patients with PBL.[9] In contrast, our patient was also positive for the pan B cell marker CD 20. A literature review from Castillo et al noted a greater expression of CD 20 and CD 56 compared to HIV-negative patients.[4-7]

Colomo et al divided patients with PBL into two major types: PBL with oral mucosa type and PBL with plasmacytic differentiation.[9] Our patient had PBL with plasmacytic differentiation. They also found more frequent association of EBV with the PBL, which is also present in our patient.

Although, there is a consistent epidemiological association between PBL and immunosuppression Colomo et al. found HIV positivity in only 33% of patients in his series. It is unclear whether HIV-related immunosuppression is responsible for the PBL or HIV infection itself. Our patient’s CD4 count was 23 and thus was severe immunosuppressed. Castillo et al. reported 112 cases of HIV positive patients with PBL[9] and only few cases in immunocompetent patients.[10,11] Castillo et al. also found EBV association with PBL in 74% of the patients.[9]
In Castillo et al. series, 58% of patients had oral mucosal involvement as primary site of PBL. 13% cases had gastrointestinal tract involvement, 6% had lymph node involvement and 23% had extra-oral non-nodal distribution. There are many other case reports that suggest PBL has predilection to oral cavity.1,2,3,4 A few cases of PBL are reported in different sites of gastrointestinal tract5 such as cecum,6,7 jejunum8 and ano-rectal junction.9 Our patient had PBL lesions in ascending colon, transverse colon, descending colon, sigmoid colon and rectum with metastases to regional lymph nodes, liver and bone marrow, confirmed by biopsy and histology of respective sites and presence of plasmablasts in specimens.

According to Ann Arbor staging classification for Hodgkin and Non-Hodgkin lymphomas, our patient had Stage IV NHL. Our patient was already on HAART, and after diagnosis of the PBL, patient underwent two cycles of the CHOP regimen. One may consider adding Rituximab to CHOP because of CD20 positivity, but it is associated with increased risk of deaths if CD4 count is less than 50 (Our patient CD4 = 23 cells/ml). Our patient died in 6 months of the diagnosis of PBL highlighting poor prognosis of patients with this type of lymphoma.

Castillo et al. from survival analysis done on 138 patients reported a median overall survival (OS) of 12 months and a 5-year OS rate of 21%. HIV-positive PBL patients have median OS of 14 months vs. 9 months in HIV-negative patients.29 Without chemotherapy, OS was reported to be 4 months in HIV-positive vs. 3 months in HIV-negative patients, while the numbers are 16 months vs. 14 months in patients treated with chemotherapy.20

Plasmablastic lymphoma is a rare aggressive subtype of DLBCL. It has predilection for immunocompromised individuals and is associated with EBV. Although, PBL is most commonly seen in oral cavity, we report its presence in unusual sites such as left sided colon. Given the aggressiveness of this disease, prompt treatment with antiretroviral and chemotherapy is a mainstay of treatment.

Conflict of interest statement: There is no Conflict of Interest of any of the authors.

REFERENCES


