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Ano Rectal Plasmablastic Lymphoma in HIV Positive Patient - A Case Report

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Plasmablastic lymphoma (PBL) is an aggressive subtype of non-Hodgkin's lymphoma (NHL), classified as a distinct entity by the WHO (2008) which frequently arises in the oral cavity of HIV infected patients [1]. It is usually associated with EBV infections, and MYC gene rearrangements [2]. PBL remains a diagnostic and a therapeutic challenge with high rate of relapse and death. There is no standard of care for this entity; current understanding & knowledge of PBL relies primarily on case reports and small case series.

We present a case of primary Ano rectal plasmablastic Lymphoma in a 24 years old male HIV positive patient from Ethiopia who presented with a 3 months history rectal bleeding & abdominal pain.

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1. INTRODUCTION

The three cancers that best describe AIDS are Kaposi's sarcoma, invasive cervical carcinoma, and non-Hodgkin lymphoma (NHL) of high-grade pathologic type and of B cell or undetermined immunologic phenotype.

“HIV-associated lymphoma is most commonly diagnosed in patients with advanced HIV, a low CD4 count (often <100/microL), high HIV viral load, and a prior diagnosis of AIDS. Since the introduction of highly active antiretroviral therapy(HAART), however, the incidence of HIV-associated lymphoma has declined and the median CD4 count at diagnosis has also increased” [3].

“PBL is one of the HIV associated Lymphomas with an estimated incidence of approximately ~2% among all HIV-related lymphomas. It most commonly affect the GI tract mainly the oral cavity but extra oral presentations are very rarely seen & reported” [4].

We present a case of primary extra oral PBL in 24 years old newly diagnosed HIV patient who presented with a 3 months history of rectal bleeding & abdominal pain.

2. CASE PRESENTATION

A 24 years old male patient started to notice rectal bleeding, which was initially with initiation of defecation and mixed with stool but later became frank dark red rectal bleeding without bowel movement, the bleeding started 3 months prior to presentation to the hospital.

In addition he also had lower abdominal pain & a painful mass which protrude during defecation and subsequently a non-reducible painful mass appeared around the anal area of 2 months duration which caused difficulty of passing stool and flatus and difficulty of sitting due to its rapid growth.

Associated with this he had low grade intermittent fever and, night sweating.

The patient also reported multiple sexual partners & history of unprotected sexual exposure but denied any homosexual or anal sex encounter.

For the mentioned symptoms he was repeatedly treated with presumed diagnosis of External hemorrhoid & subsequently he was operated for possible diagnosis of colorectal cancer, the excised mass was subjected to biopsy & the patient was put on colostomy before he was presented to our center.

On Examination he was having 2x2 cm multiple, firm, cervical lymphadenopathies, functional double barrel colostomy & around 6*8 cm protruding perianal mass to which is tender, firm, with crusting and serous discharge over the surface.

He was found to have HIV infection after admission to hospital & reported that he was not tested for HIV before the current admission.

The Imaging & laboratory findings were as follows:

T1 & T2 W Abdominal MRI showed long asymmetric rectal & anal canal wall thickening about 8.7cm long extending to anal verge with diagnostic impression of colorectal cancer.

Chest CT scan were normal.

Colorectal mass biopsy histology revealed undifferentiated high grade malignant tumor with possible differential diagnosis of high grade NHL. Immunohistochemistry for Lymphoma panel was done & revealed CD45-diffuse strong to moderate positivity~99%, CD79a- positive cells~20%, MUM1- diffuse and strong positive~99%, Ki67-Strong positive cells~80%, CD138- diffuse and strong positive~99%, CD20, CD5, TdT, CD3, CD30, Myc, BCL6, CD10 were all Negative. The diagnosis of Plasmablastic lymphoma was made from the IHC finding. His CD4 count was 215 & the viral load was > 10,000. Other hematologic & biochemical profiles were within the normal range. With the above clinical evaluation the patient was admitted with the diagnosis of Stage 3 Plasmablastic Lymphoma with IPI score of 2.

3. COURSE IN THE HOSPITAL

After admission to the hospital the patient was stabilized & was given dose adjusted infusional R- EPOCH (Rituximab, Etoposide, Prednisolone, Vincristine, Cyclophosphamide & Doxorubicin) chemotherapy regimen to be given in a 28 day

cycle. He was also started on HAART few days after chemotherapy initiation. He was doing fine for the first 2 cycles & there was clinically documented response with reduction of the size of the abdominal mass & cervical lymph nodes but after the third cycle he deteriorated & developed Neutropenic sepsis & passed away after a trial of different high dose broad spectrum antibiotics & antifungals.

4. DISCUSSION

"Cancers of the anus and anal canal represent approximately 2.4% of all GI neoplasms & it is highly prevalent in patients with HIV infection, majorities are squamous cell cancers; however, there are also less frequent tumors, including lymphoma of the anus, which is a diagnostic and therapeutic challenge" [5].

"Plasmablastic lymphoma (PBL) is a rare subtype of NHL which has a strong association with HIV infection. It is characterized by CD20 and PAX5 negativity together with the expression of CD38, CD138, MUM1/IRF4, Blimp1, and XBP1 plasmacytic differentiation markers on IHC studies. It should be carefully differentiated from other CD20-negative B-cell neoplasms like primary effusion lymphoma, anaplastic lymphoma kinase-positive (ALK) large B-cell lymphoma, and LBCL in HHV-8-associated multicentric Cattleman disease" [5]. "The incidence of HIV-associated PBL has been estimated at approximately ~2% of all HIV-related lymphomas. The M: F ratio is 5.7: 1 for the oral type and 4 : 1 for the extraoral type. PBL can also affect other extra nodal sites with a predilection for mucosal tissues. It has been also reported in HIV-negative persons, particularly those who have immunosuppression" [6].

The pathogenic pathway for PBL is poorly understood and is likely determined by the complexity of biological interplays between HIV-related immunodeficiency, molecular events, co-infecting oncogenic viruses (HHV 8 & EBV), and chronic immune activation.

PBL likely emerges from post germinal center, terminally differentiated, active B-cells that are changing from immunoblasts to plasma cells based on IHC, molecular, and genetic investigations.

Chromosomal abnormalities, abnormalities in the genes that control the cell cycle, and recurrent rearrangements of the MYC and Immunoglobin(Ig) genes have all been implicated in the pathophysiology.

"Majority of PBL patients are middle-aged adults with a mean age at presentation of 39 years in HIV-positive patients and 58 years in HIV-negative patients. Although PBL Cases have been reported from different continents & it is unclear if there is a racial or ethnic predominance due to the current scarcity of data" [5].

PBL is known for its predilection for the oral cavity but extra oral presentations like GI tract, lymph nodes & skin can occur particularly in HIV infected individuals.

Most GI tract PBL present with rapidly growing mass, sometimes destructive, advanced clinical stage (stage 3 or 4), with elevated LDH and B symptoms at diagnosis (both HIV-positive and -negative patients).

A high nuclear-cytoplasmic ratio, a moderate amount of eosinophilic cytoplasm, a high mitotic index, and the absence of neoplastic plasma cells in the background are all characteristics of monomorphic cellular proliferation of plasma blasts in PBL. Large atypical cells with immunoblastic, plasmablastic, or plasmacytic characteristics, a strong central nucleolus or peripheral nucleoli, an abundance of eosinophilic cytoplasm, and a perinuclear hof proliferate in a diffuse, cohesive sheet-like manner in PBL.

"Immunohistochemistry evaluation demonstrates little to no expression of leukocyte common antigen (LCA) or the B-cell markers CD20, CD79a, and PAX5. The plasma cell markers CD38, MUM1, and CD138 (syndecan-1); almost universally expressed. It is characterized by a high proliferation index reflected by Ki67 expression (>80%), cytoplasmic Igs are expressed in near 70% of cases. PBL is also variably positive for CD30, epithelial and endothelial markers" [7].

GI tract PBL has been reported by few case reports & case series; In a study reported by Lynette Luria, et al. 4 case reports of GI tract-PBL were analyzed of which 14 cases of GI PBL reviewed from 1998-2013, the median age was 57 years (17 to 82) with M:F= 3:4, the common symptoms reported were abdominal pain (57%), weight loss (50%), anorexia (36%), & melena (36%) & 71% of the patients displayed B symptoms. The usual locations reported were stomach (43%), Small intestine (21%), anal region (21%), cecum (14%), colon (7%), and

esophagus (7%). 4 were HIV-positive, 9 were HIV-negative, and 1 patient's status was unknown. The most common therapy administered was CHOP which was given for 57% of patients. The median survival was 3.25 months & > 50% (6 of 11) died of disease shortly after diagnosis or post chemotherapy [8].

The treatment of PBL is depends on the extent of the disease, surgical resection followed by combination chemotherapy for localized disease & systemic combination chemotherapy alone for advanced lymphomas is recommended. Although no prospective therapeutic trials have been done specifically in patients with PBL CHOP and CHOP-like regimens have been used in half of the patients reported to date. More intensive chemotherapy such as Infusional EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), HyperCVAD, or CODOX-M/IVAC is also recommended. Radiotherapy in lymphomas of the anus can be complementary, especially in local recurrences or in patients who underwent local resections with positive margins. In patients with HIV infection and PBL, the use of HAART is recommended as early as possible [1,9].

"The overall survival rate is poor for anal lymphoma. Before HAART era, survival was eight months; now, the 5-year overall survival is 50% in localized disease, while 24% at five years for advanced disease but Patients with PBL who were not treated with chemotherapy invariably die with a median survival of 3 months" [9,10].

Lack of standard treatment for PBL and its poor therapeutic outcome suggest that new therapeutic approaches are needed. Novel agents used in myeloma therapy like Bortezomib, lenalidomide in combination with chemotherapy are currently being applied for PBL treatment [10].

Our case represent a case of PBL with a unique clinical presentation, a diagnostic challenge & therapeutic difficulty commonly encountered in GI tract Lymphoma evaluation & treatment.

5. CONCLUSION

The clinical manifestations of anorectal lymphoma are similar to those of adenocarcinoma of the rectum with sensation of a perianal mass, chronic ulceration, and bleeding. B symptoms such as weight loss, abdominal pain, or fever can also occur.

Cases of Anorectal PBL can be diagnosed postoperatively after hemorrhoidectomy or perianal abscesses therefore, high index of clinical suspicion & obtaining adequate samples that allow histopathological diagnosis is vital for establishing appropriate diagnosis & treatment especially in immunocompromised individuals.

CONSENT

Written consent was obtained from the patient's families for reporting the case.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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