Plasmablastic Lymphoma Presenting as Extensive Peritoneal and Retroperitoneal Nodules in an HIV-Positive Patient

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Abstract

Plasmablastic lymphoma (PBL) is a rare but aggressive subtype of diffuse large B-cell lymphoma (DLBCL). The diagnosis of PBL is challenging as its features overlap with lymphoma and myeloma. The most common presentation involves the oral cavity/jaw in human immunodeficiency virus (HIV)–positive patients. It has also been reported in the gastrointestinal (GI) tract, lymph nodes, and soft tissues. Usually, if PBL involves the GI tract, it presents as a gut tumor mass. In this report, we present an HIV-positive patient with PBL presenting with multiple peritoneal nodules. To our knowledge, this is the first case of PBL presenting as multiple peritoneal and retroperitoneal nodules in an HIV-positive patient. This case emphasizes the rare presentation of a rare malignancy, difficulties in establishing a diagnosis, and the importance of proper and timely management.

Keywords

plasmablastic lymphoma, peritoneal nodules, HIV positive

Introduction

Plasmablastic lymphoma (PBL) is an uncommon and aggressive B-cell lymphoma characterized by the expression of plasma cell antigens and loss of pan B-cell antigens. It was initially described in 1997[1] as a subtype of diffuse large B-cell lymphoma (DLBCL) confined to the oral cavity in patients with HIV. The PBL is more commonly seen in patients with HIV infection.[2] The cell of origin is a plasmablast, an activated B cell that underwent somatic hypermutation and class switching recombination leading to the development of a plasma cell. So, PBL cells show plasmacytic differentiation markers—CD38, CD138, MUM1, Blimp1, XBP1, and MYC—with variable expression for CD45, CD79a, EMA, and CD30. Generally, there is no expression of B-cell markers (CD20 and PAX5).[3] The actual incidence of PBL is unknown. There is a male predominance in the HIV-positive population, whereas females predominate in HIV-negative group. To date, most cases reported are manifested in the oral cavity and fewer have been reported in the anorectal region, the gastrointestinal tract (GIT), skin, lungs, nasopharynx, paranasal sinuses, lymph nodes, breast, central nervous system, and soft tissues.[4,5] The GIT is the most common extraoral site, accounting for approximately 30% of extraoral PBLs.[6] Usually, when PBL involves the GIT, it presents as a thickening of the tract with few surrounding lymph nodes involved.[7] Presentation of PBL as an extensive peritoneal seeding and omental mass is unusual. There is only 1 case report in English literature of PBL presenting as such, which is also in an HIV-negative immunocompetent patient.[8] So, we report a rare case of a 69-year-old HIV-positive man, who initially presented with abdominal pain and hematuria and later was found to have CD20-negative PBL with extensive peritoneal involvement.

Case History

A 69-year-old man with a past medical history of HIV on highly active antiretroviral treatment (HAART) presented with diffuse abdominal pain and abdominal distension. He also had a low-grade fever, night sweats, hematuria, and

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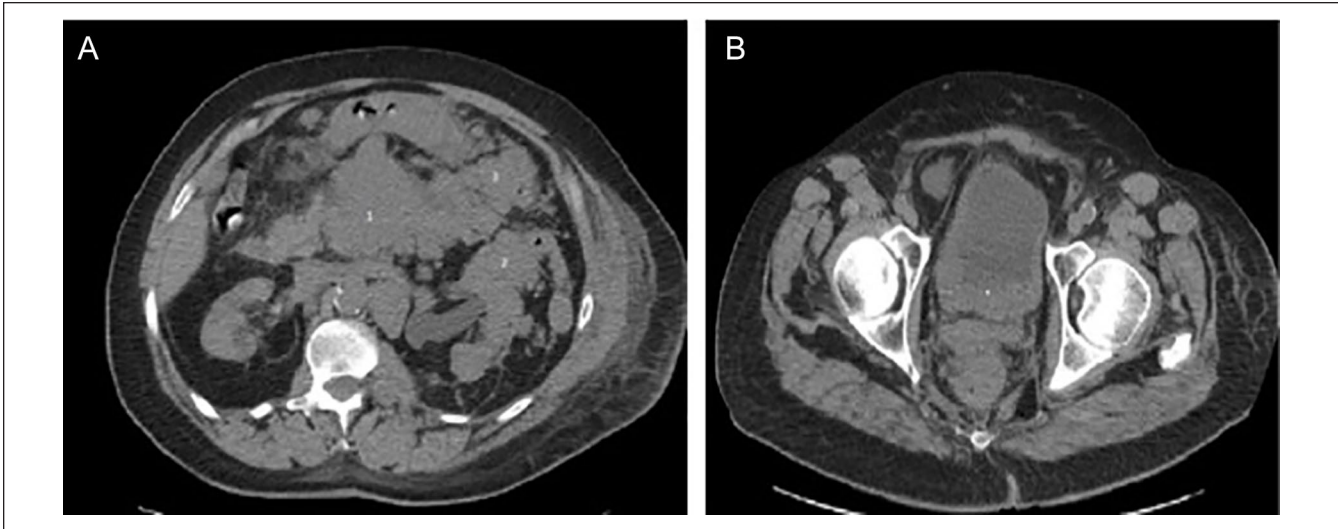Email: jcwang0005@gmail.com

Figure 1. (A) CT scan of the abdomen (noncontrast) showed diffuse peritoneal soft tissue masses seen through (1) mesenteric fat, (2) around the hydronephrotic left kidney, and (3) in the anterior omentum. (B). CT noncontrast through the pelvis showing diffuse soft tissue causing thickening (*) of the left kidney.
Abbreviation: CT, computed tomography.

nonbloody diarrhea associated with poor appetite, generalized weakness, and weight loss of around 20 pounds over 2 months. Physical examination showed distended abdomen, left upper and lower quadrant tenderness, and fullness; no fluid shift was noted. Laboratory showed white blood cell count $3.30 \times 10^3/\mu L$, hemoglobin 11.1 g/L, hematocrit 34.4%, MCV (mean corpuscular volume) 93.9 fL, RDW (red cell distribution width) 15.5%, and platelets $282 \times 10^3/\mu L$. Chemistry showed blood urea nitrogen 43 mg/dL, creatinine 3.91 mg/dL (baseline 2), bilirubin total 0.9 mg/dL, bilirubin direct 0.7 mg/dL, alkaline phosphatase 58.0, protein total 7.9 g/dL, ALT (alanine transaminase) V serum glutamate-pyruvate transaminase (SGPT) 19 U/L, aspartate aminotransferase (AST) 62 U/L, N-terminal pro B-type natriuretic peptide (NT-proBNP) 1075 (normal <450 pg/mL), troponin <0.012 (normal <0.012), and lactate dehydrogenase 1418 U/L (normal: 140–280 U/L). Serological testing was positive for HIV (HIV1 positive, HIV2 negative) and hepatitis C (HCV), hepatitis C RNA: <1.18 (normal), and negative for hepatitis B. HIV viral load was undetectable. CD4 T-cell absolute count was 229 cells/μL. Serum examination showed elevated Epstein-Barr Virus (EBV) nuclear Ag Ab to 130, EBV VCA (Viral Capsid Antigen) immunoglobulin G (IgG): 679, HHV-8: 1:20 (normal <1:20), and CD20 negative by flow cytometry. Serum and urine protein electrophoresis did not reveal any abnormal bands. Kappa and lambda light chains were also normal.

Computed tomography (CT) scan of chest/abdomen/pelvis showed multiple nodular densities within the upper abdominal mesentery consistent with mesenteric implants. The soft tissue masses have been seen through mesenteric
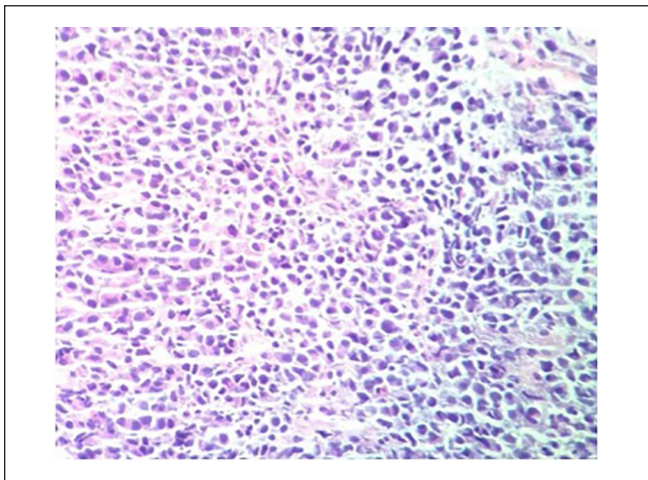

Figure 2. Omentum is involved by diffuse infiltration of tumor cells.

fat, around the hydronephrotic left kidney, and the anterior omentum (Figure 1A). Also, computed tomography (CT) noncontrast through the pelvis showed diffuse soft tissue causing thickening (*) of the posterior wall of the urinary bladder and likely causing upstream hydronephrosis of the left kidney (Figure 1B). Biopsy of the omental mass showed undifferentiated plasma cells suggesting plasmacytoma (Figure 2). Bone marrow biopsy showed hypocellular bone marrow with 30% to 40% cellularity with trilineage hematopoietic element with adequate maturation and no plasma cells infiltration. Stains negative for fibrosis by trichrome and reticulin stains. Flow cytometry analysis did not show significant numbers of circulating blasts or an abnormal
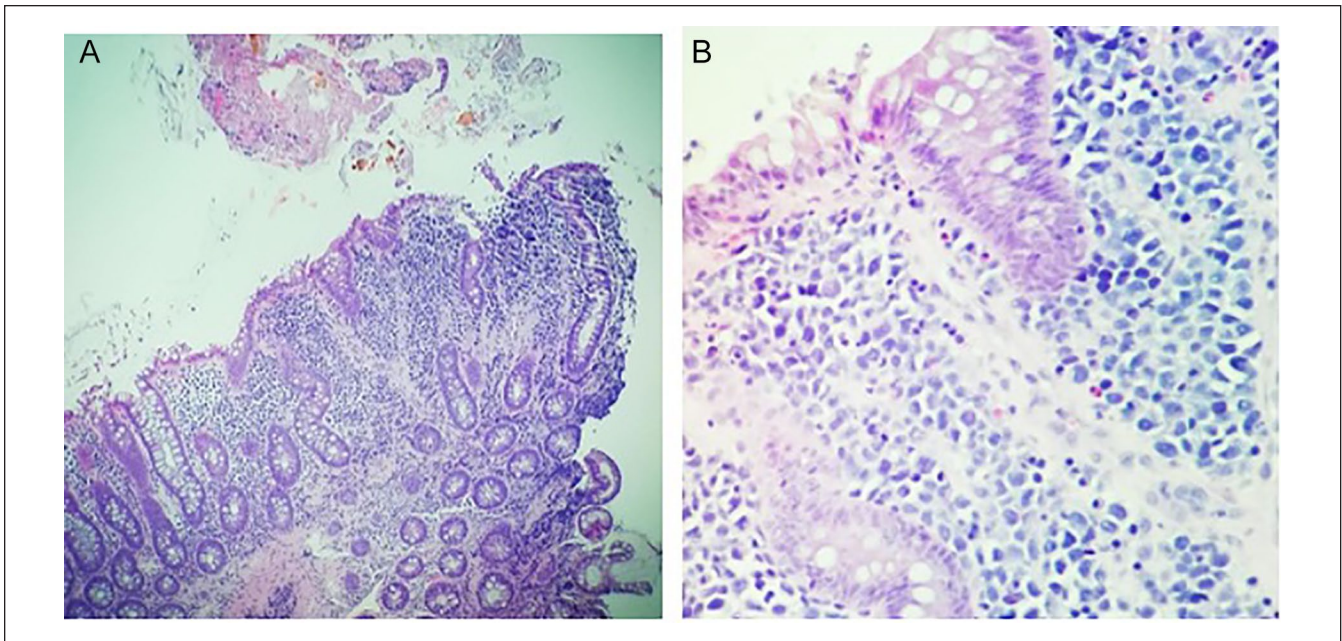
Figure 3. (A) Colon (4×). Hepatic flexure biopsy. Atypical plasmacytoid cells involving lamina propria. (B) At higher magnification (40×), atypia is apparent with diffuse sheets of neoplastic cells.

lymphoid or myeloid population; no evidence of plasma cell neoplasm. He underwent colonoscopy, which showed the presence of hemorrhoids, radiation rectal proctitis, and cystic lesions throughout the colon. Biopsy of the hepatic flexure thickening seen on imaging was done, which showed very immature plasmacytoid cells (Figure 3A & B). We sent slides to the National Institute of Health and consultation was done with Dr Elaine Jaffe, where the diagnosis concurred as PBL as further testing showed neoplastic cells positive for CD138, CD79a, MYC (100%), Ki67 (100%), and kappa light chain restriction by immunohistochemistry (IHC) (Figure 4A–C). The patient also had a cystoscopy and bilateral retrograde uretero-pyelogram examination. There were multiple fleshy-appearing tumor implants upon cystoscopy and ureteral orifices were visualized amid trigonal tumor implants. Bladder biopsy showed the urothelial tissue and muscularis propria extensively involved by plasma cell neoplasm (Figure 5A & B). He was then treated with bortezomib and EPOCH (etoposide phosphate, prednisone, vincristine sulfate, cyclophosphamide, and doxorubicin hydrochloride). He was also treated with intrathecal methotrexate for central nervous system (CNS) prophylaxis. After 5 cycles, the patient had a repeat CT scan that showed a significant response to treatment (Figure 6). The plan was to send him for bone marrow transplant evaluation after 4 or 5 cycles of bortezomib + EPOCH. Unfortunately, the patient developed extended spectrum B-lactamase *Klebsiella pneumoniae* sepsis after the fifth cycle and succumbed to septic shock and multiorgan failure despite our best efforts, 5 months after the first presentation to the hospital.

Discussion

Our case presented with extensive peritoneal and retroperitoneal nodules and the initial differential diagnoses considered were abdominal carcinomatosis, amyloidosis, and abdominal tuberculosis. Abdominal tuberculosis was ruled out after Quantiferon gold was negative. Commonly, GI or genitourinary tract malignancies, including pancreas, appendix, small intestine, endometrium, and prostate cancers, present with peritoneal metastases.[9] A biopsy of the anterior omental nodule and hepatic flexure through colonoscopy was done to confirm the diagnosis. After the biopsy showed very immature plasmacytoid cells (Figures 2 and 3), differentials were narrowed down to multiple myeloma, plasmacytoma, and PBL. Myeloma was unlikely as serum and urine protein electrophoresis did not reveal any abnormal bands and immunofixation was negative. Kappa and lambda light chains were also normal and bone marrow biopsy was negative for plasma cells infiltrate. To differentiate PBL from nonsecreting multiple myeloma is difficult sometimes, but GI involvement in an HIV patient with EBV-positive status favors the diagnosis of PBL.

The PBL is a rare neoplasm generally presented with clinical features of fever, night sweats, and weight loss. It commonly involves the oral cavity. Apart from that, GIT, lymph nodes, and sometimes skin are involved.[10] There are a couple of case series and a few case reports of PBL in GI.[7,11-13] Depending upon the location of the tumor in GIT, PBL presented with various symptoms. PBL in the stomach[7] presented with epigastric abdominal pain and vomiting; CT scan
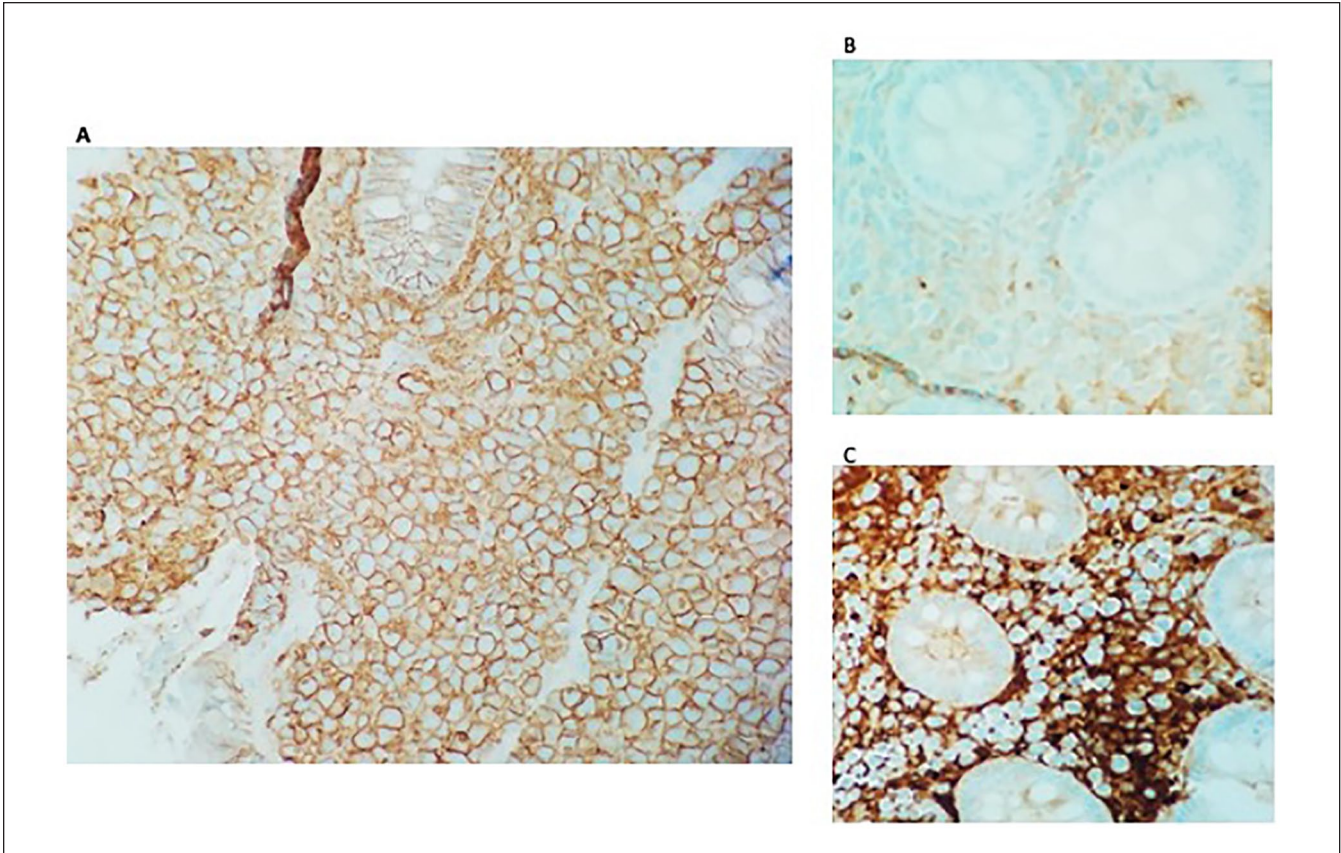
Figure 4. (A) Immunochemical stains of hepatic flexure biopsy revealed diffuse membranous stains for CD138, plasma cell marker at 10× shows diffuse membranous staining. (B) Kappa is negative in the tumor. (C) Lambda is strongly positive.
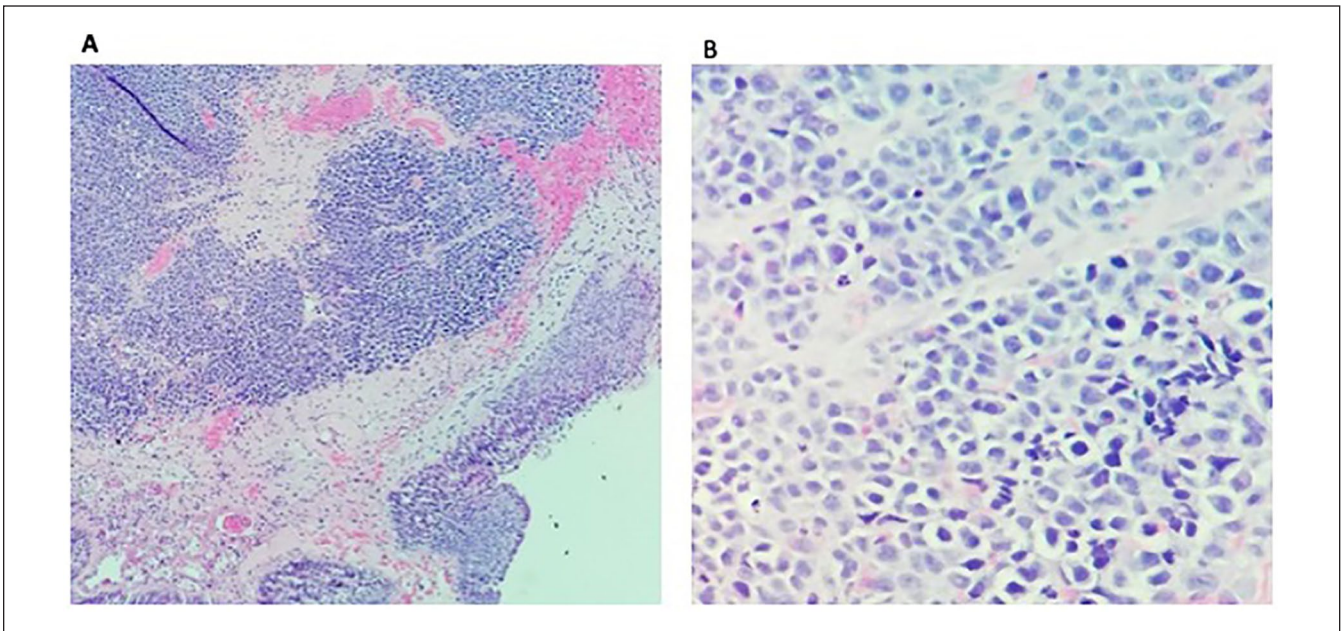

Figure 5. (A) Bladder biopsy at 4×: Lamina propria infiltrated by atypical plasmablastic lymphoma cells. (B) Bladder biopsy at 40×: Invasion of muscularis propria by lymphoma cells.
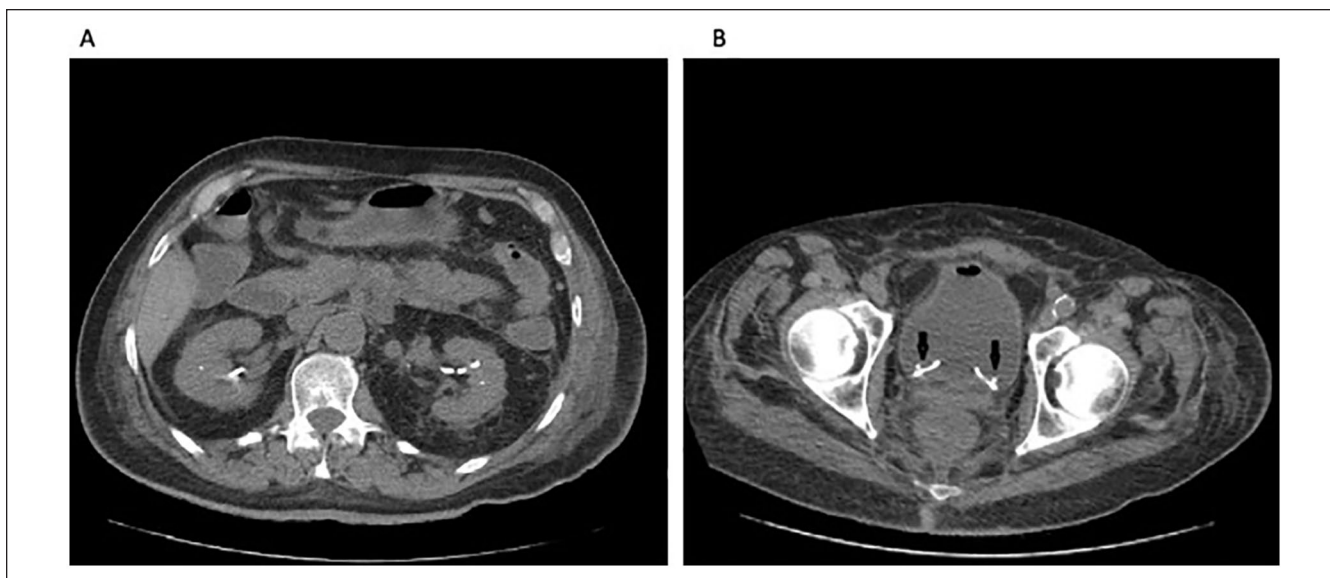
Figure 6. (A) CT noncontrast through the abdomen 3 months later shows significant interval resolution of soft tissue nodularity previously studding the mesentery, omentum, and left perinephric fat. Interval placement of bilateral ureteral stents (*) and resolution of hydronephrosis are seen. (B) CT noncontrast pelvis shows interval resolution of soft tissue thickening posterior bladder wall and placement of bilateral ureteral double J stents. A small amount of air in the bladder is related to stent placement.
Abbreviation: CT, computed tomography.

showed diffuse wall thickening with few perigastric lymph nodes. In caecum,[7] it presented with right iliac fossa pain with tenderness and recent onset of abdominal distension and imaging showed a mass lesion in the cecum extending to the ileocecal junction, mediastinal lymphadenopathy, multiple lesions in the liver and spleen, and bone marrow was found to be involved. In ascending colon,[7] it presented with abdominal pain and imaging showed a large polypoidal mass in the ascending colon. In the rectum,[7] it presented with altered bowel habits, bleeding per rectum, and icterus. Imaging showed both supradiaphragmatic and infradiaphragmatic disease with multiple hypodensities in the liver. Colonoscopy showed a polypoidal growth in the lower one-third of the rectum. In a case series of 4 patients, only 1 survived to complete the full chemotherapy treatment but relapsed 6 months later.[7] Although PBL in the GIT can present in various ways, it rarely involves extensive mesenteric and omental lymph nodes. There is 1 case report in literature where PBL presented diffuse involvement of omentum and peritoneal cavity in an immunocompetent woman mimicking ovarian carcinomatosis.[8]

Before introducing HAART, Kaposi sarcoma and non-Hodgkin lymphoma were commonly acquired immune deficiency syndrome (AIDS) defining cancers (ADCs).[14] After the introduction of HAART, with the extension of life expectancy, AIDS-defining and non-AIDS-defining cancers (NADCs) increased. As per a descriptive epidemiologic study in 2017, the most common ADCs were non-Hodgkin lymphoma (53.6%), followed by Kaposi sarcoma (17.9%).

Common NADCs were lung cancer (25%) and hepatocellular carcinoma (25%).[15] Primary CNS lymphoma accounts for up to 15% of non-Hodgkin lymphomas in HIV patients.[16] The association of HIV with plasma cell tumors is well established. There is a case report where a HIV-positive patient presented with hepatic capsular implants, large volume abdominopelvic ascites with extensive peritoneal soft tissue thickening/omental caking compatible with peritoneal carcinomatosis, mass-like thickening of the rectum, numerous lytic lesions involving multiple bones, and was found to have plasma cell neoplasm.[17] The incidence of HIV-associated PBL accounts for approximately 2% of all AIDS-related lymphomas. Several case reports and case series have been published, accounting for no more than 250 cases.[18]

Morphologically, PBL shows some degree of plasmacytic differentiation, including eccentric nuclei, smaller nucleoli, and frequent para nuclear hofs.[5] Frequent mitotic figures, apoptotic bodies, and intermixed tingible body macrophages (starry sky appearance) are characteristic of PBL.[19] Immunohistochemically, PBL shows features of plasmacytic differentiation as well as B-cell neoplasm. The immunophenotype of PBL is positive for CD138, CD38, and IRF4/MUM1, which are markers of plasmacytic differentiation, along with CD79a (seen in B-cell neoplasm). CD4, CD10, CD30, and/or CD56 may also be positive. Ki67 proliferation index is generally >90%. In situ, hybridization for EBV-encoded RNA is positive in most cases. Around 75% of PBL in HIV-positive patients are positive for EBV. Approximately 50% of PBL shows MYC gene rearrangement or gains of

MYC,[20] which may also be positive for MYC in immunohistochemistry (IHC).[21] PBL can be differentiated from DLBCL as DLBCL shows the expression of CD20 and common leukocyte antigen, which is negative in PBL.[22] Morphologic and immunophenotypic features of PBL and myeloma, especially plasmablastic variant, are virtually identical.[23] Clinical, laboratory, and radiograph findings must be extensively analyzed for reaching the diagnosis. Osteolytic lesions, bone marrow involvement, hypercalcemia, and paraproteinemia point toward myeloma.[24] EBV-positive status, HIV infection, and high Ki67 proliferation index point toward PBL. Also, in our case, neoplastic cells were positive for CD138, CD79a, MYC (100%), Ki67 (100%), and kappa light chain restriction by IHC.

Involvement of the urinary tract, especially the bladder, is also very rare with PBL. We could find 4 cases in the English literature search where PBL presented in the urinary tract. There was a case report with 2 cases where PBL presented in the urinary tract causing hydronephrosis.[25] There was 1 case that presented as ureteral polypoid mass.[26] To our knowledge, there has only been 1 case where PBL presented in the bladder similar to how it presented in our case with hydronephrosis and acute kidney injury (AKI).[27]

Etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin (EPOCH) are used to treat PBL rather than cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) based on the results of a meta-analysis. Other regimens include cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate (CODOX-M) alternating with ifosfamide, hyperfractionated cyclophosphamide, vincristine, methotrexate, and cytarabine (hyper-CVAD). Six to eight cycles of chemotherapy are usually given. In a refractory setting, bortezomib with doxorubicin or lenalidomide can be considered. Autologous stem cell transplant should be considered for chemosensitive patients in the first remission. The HAART should be given to HIV-positive patient.[10] The prognosis is also extremely poor. A systematic review conducted in 2008 on 112 HIV-positive patients with PBL revealed a median overall survival (OS) of 15 months and a 3-year OS rate of 25%.[11] Later, in 2014, Morscio et al conducted a systematic review of more than 300 patients with PBL, both immunocompromised and immunocompetent, showed a median OS of 8 months.[12] A case report shows a patient with PBL achieved long-term complete remission after thalidomide-dexamethasone induction and double autologous stem cell transplantation.[28] Recently, successful management of a refractory PBL who could not tolerate miniCHOP and bortezomib was treated with tislelizumab and lenalidomide and achieved full remission, indicating immunotherapy could be the future of PBL treatment.[29]

Conclusion

We presented a rare case of PBL with peritoneal seeding, omental mass, and bladder tumor mass in an HIV-positive patient. Awareness of this rare presentation may lead to an early diagnosis and prompt treatment when a patient presents with similar features.

Declaration of Conflicting Interests

Funding

Ethics Approval

Ethics approval to report this case was obtained from Brookdale Hospital IRB Review Board. Our institution does not require ethical approval for reporting individual case reports.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report.

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