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A Case Report of Plasmablastic Lymphoma with Unusual Presentation: How Do Socioeconomic Factors Contribute to Cancer Survival?

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ABSTRACT

Plasmablastic lymphoma (PBL) is an uncommon but aggressive subtype of diffuse large B-cell lymphoma (DLBCL) that is mostly seen in HIV positive patients. This case report details an HIV-positive patient with two unusual sites of PBL manifestation, the pleural space and the rectum. The patient was initiated on treatment but subsequently developed complications leading to the inability to temporarily continue therapy. In addition to illustrating less common site manifestations of PBL as well as its therapeutic challenges, this case also exhibits how a patient's socioeconomic and health insurance status can contribute to treatment delays, and hence their overall prognosis and survival.

Keywords: *Plasmablastic Lymphoma, HIV, AIDS, Health Insurance, Cancer Survival*

Case Presentation

The patient is a 30-year-old male who initially presented to an outside hospital with complaints of rectal discomfort with intermittent discharge from the perirectal area. Computed tomography (CT) scan of the abdomen and pelvis was performed, and he was noted to have a perirectal mass concerning for a malignancy versus a soft tissue nodule. A biopsy of the rectal mass was performed, and pathology was reported as plasmablastic lymphoma. He was also subsequently diagnosed with HIV and was started on treatment with appropriate triple therapy. The patient was advised to follow up with an outpatient oncology clinic in order to determine appropriate treatment for his cancer but was unable to do so due to his uninsured status, despite social worker assistance.

He then presented to our facility 66 days later with complaints of left-sided chest wall swelling and pain that radiated around the left chest wall to his axilla and was worse with movement, including coughing or sneezing. He denied constitutional symptoms, such as fevers, chills, or weight loss. He continued to have rectal pain with streaks of blood when wiping. Of note, the patient had no past medical history prior to his initial diagnosis of HIV.

Physical examination on admission revealed: A diffuse left upper chest wall area swelling, tenderness on palpation, a large fungating rectal mass with dark reddish-brown serosanguineous drainage, protruding adipose tissues with overall foul smell present measured at approximately 2-3cm in depth all around (Fig. 1).

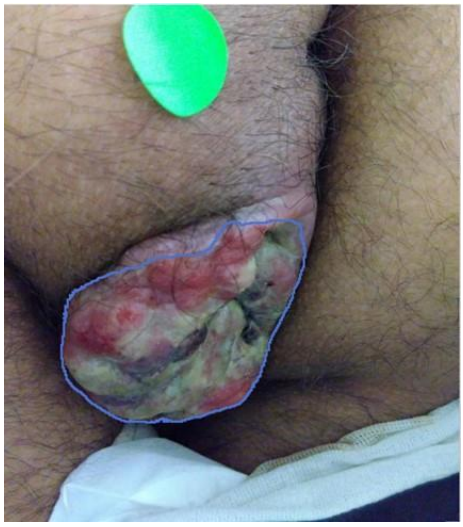

Figure 1: Photographed image of recto-anal mass at initial presentation.

Initial evaluation included a computed thoracic angiography (CTA) scan which was performed to rule out a pulmonary embolism. This demonstrated a large, left chest wall mass with osseous destruction and pathologic fourth rib fracture as well as moderate left pleural effusion (Fig. 2). CT of the abdomen and pelvis demonstrated large ileal inguinal lymph nodes and a large, abnormal soft tissue density at the left lower rectum/anus posterior to the gluteal crease. Bone marrow biopsy results from the outside facility were reviewed and they confirmed no involvement of the bone marrow.

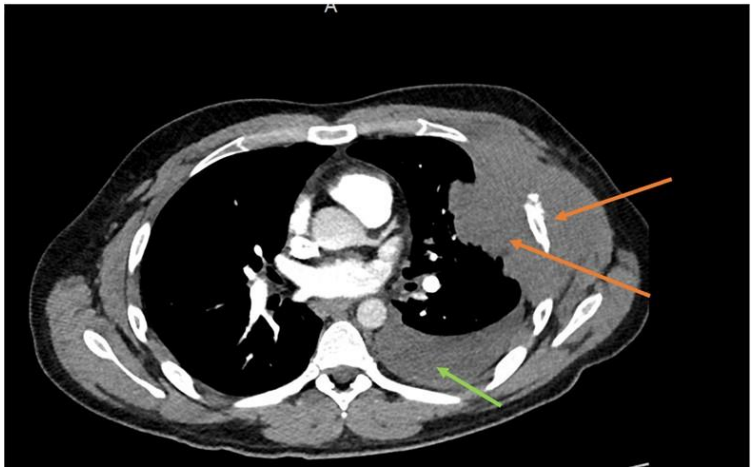

Figure 2: CTA Thorax, with orange arrows indicating a destructive left sided thoracic mass. Green arrow shows moderate left pleural effusion.

Treatment Course and Complications

Given this patient's uninsured status and already significant delays in initiating systemic therapy, it was determined that he would benefit from the urgent start of inpatient systemic chemotherapy. National Comprehensive Cancer Network (NCCN) guidelines were reviewed, and he was started on a dose adjusted EPOCH-R regimen1 (Etoposide, Prednisone, Vincrisitine, Cyclophosphamide, Doxorubicin and Rituximab) in addition to CNS prophylaxis with intrathecal methotrexate and G-CSF (granulocyte colony-stimulating factor) supplementation [3].

Results of initial presenting lab work as well as other preliminary testing before starting chemotherapy are summarized in the table below (Table 1).

Table 1: Table demonstrating results of preliminary laboratory testing at initial presentation.

Labs	**Ranges**	**Labs**	**Ranges**
WBC	9.1 (4.5-11.0 x 10^3/ul)	Glucose	135 (70-100mg/dL)
RBC	4.42 (4.5-5.9 x 10^6/ul)	Sodium	135 (132-144 mmol/L)
Hemoglobin	13.3 (14.0-17.5 g/dL)	Potassium	3.9 (3.5-5.1 mmol/L)
Hematocrit	39.1 (40.0 -52.0 %)	Chloride	103 (98-110 mmol/L)
MCV	88.5 (80.0- 100.0 fL)	Carbon dioxide, serum	27 (21-32 mmol/L)
Platelet	282 (150-400 x 10^3/ul)	Blood urea nitrogen	7 (6-20 mg/dL)
Segmented neutrophils	67 (29-66%)	Creatinine, serum	0.97 (0.70-1.30 mg/dL)
Lymphocytes	20 (15-49%)	Estimated GFR	>60 (>60 mL/mn)
Monocytes	8 (2-14%)	Calcium	9.4 (8.3-9.9 mg/dL)
Eosinophils	3 (0-5%)	Magnesium	2.2 (1.6-2.5 mg/dL)
Basophils	1 (0-2%)	Beta 2 microglobulin	3.53 (<2.51)
		Lactate Dehydrogenase	372 (87-241 U/L)
Lymph count, Absolute CD45	1150 (850-3900)	Uric acid	6.4 (3.5-7.2) mg/dL
CD3 (T cells)	825 (840-3060) cells/uL	Hepatitis A Ab IgM	Non-reactive
% CD3 (T cells)	72 (57-85) %	Hepatitis A Ab Total	Non-reactive
CD 4 (Helper cells)	103 (490-1740) cells/uL	Hepatitis B surface Ab	Non-reactive
%CD4 (Helper cells)	9 (30-61) %	Hepatitis B surface Ag	Non-reactive
CD 8 (Suppressor cells)	726 (180-1170) cells/uL	Hepatitis B core Ab Total	Non-reactive
%CD8 (Suppressor cells)	63 (12-42) %	Hepatitis B core IgM	Non-reactive
H/S ratio	0.14 (0.86-5)	Hepatitis C Ab	Non-reactive
Peripheral blood flow cytometry done showed T-cells with a skewed/inverted CD4:CD8 ratio; polytypic B-cells with no increase in blasts. 12% of total cells represented a population of T cells which demonstrated the following immunophenotype: CD2+, CD3+, CD4-, CD5+, CD7+, CD8+, and CD56-.			
KEY: WBC-White blood cells; RBC-Red blood cells; MCV- Mean Corpuscular volume; CD; GFR-Glomerular filtration rate; Ab-Antibody; Ag-Antigen; Ig-Immunoglobulin			

Two days after admission and while preliminary testing before initiating chemotherapy was still pending, the patient suddenly developed numbness and tingling in his bilateral legs along with acute urinary retention. Initial motor exam showed 5/5 strength in the upper extremities but 0/5 strength in

the lower extremities bilaterally. The sensory exam showed a T5 sensory level and there were absent reflexes in the lower extremities. Urgent magnetic resonance imaging (MRI) of the thoracic spine was obtained, which revealed an enhancing extradural mass in the upper thoracic spine extending from cord levels T2-T5 (Fig. 3). He was immediately started on intravenous dexamethasone. Neurology and neurosurgery consultations were obtained. He subsequently underwent urgent surgical decompression/laminectomy. However, he remained paraplegic. Lumbar puncture was performed given concerning neurologic findings. The cerebrospinal fluid did not reveal any malignant cells and flow cytometry report of the cerebrospinal fluid showed no overt evidence of clonal B cell or abnormal T cell populations.

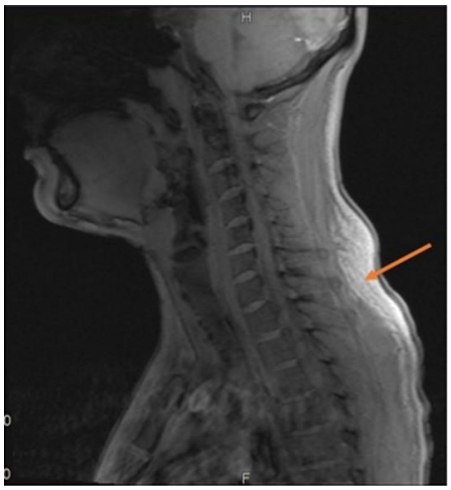

Figure 3: MRI of thoracic spine with orange arrow indicating thoracic epidural mass.

The thoracic epidural mass biopsy demonstrated sheets of plasmacytoid cells with increased mitotic and apoptotic activity (Fig. 4). The malignant cells were reactive for MUM1 and CD30 with no significant reactivity for CD138, ALK, CD20, CD3, Pax5, or CD79a. Additionally, an Epstein-Barr virus in situ hybridization study was positive.

This immunostaining is consistent with prior studies which demonstrate that the neoplastic cells in PBL are negative for B-cell markers such as CD19, CD20, and PAX-5; most or all neoplastic cells are positive for Ki-67 and about 70% of cases express EBV-encoded RNA (EBER) (Pathak *et al*., 2021; Castillo *et al*., 2015; Al Sbihi *et al*., 2020). There is variable expression for CD38 and CD138 in general, and in most cases is positive but was negative in this patient (Al Sbihi *et al*., 2020). MUM1 immunostains are usually positive in PBL patients which was consistent in this case (Al Sbihi *et al*., 2020).

Based on these findings, the epidural mass was classified as involvement by the patient's known plasmablastic lymphoma.

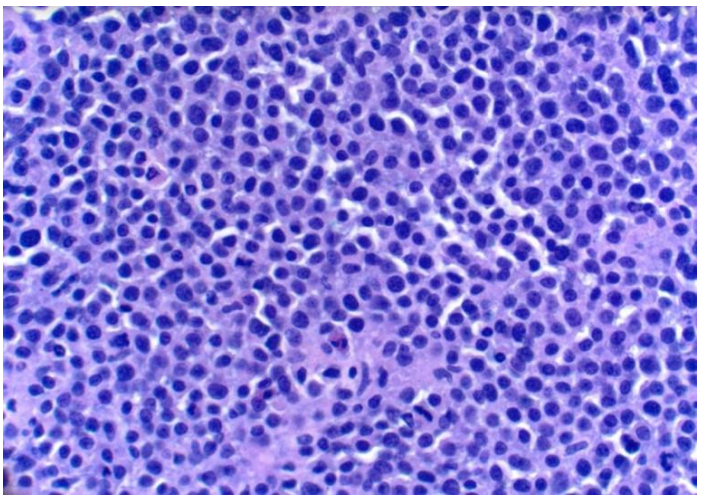

Figure 4: Histopathologic features of PBL-High magnification displays large cells with an immunoblastic appearance, with central oval nuclei with prominent nucleoli and moderately abundant cytoplasm.

Initiation of chemotherapy was delayed allowing for adequate healing time. During this period, the patient's case was presented at a tumor board meeting. Due to his multiple comorbidities, requirements for extensive coordination of care with systemic chemotherapy, intrathecal chemotherapy, radiation, as well as ongoing intense physical therapy and rehabilitation, it was deemed that his care would be best provided at a higher level/national cancer center. A transfer request was placed; however, this was denied.

The patient received his first cycle of chemotherapy ten days postoperatively. He tolerated treatment well but developed chemotherapy-induced pancytopenia. He was also started on inpatient radiotherapy3 since his Medicaid insurance would not cover transportation costs if he was to be discharged and had to be transported from rehabilitation to radiation. Due to ongoing radiation treatments, initiation of the second cycle of chemotherapy was delayed to mitigate the risk of overlapping radiotherapy and systemic chemotherapy. He was successfully tolerating radiotherapy when he then developed a large subfascial thoracic wound dehiscence. He underwent surgery again for delayed primary wound closure and subsequent wound vac placement. Due to this complication and to allow for adequate recovery, receipt of the second cycle of chemotherapy was delayed for an additional 8 days.

Following receipt of cycle 2 of therapy, the patient developed severe oral mucositis despite prophylaxis and worsening pancytopenia despite G-CSF support (Table 2). He also eventually developed repeated neutropenic fevers. Blood cultures were obtained, and the patient was started on broad spectrum antibiotics including Vancomycin and Cefepime, which was later switched to Meropenem and Posaconazole. The patient was already on atovaquone and acyclovir for prophylaxis given his CD4 count [2].

Table 2: Table demonstrating Complete blood cell counts and other laboratory parameters post cycle 1 and 2 of treatment.

	7 days after end of cycle 1	7 days after end of cycle 2
WBC	0.8 (4.5-11.0 x 10^3/µl)	0.2 (4.5-11.0 x 10^3/µl)
RBC	2.11 (4.5-5.9 x 10^6/µl)	2.52 (4.5-5.9 x 10^6/µl)
Hemoglobin	6.7 (14.0-17.5 g/dL)	7.8 (14.0-17.5 g/dL)
Hematocrit	18.9 (40.0 -52.0 %)	23.8 (40.0 -52.0 %)
MCV	89.6 (80.0- 100.0 fL)	94.4 (80.0- 100.0 fL)
MCH	31.8 (25.0-32.0 pg)	31.0 (25.0-32.0 pg)
Platelet	92 (150-400 x 10^3/µl)	16 (150-400 x 10^3/µl)
MPV	10.4 (8.2-12.2 fL)	11.2 (8.2-12.2 fL)
Segmented neutrophils	67 (29-66%)	0 (29-66%)
Lympocytes	18 (15-49%)	47 (15-49%)
Monocytes	14 (2-14%)	33 (2-14%)
Eosinophils	0 (0-5%)	0 (0-5%)
Basophils	0 (0-2%)	1 (0-2%)
Glucose	123 (70-100mg/dL)	80 (70-100mg/dL)
Sodium	130 (132-144 mmol/L)	135 (132-144 mmol/L)
Potassium	3.8 (3.5-5.1 mmol/L)	2.9 (3.5-5.1 mmol/L)
Chloride	99 (98-110 mmol/L)	101 (98-110 mmol/L)
Carbon dioxide, serum	24 (21-32 mmol/L)	29 (21-32 mmol/L)
Blood urea nitrogen	20 (6-20 mg/dL)	4 (6-20 mg/dL)
Creatinine, serum	0.68 (0.70-1.30 mg/dL)	0.31 (0.70-1.30 mg/dL)
Estimated GFR	>60 (>60 mL/mn)	>60 (>60 mL/mn)
Calcium	8.1 (8.3-9.9 mg/dL)	9.4 (8.3-9.9 mg/dL)
Magnesium	2.6 (1.6-2.5 mg/dL)	2.2 (1.6-2.5 mg/dL)

With initiation of broad-spectrum antibiotics, the patient defervesced and started to feel much improved however, he then developed severe diarrhea. This was found to be Clostridium difficile infection and oral Vancomycin was started. Due to severe mucositis and esophagitis, the patient developed dysphagia which led to worsened nutrition status.

The patient's fevers and diarrhea gradually resolved, however, he remained in the hospital as several rehabilitation facilities denied requests for placement given his insurance status and transportation needs. Restaging scans were performed after a new 3-4 cm fleshy mass was noted along the perianal area. This mass involved the anus at the rectum level of the sphincters. About half of the mass was removed for a biopsy specimen. Restaging scans were consistent with progression of the disease and pathology with immunohistochemical stains again confirmed PBL. The decision was then made not to proceed with any further cycles of inpatient chemotherapy given his extremely poor and worsening performance status. It was deemed that aggressive chemotherapy would further worsen infectious

complications and delay discharge from the hospital. Palliative care was advised, and the patient was discharged home with home health according to his wishes (Fig. 3).

Discussion

Plasmablastic lymphoma (PBL) is an aggressive subtype of DLBCL (Pokhrel *et al*., 2022). It is quite rare and thought to account for approximately 2.6% of all AIDS-related lymphomas, although, the exact rate of incidence is unknown (Castillo and Reagan, 2011). PBL has also been reported in patients with other causes of immunodeficiency, such as recipients of solid organ transplantation or in elderly patients (Castillo *et al*., 2015). It is generally thought to be confined to the oral cavity in patients with HIV infection but also often involves the nasal cavity, gastrointestinal tract, lymph node, and skin (Morscio *et al*., 2014). PBL is characterized by plasmablasts, which are lymphoid cells that have lost the characteristic B-cell surface markers and have instead acquired plasma cell surface markers (Nwanwene *et al*., 2021), its features overlap with myeloma and lymphoma making diagnosis difficult. Hence, PBL cells show plasmacytic differentiation markers-CD38, CD138, MUM1, Blimp1, XBP1, and MYC-with variable expression for CD45, CD79a, EMA, and CD30 (Pathak *et al*., 2021). Generally, there is no expression of B-cell markers (CD20 and PAX5) (Pathak *et al*., 2021). Given its rarity and overall dismal prognosis of patients with PBL, there is no established standard of care for patients with this disease (Castillo *et al*., 2015).

Recently however, the use of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) has been considered inadequate therapy, and current guidelines recommend more intensive regimens (Castillo *et al*., 2015). Small case series have shown that intensive chemotherapies combined with anti-myeloma agents, such as Bortezomib and Lenalidomide may be effective in treating PBL (Castillo *et al*., 2015). The prognosis of patients with PBL is generally poor with a median overall survival of 6-19 months, and there are no clear-cut differences between HIV-positive and HIV-negative patients based on a meta-analysis of 277 patients (Pathak *et al*., 2021; Morscio *et al*., 2014)

The patient in this case report was treated with R-EPOCH therapy and received two cycles of inpatient chemotherapy with multiple complications. This patient had treatment delays totaling 88 days including 66 days from initial presentation before presenting to our facility, Overall, the patient was in the hospital for 94 days during which he was only able to complete 2 cycles of chemotherapy because of multiple complications including paraplegia, thoracic wound dehiscence, profound bone marrow suppression, infections, clostridium difficile diarrhea, mucositis, esophagitis, and poor nutrition. These extensive complications all contributed to his lowered performance status and inability to further continue treatment.

As evident in this case report, the patient's poor health insurance status played a factor in his treatment delays and his available treatment options. In general, treatment delays contribute to a worse prognosis in patients with cancer. According to a systematic review and meta-analysis, even a four-week delay in cancer treatment is associated with increased mortality across surgical, systemic treatment, and radiotherapy indications for seven cancers (Hanna *et al*., 2020). In the United States, adolescents and young adults diagnosed with cancer have had less survival improvement than older patients, a deficit that may be a result of delays in diagnosis in an age group with the lowest rates of health insurance (Martin *et al*., 2007). In a study, evaluating the relationship between health insurance status and the time from the onset of first cancer-specific symptom or sign to definitive diagnosis, the mean lagtime in patients with public or no health insurance was 13.1 weeks longer than in patients with private health insurance (Tao *et al*., 2014). In a different study carried out evaluating socioeconomic disparities in mortality after DLBCL in California, 43% of the population aged 18 to 65 years was uninsured or underinsured, meanwhile 97% of the population older than 65 years was covered by Medicare (Tao *et al*., 2014). They found that younger DLBCL patients residing in the lowest socioeconomic status neighborhoods had a 50% increased mortality risk compared to older patients (Tao *et al*., 2014). Although cancer incidence and mortality overall are declining in all population groups in the United States, certain groups continue to be at increased risk of developing or dying from particular cancers [1].

In a study, the National Cancer Database was used to evaluate 43,648 patients with follicular lymphoma diagnosed between 2004 and 2014. In this study, patients who were uninsured or had Medicaid more commonly had poorer socioeconomic status, advanced stage, B symptoms, and multiple comorbidities, likely contributing to observed survival difference (Goldstein *et al*., 2018). The findings of the study indicate that improving access to affordable quality health care may reduce disparities in survival for those currently lacking coverage (Goldstein *et al*., 2018). In a ssytematic review of public literature, it was also found that health insurance coverage disruptions were consistently adversely associated with receipt of cancer prevention and screening and among those diagnosed with cancer, later stage of disease, delayed treatment if any, and poorer survival (Yabroff *et al*., 2020).

Conclusion

In this case, we reported an HIV-positive patient who presented with two unusual sites of PBL manifestation namely the pleural space and the rectum. Due to the rarity of the disease, the description of various clinical presentations of PBL may prove to be helpful in recognizing the disease and preventing delays in treatment. We also illustrate how a patient's socioeconomic and health insurance status may lead to substantial treatment delays and decreased treatment options. We conclude that managing factors, such as access to quality health insurance coverage that contribute to treatment delays, could

help improve population-level survival outcomes from cancers. Additional studies are required to further determine the association between a patient's socioeconomic and health insurance status and overall survival from uncommon malignancies like PBL.

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