

Case of plasmablastic lymphoma of the sigmoid colon and literature review

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Abstract

Plasmablastic lymphoma (PBL) is a rare form of non-Hodgkin's lymphoma that is associated with human immunodeficiency virus (HIV) infection. Although PBL is most commonly observed in the oral cavity of HIV-positive patients, it can also be observed at extra-oral sites in HIV-negative patients. This report represents an unusual case of HIV-negative PBL that occurred in the sigmoid colon. This patient had a history of *systemic lupus erythematosus* and an underlying immunosuppressive state from long term steroid therapy. The lymphoma cells were positive for CD138, kappa light chain restriction and Epstein-Barr virus and negative for CD20/L26, CD3, CD79a, UCHL1 (CD45RO) and cytokeratin (AE1/AE3). The patient died approximately 2 mo after the operation. In the present paper, we review cases of PBL of the colon in HIV-negative patients.

Key words: Plasmablastic lymphoma; Sigmoid colon; Human immunodeficiency virus-negative; Immunosuppressive state; Extra-oral site

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Core tip: Plasmablastic lymphoma (PBL) is a rare form of non-Hodgkin's lymphoma that is associated with human immunodeficiency virus (HIV) infection. Although PBL is most commonly observed in the oral cavity of HIV-positive patients, it can also be observed at extra-oral sites in HIV-negative patients with an underlying immunosuppressive state. The gastrointestinal tract and skin are the most commonly involved extra-oral organ systems and cases

of PBL in the colon are unusual. We report a case of HIV-negative PBL that occurred in the sigmoid colon.

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INTRODUCTION

Considered as a diffuse large B-cell non-Hodgkin's lymphoma variant, plasmablastic lymphoma (PBL) is an aggressive and rapidly growing lymphoma characterized by weak/absent expression of conventional B-cell markers and by strong expression of plasma cell markers. PBL was described as a new disease entity in the 4th WHO classification^[1]. PBL was first reported in the oral cavity in the setting of human immunodeficiency virus (HIV) in 1997 by Delecluse *et al*^[2], originally described in 16 cases of a variant of diffuse large B-cell lymphoma (DLBCL). Although PBL is strongly associated with HIV infection, an increasing number of cases have recently been recognized in a non-HIV population, as in our case^[3]. These cases often occur in patients with an underlying immunosuppressive state, such as from solid organ and bone marrow transplantation, and from lymphoproliferative or autoimmune disorders. A characteristic feature of PBL is its rapidly progressive clinical course. However, the overall survival is better in HIV-positive patients treated with highly active antiretroviral therapy (HAART) and appropriate chemotherapy than in HIV-negative patients^[4].

Several reports have described the occurrence of PBL in extra-oral sites, including the skin, stomach, small intestine, anal mucosa or perianal area, lung, liver, retroperitoneum and other regions^[5-10].

We describe a case of PBL of the sigmoid colon in a HIV-negative but Epstein-Barr virus (EBV)-positive patient who presented with gastrointestinal bleeding.

According to our research, before our case, there have only been four cases of PBL of the colon in an HIV-negative patient. Herein, we review the literature of rare cases of PBL of the colon.

CASE REPORT

An 86-year-old female was admitted to our hospital's emergency department because of bloody stool. On physical examination, she had no abdominal pain and no tenderness with guarding or rebound. At presentation, laboratory data revealed the following results: white blood count at 13100 cells/mm², hemoglobin at 13.2 mg/dL, C-reactive protein at 2.1 mg/dL, and negative status for hepatitis B and C and

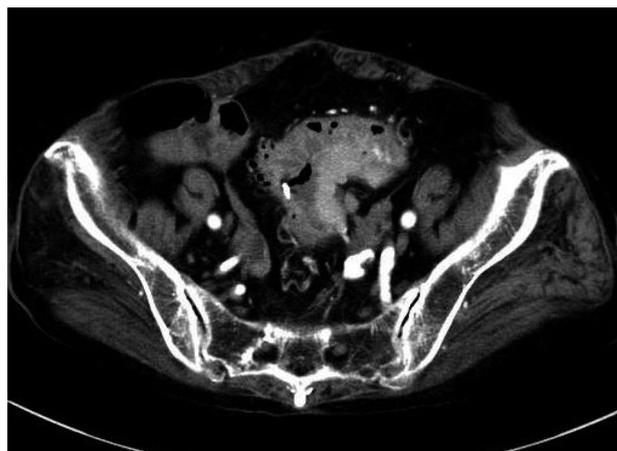


Figure 1 Computed tomography of abdomen. Computed tomography scan showed a mass measuring 5 cm in diameter, multiple diverticula in the sigmoid colon and enlarged lymph nodes in the sigmoid mesentery.



Figure 2 Gross appearance of the primary tumor lesion. A: A tumor (5 cm in diameter) is present in the sigmoid colon. Coagulation is on the surface; B: The tumor showed hemorrhage on the surface and a white mass within and was soft in consistency.

for human T-cell lymphotropic virus 1. The patient was known to have *systemic lupus erythematosus* (SLE) and type 2 diabetes mellitus. The patient was receiving steroidal treatment for SLE. A computed tomography scan of her abdomen revealed a mass measuring 5 cm, multiple diverticula in the sigmoid colon and enlarged lymph nodes in the sigmoid mesentery (Figure 1). Free air was not detected in the abdominal cavity. Colonoscopy was performed and a tumor with bleeding in the sigmoid colon was revealed. Because bleeding due to sigmoid colon cancer was suspected, sigmoidectomy with Hartmann's procedure was urgently performed. The excised material revealed the tumor to be tender, 5 cm × 4.5 cm in size, and displaying the diverticulosis (Figure 2A). On the cut surface, the tumor was soft, consistent with hemorrhage (Figure 2B). Microscopically, the tumor cells had large hyperchromatic nuclei with prominent

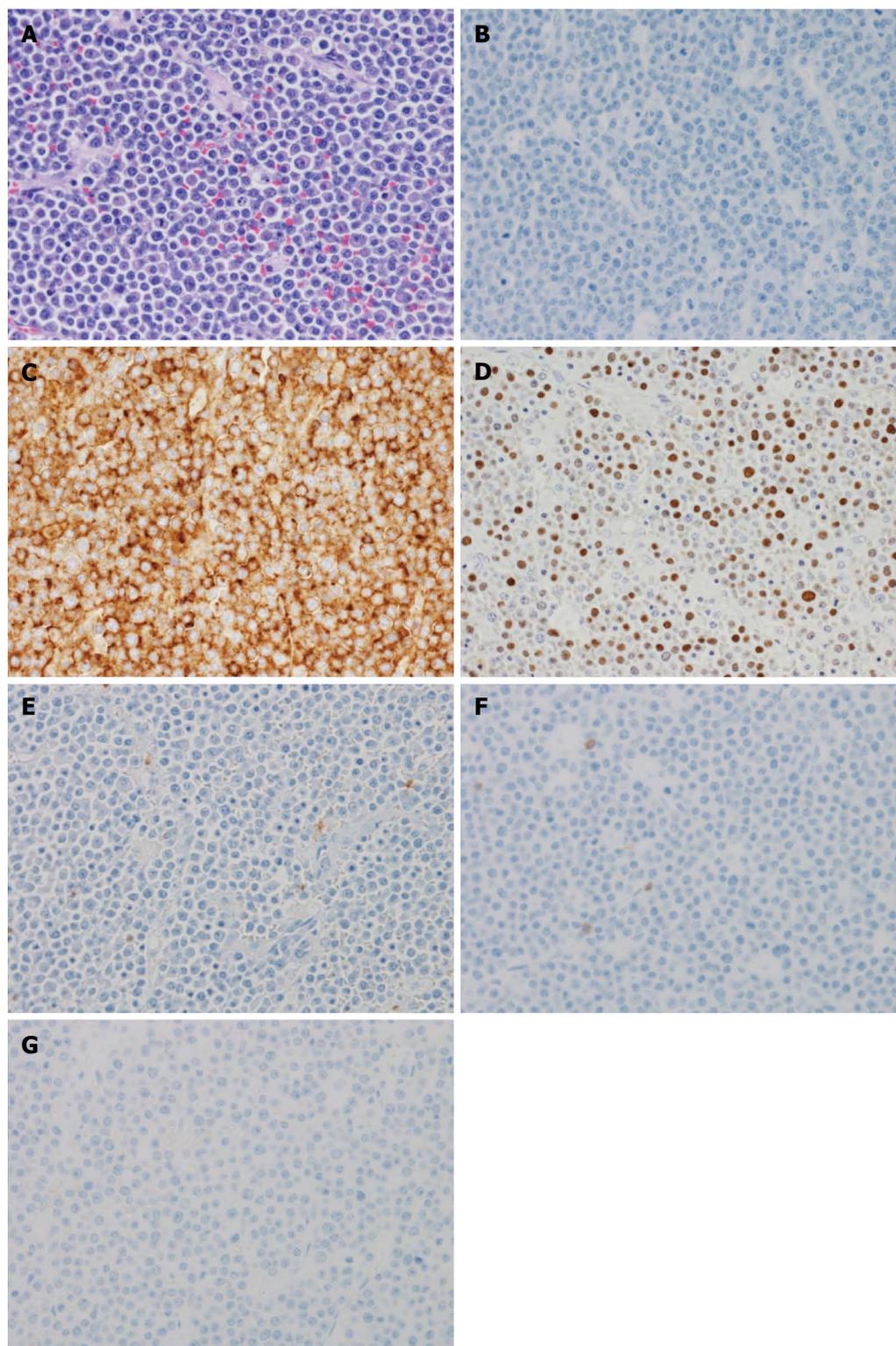


Figure 3 Plasmablastic lymphoma of the sigmoid colon. A: Tumor cells have large hyperchromatic nuclei with prominent nucleoli. Some tumor cells showed plasmacytic differentiation [hematoxylin and eosin (HE) staining, original magnification $\times 400$]; B: The atypical cells are negative for the B-cell marker CD20 (original magnification $\times 400$); C: The atypical cells are diffusely positive for the plasma cell marker CD138 (original magnification $\times 400$); D: The nuclei of the atypical cells are positive for EBER, which is Epstein-Barr encoded RNA (original magnification $\times 400$); E: The atypical cells are negative for the leukocyte common antigen CD45RO (UCHL1) (original magnification $\times 400$); F: The atypical cells are negative for the T-cell marker CD3 (original magnification $\times 400$); G: The atypical cells are negative for the pan-B-cell marker CD79a (original magnification $\times 400$).

nucleoli. Some tumor cells showed plasmacytic differentiation (Figure 3A). There was no epithelial component. Therefore, malignant lymphoma or diffuse

lymphoma was suspected.

Immunohistochemical examination revealed that the tumor cells were negative for CD20/L26 (Figure

Table 1 Patient clinical, tumor, immunohistochemical and Epstein-Barr virus status characteristics

Patient	Age	Gender	Primary site	CD3	CD20	CD45	CD79a	CD138	EBV	Cyclin D1	CD56
1	56	M	Sigmoid	-	-	-	-	+	-	ND	ND
2 ¹	29	M	Colon	-	-	+/-	-	+	+	ND	ND
3	75	M	Cecum	-	-	-	-	+	-	-	-
4	77	F	Cecum	-	-	ND	+/-	+	ND	-	ND
5 ²	86	F	Sigmoid	-	-	-	-	+	+	ND	ND

¹Patient with history of ulcerative colitis; ²Present patient. M: Male; F: Female; ND: Not determined; CD3: T-cell marker; CD20: B-cell marker; CD45: Leukocyte common antigen; CD79a: Pan-B-cell marker; CD138: Plasma cell marker; EBV: Epstein-Barr virus; Cyclin D1: Mantle cell lymphoma marker; CD56: NK-cell marker.

3B), CD3, CD79a, UCHL1 (CD45RO) and cytokeratin (AE1/AE3), but positive for CD138 (Figure 3C), kappa light chain restriction and EBV (Figure 3D). The patient's HIV negative status was proven after the surgery. Based on these results, our final diagnosis was PBL. The patient continued to deteriorate clinically and developed multiorgan failure. The patient died approximately 2 mo after surgery after refusing chemotherapy and radiotherapy. Autopsy was not performed.

DISCUSSION

PBL has been recognized as a distinct entity, a subtype of diffuse large B-cell lymphoma, by the WHO classification of lymphoproliferative disorders^[11]. PBL accounts for 1.5% of all nodal non-Hodgkin's lymphomas and has a strong predilection for immunodeficiency, particularly HIV. In patients with PBL in HIV infection, the median age was 38 years with a male predominance of 7:1. The prognosis remains poorer than that of other DLBCL^[12]. The risk of developing non-Hodgkin's lymphoma is 200 times higher in HIV-positive patients than in otherwise healthy persons. However, an increasing number of PBL cases have recently been recognized in patients without HIV infection. In HIV-negative individuals, PBL cases have been reported after solid organ transplantation, in association with steroid therapy for autoimmune disease, and some other types of immunosuppression^[13,14]. About one-third of PBL-diagnosed HIV negative patients have presented with an underlying immunosuppressive state^[15]. The present patient had a diagnosis of *SLE* and a history of steroidal treatment for 35 years before developing lymphoma. This steroidal therapy probably led to the iatrogenic immunocompromised state. There was no family history of any hematological malignancies. Except for the steroidal therapy, our patient had never received any other treatment which could lead to an iatrogenic immunocompromised state.

The present case is HIV-negative but EBV-positive. EBV plays an important role in the tumorigenesis of HIV-associated PBL^[16]. HIV infection creates a favorable environment for chronic EBV infection, with a subsequent latency that predisposes EBV-transformed B-cells to become malignant. It has been reported that

EBV infection was detected in 72% of PBL cases^[17]. However, EBV infection has been detected in only 17% of HIV-negative PBL cases, which suggests that PBL pathogenesis is not specific to EBV infection^[5].

The histological appearance of PBL is usually monomorphic with a diffuse lymphoid infiltrate and cohesive growth pattern^[18]. The main differential diagnosis of PBL includes other forms of DLBCL, plasmacytoma/myeloma, Burkitt's lymphomas, poorly differentiated carcinoma and malignant melanoma; for such a differential diagnosis, the help of morphological characteristics and behavior are often effective^[16]. Unlike PBL, DLBCL always expresses CD20, CD45-RA and CD79a. Plasmacytoma typically consists of mature plasma cells without a high rate of mitotic activity. Burkitt's lymphomas express a membrane-bound IgM heavy chain isotype. PBL expresses immunoreactivity for plasma cell markers (CD38, CD138) and is weakly positive or negative for CD45 and CD20. CD79a is positive in approximately 50%-85% of all PBL cases^[16]. CD138 is a highly specific and sensitive marker of plasmacytic differentiation within the spectrum of hematological malignancy. CD138 reactivity has been reported with variable frequency in immunoblastic diffuse large B-cell lymphoma. CD56 and cyclin D1 are usually negative. However, a differential diagnosis between PBL and plasmacytoma is difficult without histological examination.

The most notable feature of PBL is its predilection for the oral cavity. Most patients with PBL present with a primary oral lesion, often complaining of a toothache or tooth abscess^[19]. PBL can be observed at extra-oral sites in HIV-negative patients. As for extra-oral organ systems, the gastrointestinal tract and skin are the most commonly involved^[19] but only four PBL cases of the colon in HIV-negative patients have been reported before our case^[4,20,21] (Table 1).

The general prognosis of PBL is very poor, with a rapidly progressive clinical course^[19]. However, clinicopathological characteristics of PBL patients differ between HIV-positive and HIV-negative status, where HIV-positive patients have better response to chemotherapy and longer survival^[5]. For HIV-positive PBL patients, recent reports have noted improved survival when treating with both HAART and appropriate chemotherapy, such as cyclophosphamide,

doxorubicin, vincristine and prednisone, with similar outcomes for HIV-infected patients to other non-Hodgkin's lymphomas^[19]. Several patients have been documented to have survived for more than 3 years from the time of initial diagnosis of PBL, usually with a combination of HAART plus chemotherapy^[19].

Extra-oral PBL can often occur in HIV-negative patients and is highly aggressive, with a poor prognosis. Although identifying extra-oral PBL requires familiarity with lymphoma variants and related differential diagnosis procedures, PBL should be suspected if the patient is immunosuppressed. A high index of suspicion by the clinician and pathologist might lead to initiating appropriate treatments and account for better outcomes.

COMMENTS

Case characteristics

An 86-year-old female was admitted to our hospital's emergency department because of bloody stool.

Clinical diagnosis

The physical sign of our case was bloody stool; on physical examination, she had no abdominal pain and no tenderness with guarding or rebound.

Differential diagnosis

Diffuse large B-cell lymphoma, plasmacytoma/myeloma, Burkitt's lymphomas, poorly differentiated carcinoma and malignant melanoma.

Laboratory diagnosis

Laboratory data revealed the following results: white blood count at 13,100 cells/mm², hemoglobin at 13.2 mg/dL, C-reactive protein at 2.1 mg/dL, and negative status for hepatitis B and C and for human T-cell lymphotropic virus 1.

Imaging diagnosis

A computed tomography scan of our patient's abdomen revealed a mass measuring 5 cm, multiple diverticula in the sigmoid colon and enlarged lymph nodes in the sigmoid mesentery.

Pathological diagnosis

Microscopically, the tumor cells had large hyperchromatic nuclei with prominent nucleoli and some tumor cells showed plasmacytic differentiation, while immunohistochemical examination revealed that the tumor cells were negative for CD20/L26, CD3, CD79a, UCHL1 (CD45RO) and cytokeratin (AE1/AE3), but positive for CD138, kappa light chain restriction and Epstein-Barr virus (EBV).

Treatment

Sigmoidectomy with Hartmann's procedure was performed.

Term explanation

Considered as a diffuse large B-cell non-Hodgkin's lymphoma variant, plasmablastic lymphoma (PBL) was described as a new disease entity in the 4th WHO classification.

Experiences and lessons

Extra-oral PBL can often occur in human immunodeficiency virus (HIV)-negative patients and is highly aggressive with a poor prognosis. However, a high index of suspicion by the clinician and pathologist might lead to initiating appropriate treatments and account for better outcomes.

Peer-review

This is a case report of PBL which is a rare form of non-Hodgkin's lymphoma that is associated with HIV infection. The author of this manuscript should give more information about this kind of lymphoma, including the epidemiology and distribution of the disease.

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