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Plasmablastic lymphoma in an HIV-negative patient with complete remission after chemotherapy with DA-EPOCH

Joseph Alburqueque-Melgarejo[1], Juan Carlos Roque-Quezada[1], Javier Dulanto Moscoso[2], Emanuel Salcedo Davila[1], Brady Beltrán Gárate[3]

[1]Institute in Biomedical Sciences, Faculty of Human Medicine of the Ricardo Palma University, Lima, Peru
[2]Department of Haematology of Naval Hospital Medical Centre, Lima, Peru
[3]Medical Oncology Service, Edgardo Rebagliati Martins Hospital, Lima, Peru

Abstract

Plasmablastic lymphoma (PBL) is a rare subtype of diffuse large B-cell lymphoma originally described in human immunodeficiency virus (HIV)-positive patients. However, recent reports have described this neoplasia in HIV-negative patients. This neoplasia usually arises in extranodal tissues, such as the gastrointestinal tract, abdominal cavity and retroperitoneum. Here a case is presented of an HIV-negative patient with a history of stage II rectal cancer for which he received chemotherapy and radiotherapy with a complete response. However, in the following years, the patient presented clinical deterioration and the presence of an exophytic mass with fistulous tracts. For this reason, the patient underwent a new biopsy of the rectum which showed a plasmablastic lymphoma of the rectum, with an extensive local compromise that presented complete remission after 6 cycles of chemotherapy with a DA-EPOCH regimen.

Key words: plasmablastic lymphoma, non-Hodgkin lymphoma, diffuse large B-cell lymphoma

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Introduction

Plasmablastic lymphoma (PBL) is a rare and highly aggressive subtype of diffuse large B-cell lymphoma (DLCBL), originating from plasmablasts with a CD20-negative phenotype (CD20–). This was first described in 1997 in the oral cavity of patients with human immunodeficiency virus (HIV) infection. This began being considered an acquired immunodeficiency syndrome (AIDS)-defining neoplasm [1–5]. This represents approximately 2% of HIV-related lymphomas and less than 3% of all non-Hodgkin lymphomas [1, 4].

Although this type of lymphoma was initially described in patients with HIV infection, several case series have shown its presence in immunocompetent patients, with the denomination of HIV-negative PBL [3, 4]. This has been reported in several locations other than the one initially described in the oral cavity. The gastrointestinal tract, lymph nodes, and skin stand out, with the gastrointestinal tract being a rather challenging location in terms of its diagnosis [1–5]. Due to its difficult diagnosis because of its clinical presentation and variable location, it can initially be confused with other neoplasms of the gastrointestinal tract [1].

This article illustrates the case of a 68-year-old male patient with a history of rectal cancer in remission who presented to the emergency of the hospital because of the presence of an exophytic

Address for correspondence: Joseph Alburqueque-Melgarejo,, Ricardo Palma University, Lima, Peru, Carmen de la Legua, Reynoso 573, Lima 01 Lima, Peru, e-mail: joseph.alburqueque@urp.edu.pe

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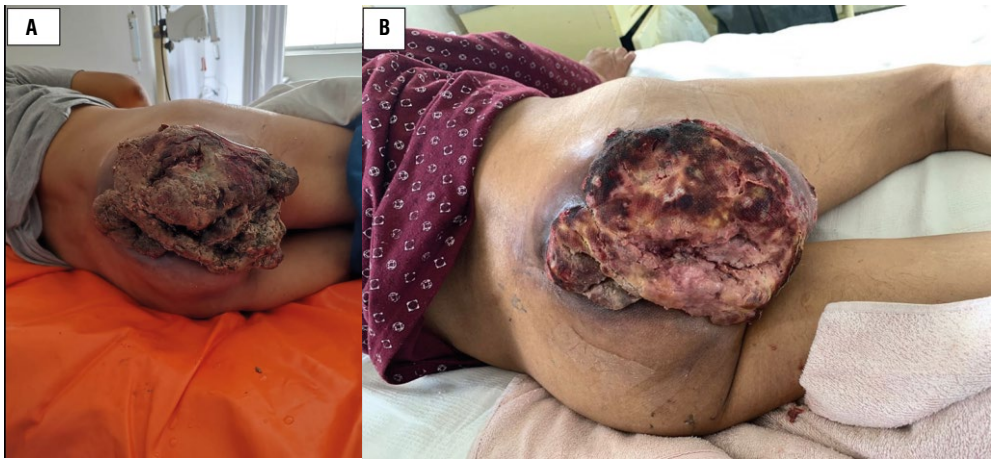

Figure 1A, B. Patient's injury on admission. A mass of approximately 7 × 10 cm in transverse and longitudinal diameter is observed located in the right buttock with irregular edges and signs of local inflammation, painful on palpation

mass with fistulous tracts and clinical deterioration. The biopsy of the rectum revealed a PBL, that achieve complete remission of the disease after 6 cycles of chemotherapy with the DA-EPOCH (dose-adjusted of etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin) scheme.

Case report

A 68-year-old male patient presented to the hospital emergency room reporting that for 1 month he had presented a tumour in the right gluteal region, painful on palpation that made sitting difficult and was draining purulent secretions. In addition, the patient reported having lost 8 kg in the last 4 months and having had an episode of fever the day prior. The patient had a history of stage II rectal cancer diagnosed in 2011 for which he received chemotherapy and radiotherapy with complete response.

Physical examination revealed a pasty exophytic mass with signs of local inflammation with irregular edges, located in the right gluteal area. It measured approximately 7 × 10 cm in diameter, with an ulcerated centre covered by scar tissue and little necrotic tissue. It was friable to the touch, with a central fistulous orifice, 2.5 cm in diameter, and presented with bad-smelling serous secretion (Figure 1).

His laboratories at admission showed haemoglobin (Hb) 8.1 g/dL, hematocrit (Hct) 24.4%, platelets 443 G/L, leukocytes 16.44 G/L, band 1%, segmented 78%, urea 27.1 mg/dL, creatinine 0.7 mg/dL, glucose 114 mg/dL, total proteins 6.7 g/dL, albumin: 2.91 g/dL, carcinoembryonic antigen (CEA) 0.82 pg/mL, alpha-fetoprotein (AFP) 1.96 ng/mL, lactate dehydrogenase (LDH) 624 U/L. His serology was negative for hepatitis B, hepatitis C, HIV, and syphilis.

Contrast-enhanced tomography of the abdomen and pelvis showed a 133 × 95 mm collection with irregular borders that were enhanced with contrast administration located in the right ischiorectal fossa (Figure 2). It extended to the lateral wall of the rectum and tissues adjacent to the coccyx, with the involvement of the obturator internus on the right side, gluteus maximus, and soft skin tissues. The presence of a fistulous tract that extended from the rectum to the skin of the right gluteus was evidenced. No mesenteric or retroperitoneal adenopathies were observed. The presence of a hydrocele in the right testicle was also observed.

Magnetic resonance imaging of the pelvis with contrast showed a concentric thickening of the wall of the rectum and anus that caused stenosis of the same. There was an infiltration of the mesorectum, ischiorectal fossa, presacral fat, and obturator internus on the right side, which extended through the greater sciatic foramen infiltrating the gluteus maximus muscle and the subcutaneous cellular tissue on the right side. There was also evidence of an exophytic mass of approximately 17 × 15 × × 93.5 cm, which presented peripheral enhancement with contrast administration, as well as areas of peripheral restriction of diffusion (Figure 3).

Because of the extensive involvement of the rectum and the presence of large loop obstruction, it was decided to perform a Hartman-type colostomy to defunctionalize intestinal transit. The

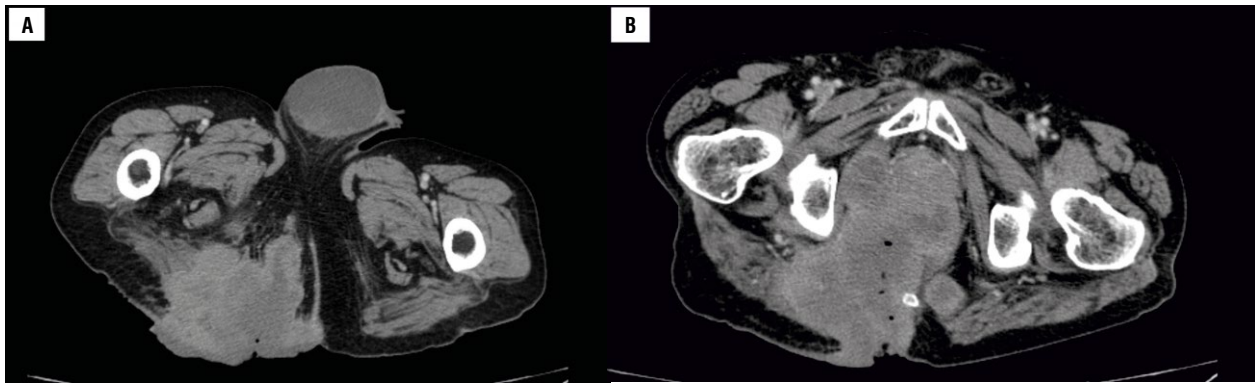

Figure 2. Computed tomography of the abdomen and pelvis with contrast. There is evidence of a mass with irregular edges that compromises the right ischiorectal fossa, right gluteus maximus, surrounding soft tissues and the skin on the same side with a central necrotic component and peripheral enhancement when contrast is administered, extending from the lateral wall of the rectum (**A**). The presence of a fistula extending from the posterior wall of the rectum towards the skin (air extending towards the skin) is also evident (**B**)

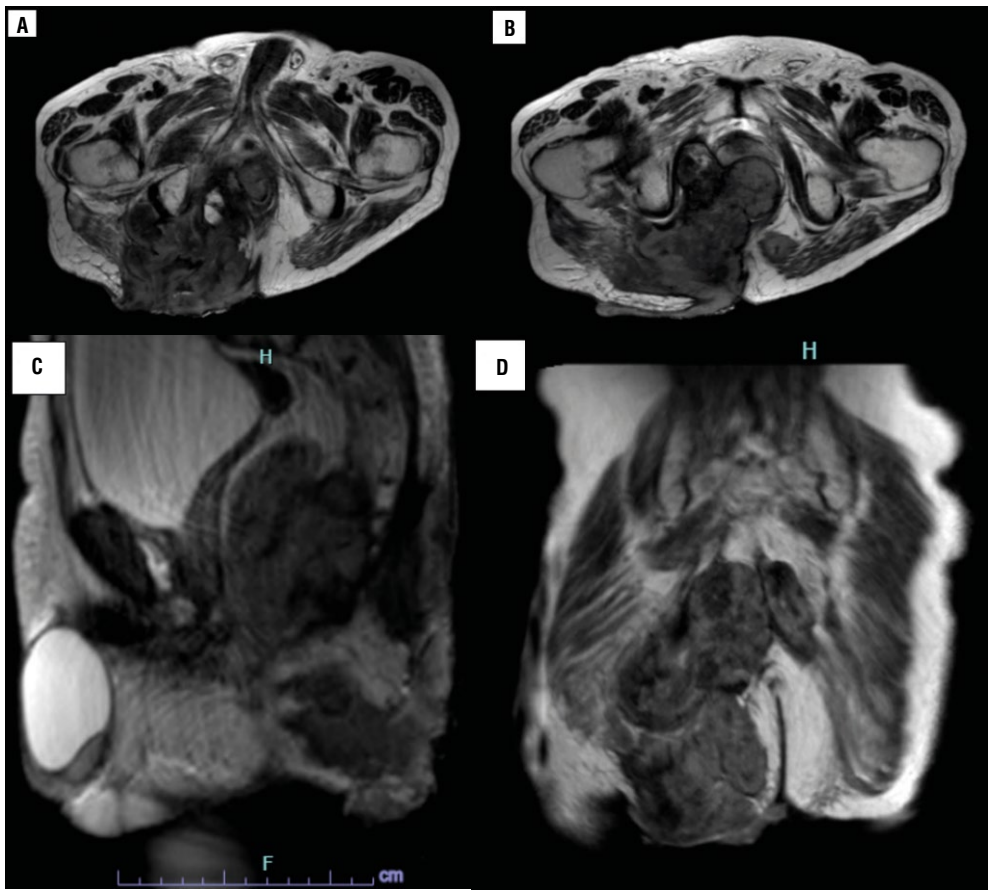

Figure 3. Magnetic resonance with contrast of the pelvis. A concentric mural thickening of the upper, middle and lower rectum wall was evidenced, with extension to the anal canal. At T2 (**A, B**) a high signal was observed in the mass and diffusion restriction. Infiltration of the mesorectal fascia, mesorectal fat, presacral fat, right ischiorectal fossa, obturator internus on the right side, gluteus maximus muscle, and soft tissues on the same side were observed, forming an abscessed collection of approximately 17 × 15 × 93.5 cm that showed peripheral enhancement with contrast administration and areas of diffusion restriction. Figures **C** and **D** show the sagittal and coronal planes.

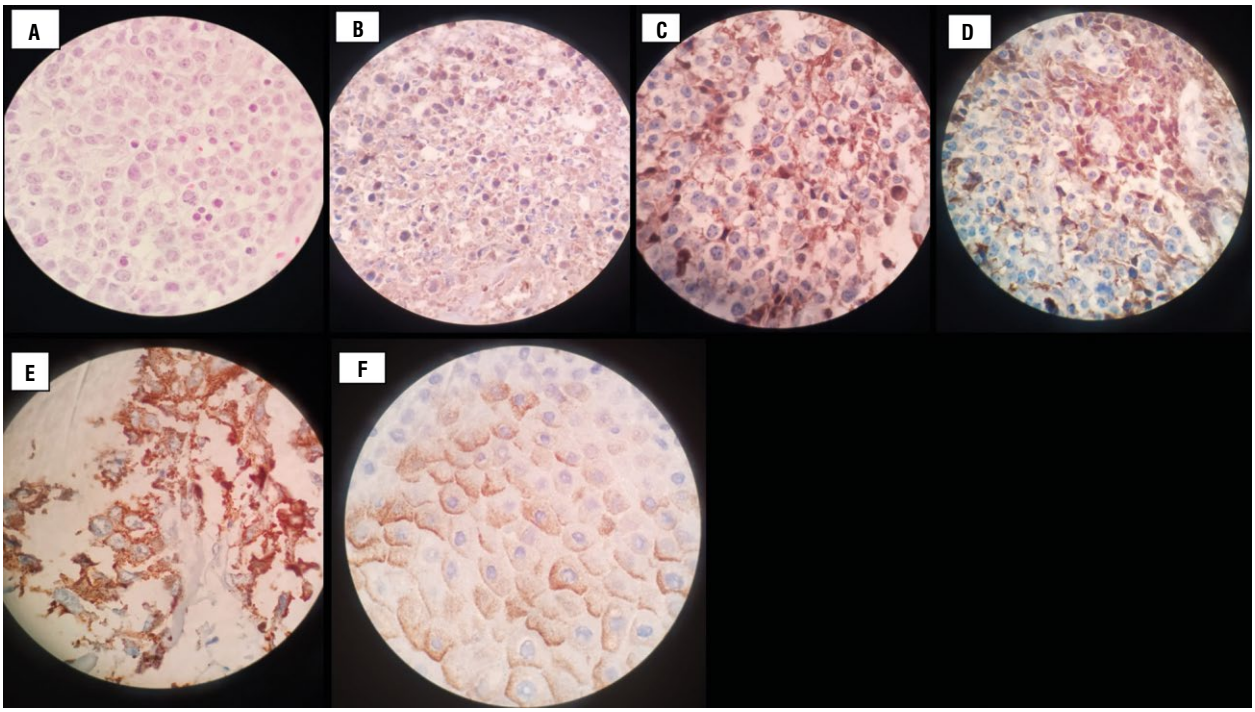

Figure 4A–F. Histopathology. Microscopic examination revealed the presence of round cells with a neoplastic appearance and plasmablastic differentiation, with the presence of an ulcerous bed with granulation tissue. Histopathology showed positivity for MUM-1 (× 100), kappa chain (× 100), lambda chain (× 100), LMP-1 (× 100), and HMB-45 (× 100)

patient received broad-spectrum antibiotic treatment and daily dressings for the soft tissue infection that he presented. He also received negative pressure therapy with a vacuum-assisted closure device. However, the patient showed no apparent improvement.

It was decided to take a new biopsy of the rectum, which showed a malignant neoplasm of poorly differentiated round cells with a lymphoid appearance associated with an ulcerous bed with granulation tissue, which suggested plasmablastic differentiation.

Immunohistochemistry indicated positivity for CD38, CD138, ACL, MUM-1, kappa chain, and LMP1, and negativity for pancreatin, synaptophysin, CD20, CD30, ALK, EMA, lambda chain, S-100, calretinin, and HMB45 (Figure 4). Furthermore, the sample was negative for human herpesvirus type 8 latent nuclear antigen (HHV-8 LNA). The tumour mass showed a Ki-67 proliferation index of 90%. The final diagnosis was a PBL of the rectum with a bulky mass in clinical stage II.

Six cycles of chemotherapy were started with the DA-EPOCH scheme, to which the patient responded favourably. This was evidenced by a notable reduction in the size of the mass (Figure 5). In the last cycle of chemotherapy, the patient presented severe neutropenia, for which he received filgrastim (G-CSF, granulocyte-colony stimulating factor). No other complications related to chemotherapy were reported. Control imaging studies did not show distant metastases. The positron emission tomography–computed tomography (PET-CT) scan showed no metabolic uptake in the chest, abdomen, and pelvis. The patient achieved complete remission after 10 months from the last cycle of chemotherapy. He is alive and remains in control by external consultation at the hospital.

Discussion

PBL is a high-grade lymphoma that was initially described in patients with HIV, but in recent years it has been described in other populations, including post-transplant patients, in the context of immunological or lymphoproliferative diseases, and immunocompetent patients [1, 3, 4].

This neoplasm presents variable clinical characteristics according to the affected population. This is reflected in the presentation at early ages, with a mean age of 28 years in HIV-positive patients, in contrast to its presentation at advanced ages, with

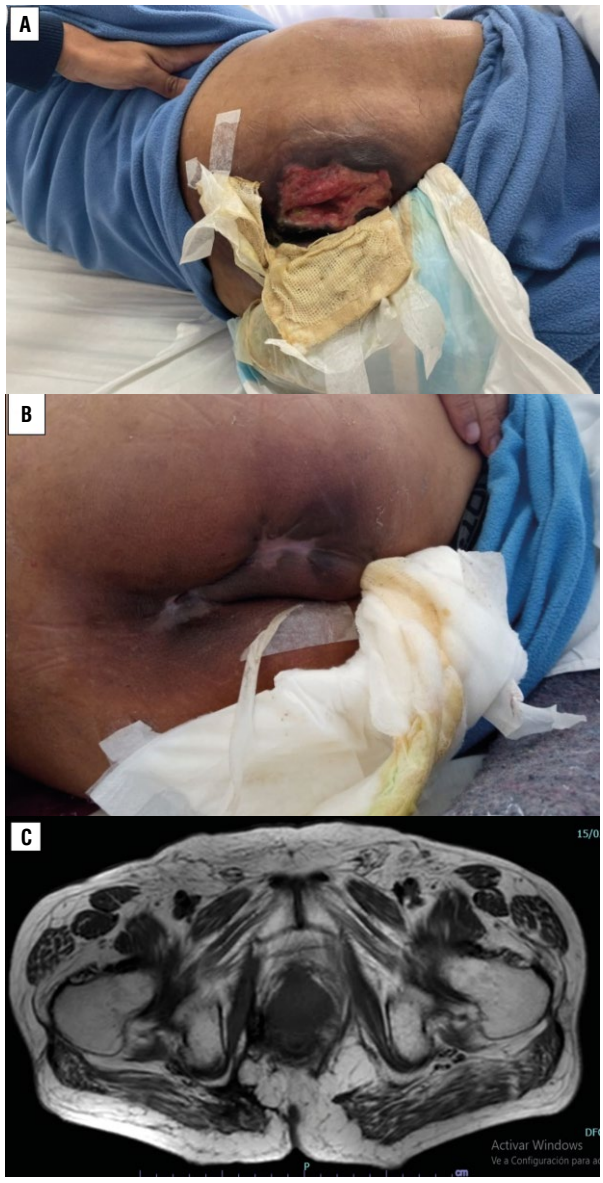

Figure 5. Evolution of the lesion after 6 cycles of chemotherapy with the DA-EPOCH (dose-adjusted of etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin) scheme. A decrease in the size of the mass is observed in relation to the beginning, as well as the presence of scar tissue that covers the lesion (**A, B**). Control magnetic resonance showed a decreased mass and the presence of hypointense scar tissue around the mesorectum, and mesorectal fat on the right side, with retraction of the rectal wall (**C**)

a mean age of 57 years, in HIV-negative patients. These differences highlight the role of immunosenescence in the pathogenesis of this neoplasm. The exact prevalence of PBL in HIV-negative patients is unknown due to its rarity and underreporting, especially in low-income countries [3, 4].

A series of cases showed that this neoplasm usually has a predilection for male patients, in the same way approximately 60% of patients presented an advanced clinical stage (III or IV), as well as 50% presented B symptoms. In HIV-negative patients, PL usually has its origin in extranodal locations, among which the oral cavity, gastrointestinal tract, soft tissues, and bone marrow stand out [3, 4].

Primary involvement of the rectum in patients with PBL is rare, so information regarding clinical characteristics, diagnosis, management, and prognosis is scarce. Isolated cases of plasmablastic lymphoma have been reported in the rectum with a presentation similar to that of the case presented, such as a rectal mass with signs of local inflammation. The mass tends to be painful on palpation, friable to the touch and protrudes through the anal canal with local invasion of surrounding tissues, which can be accompanied by rectal bleeding and pain on defecation [5–8]. Only scarce cases of plasmablastic lymphoma of the rectum have been reported in HIV-negative patients. Table 1 summarizes the clinical features of plasmablastic lymphoma of the rectum in HIV-negative patients [6, 8–11].

In images such as computed tomography or nuclear magnetic resonance, most cases of lymphoma of the gastrointestinal tract usually present as a concentric mural mass that infiltrates adjacent tissues. It may or may not cause luminal stenosis, as well as the formation of fistulas [2, 6]. In the present case, there is evidence of wall thickening with the involvement of the ischiorectal fossa, levator ani muscle, obturator internus, seminal vesicles, and the formation of a complex anorectal fistula. Due to the highly variable presentation of the various lesions in the anorectal region, other possible differential diagnoses should be taken into account in similar cases in addition to adenocarcinoma of the rectum. This would include inflammatory bowel disease, pelvic actinomycosis, tuberculosis, nocardiosis, neoplasms of epithelial origin, melanoma, and lymphoma [2].

This neoplasm originates from a plasmablast, an activated B cell that has undergone somatic hypermutation and class-switching recombination in the process of becoming a plasma cell. These cells usually express plasmablast markers such as CD138, IRF-4/MUM-1, and CD19, but do not express CD20 and have a variable expression of CD34. It usually presents cytoplasmic immunoglobulins and has a high proliferation index (> 90%) Its pathogenesis is associated with Epstein-Bárr virus (EBV), HIV and Kaposi's sarcoma-associated herpesvirus (KSHV) infection [12, 13].

Table 1. Summary of studies that report cases of plasmablastic lymphoma of the rectum

Study	Age	Sex	HIV status	Location	Signs and symptoms	Chemotherapy
Al Mohamedi et al. [6]	27	Male	Negative	Rectum	Rectal mass, abdominal pain, abdominal distention, postprandial abdominal discomfort, mucous and bloody stools, constipation, night sweats, undesired weight loss (25 kg in 3 months)	EPOCH
Brahmania et al. [8]	59	Male	Negative	Anorectal junction	Recurrent rectal bleeding	CHOP
Escudero et al. [9]	63	Male	Negative	Rectum, para-rectal space, presacral space	Rectal bleeding, anaemia	V-CHOP

EPOCH — etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone; CHOP — cyclophosphamide, hydroxydaunorubicin, oncovin (vincristine), prednisone; V-CHOP — bortezomib, cyclophosphamide, hydroxydaunorubicin, oncovin (vincristine), prednisone;

PBL shares similar morphological characteristics to diffuse large B-cell lymphoma, such as architectural distortion of the lymph node, which is why the World Health Organization (WHO) classifies it as a variant [13]. Histopathologically, this neoplasm can be confused with other entities that also present plasmablastic morphology such as plasma cell myeloma, Burkitt's lymphoma, diffuse large B-cell lymphoma (DLBCL) with plasmacytoid differentiation, pleural effusion lymphoma, anaplastic ALK lymphoma, among others [13–15]. Haemopathologists must be aware of all these entities and keep a high index of suspicion.

Among the prognostic factors, complete remission after chemotherapy, Ki-67 expression greater than 80%, and male sex stand out, with response to chemotherapy being the most associated with total survival [6–8].

There is currently no standard handling for PL. However, several organizations recommend CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)chemotherapy schemes and more intense chemotherapy schemes such as EPOCH (infusion of etoposide, vincristine, doxorubicin + bolus of cyclophosphamide and prednisone), CODOX-M/IVAC (cyclophosphamide, vincristine, doxorubicin, methotrexate altering with ifosfamide, etoposide and cytarabine), and hyper-CVAD (hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone) [6–8].

Some studies have shown a benefit in survival with the EPOCH scheme compared to the CHOP scheme in cases of high-risk diffuse large B-cell lymphoma and HIV-associated lymphomas, for which it has become the first-line management. However, this is not better compared to the other schemes [3, 4, 16]. Furthermore, a study conducted by Castillo et al. [17] showed an effective response to treatment in patients with PBL that received a regimen with bortezomib plus EPOCH (V-EPOCH). This article presents a patient with plasmablastic lymphoma who presented a complete response after receiving 6 cycles of DA-EPOCH chemotherapy.

Conclusion

The present case illustrates the variable clinical presentation and diagnostic challenge that PBL represents in clinical practice. Likewise, complete remission was evidenced after 6 cycles with the DA-EPOCH scheme, which has been reported in these neoplasms.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Financing

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