Case Report

Transient atypical lymphoplasmacytic proliferation of the endometrium associated with pyometra: a case report

Tomoyuki Otani1,4, Kosuke Murakami2, Masatomo Kimura4, Mitsuru Matsuki3, Takao Satou4, Noriomi Matsumura2, Akihiko Ito1

Departments of 1Pathology, 2Obstetrics and Gynecology, 3Radiology, Kindai University Faculty of Medicine, Osaka 589-8511, Japan; 4Division of Hospital Pathology, Kindai University Hospital, Osaka 589-8511, Japan

Received March 10, 2021; Accepted May 10, 2022; Epub July 15, 2022; Published July 30, 2022

Abstract: Plasmablastic lymphoma is a mature B-cell neoplasm with plasmablastic differentiation, often associated with human immunodeficiency virus (HIV) infection and other forms of immunosuppression. Although it is usually an aggressive disease, spontaneous regression has been seen in a few cases. Plasmablastic lymphoma of the uterus is rare. We report a case of atypical lymphoplasmacytic proliferation resembling plasmablastic lymphoma associated with pyometra that disappeared completely as the pyometra resolved. A 76-year-old HIV-negative woman presented with abnormal vaginal bleeding. Ultrasound and MRI findings were consistent with pyometra diagnosis. Endometrial biopsy revealed large plasmablastoid cells with abundant cytoplasm and prominent nucleoli proliferating in the endometrium. Immunohistochemistry showed that large cells stained positive for CD138, CD79a, and MUM1, and negative for CD20, PAX5, CD3, and CD5. Ki67 labelled at least 80% of the large cells. Epstein-Barr virus was detected in a small number of cells. The histologic picture was highly indicative of lymphoma, especially plasmablastic lymphoma, though the clinical context was unusual. As the pyometra was treated and resolved, the intrauterine abnormality disappeared completely. The patient has been well after 16 months with no sign of recurrent disease. This case underscores the sometimes blurry distinction between benign inflammation and lymphoma.

Keywords: Plasmablastic lymphoma, spontaneous regression, uterus, endometrium, case report

Introduction

Distinguishing between lymphomas and benign lymphoma-like lesions can be difficult, in endometrium [1] and other organs. Further complicating the situation is the blurry distinction between lymphomas and benign inflammation, with an increasing number of “lymphoproliferative diseases” of variable prognoses being recognized. Here, we report a case of atypical lymphoplasmacytic proliferation resembling plasmablastic lymphoma associated with pyometra, which spontaneously regressed as the pyometra resolved.

Case report

A 76-year-old, human immunodeficiency virus (HIV)-negative woman presented with abnormal vaginal bleeding. She had no significant past medical history. The discharge was blood-tinted and malodorous purulent material, and transvaginal ultrasonography revealed a uterus filled with irregular echogenicity (Figure 1A). Culture of the vaginal discharge grew *Escherichia coli* and, on MRI, inside of the uterine cavity was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging and showed diffusion restriction on diffusion-weighted imaging (Figure 2). These findings were consistent with the diagnosis of pyometra.

Histopathologic examination of the biopsy specimen from the endometrium revealed a dense cellular infiltrate expanding the endometrial stroma (Figure 3A). Remarkably, among that mixed inflammatory infiltrate was a significant population of large lymphoid or plasma-
Transient plasmablastic proliferation with pyometra

![A](image1.png) ![B](image2.png)

**Figure 1.** Ultrasonographic imaging. The uterus was filled with irregular echogenicity (A), which disappeared completely after repeated irrigation (B).

![A](image3.png) ![B](image4.png) ![C](image5.png)

**Figure 2.** MRI. Inside of the uterine cavity was T1-hypointense (A), T2-hyperintense (B), and diffusion-restricted (C), consistent with pyometra.

blastoid cells with abundant cytoplasm and prominent nucleoli. Mitotic figures were scattered (**Figure 3B**). On immunohistochemistry, large cells stained positive for CD138, CD79a, and MUM1, and negative for CD20, PAX5, CD3, CD5, CD10, CD56, ALK, HHV8, Cyclin D1, and MYC (**Figure 3C, 3D**). Ki67 labelled at least 80% of the large cells (**Figure 3E**). The cellular morphology and immunophenotype were suggestive of plasmablastic differentiation. Epstein-Barr virus (EBV) was detected in a small number of cells by EBV-encoded small RNA (EBER) in situ hybridization (**Figure 3F**). Since the positive cells did not have obvious large nuclei, it could not be determined whether they belonged to the large proliferating cell population or the admixed inflammatory cells. Immunohistochemistry for immunoglobulin kappa and lambda light chains and in situ hybridization for kappa and lambda light chains mRNA did not demonstrate light chain restriction. The histologic picture was highly indicative of lymphoma, especially plasmablastic lymphoma or aggressive B-cell lymphoma, though the unusual clinical context was deemed problematic for a definitive diagnosis.

After repeated irrigation with saline, the intrauterine echogenicity completely disappeared (**Figure 1B**). Since the entire biopsy specimen described histologically above had been submitted for histopathologic examination, another endometrial specimen was obtained and sent for flow cytometry and PCR analysis of immunoglobulin heavy chain gene rearrangement, but no significant findings were obtained from this specimen. Further work-up with PET-CT and bone marrow biopsy did not reveal any lymphoproliferative lesion or plasma cell neoplasm. An FDG-avid lesion in the sigmoid colon was resected endoscopically and diagnosed as intramucosal adenocarcinoma. The patient has been well after 16 months with no signs of recurrent disease.
Discussion

Lymphomas arising primarily in the female genital tract are rare, though secondary involvements are not uncommon. Transient lesions mimicking lymphomas are known under the name of “florid reactive lymphoid hyperplasia”, “pseudolymphoma”, or “lymphoma-like lesion” [1]. In a case series by Geyer et al. [1], lymphoma-like lesions of the endometrium were always associated with chronic endometritis, and one of these three cases was associated with EBV reactivation. Though traditional reasoning suggests that lymphoma-like lesions are of polyclonal origin, some of them have been proven to be a monoclonal proliferation [1]. This underscores the sometimes blurry distinction between benign inflammation and lymphoma.

Plasmablastic lymphoma is a mature B-cell neoplasm with plasmablastic differentiation, often associated with HIV infection and other forms of immunosuppression [2, 3]. EBV is positive in 60-75% of cases [2]. In HIV-negative, non-transplant patients, Tchernonog et al. [4] included local inflammation, such as anal fistula and skin abscess, as a type of immune dysregulation predisposing to the disease, in addition to systemic inflammation, malignancy, and old age. Although it is usually an aggressive disease, spontaneous regression has been seen in a few cases: in HIV-positive patients on antiretroviral therapy [5, 6], in patients with autoimmune disease after decreasing [7] or stopping [8] immunosuppressive therapy, and in an HIV-negative patient who had not undergone any intervention [9].

Plasmablastic lymphoma in the uterus has been very rarely reported. After excluding secondary involvement [10], we identified four reported cases of patients aged 47 years [11], 54 years [12], 61 years [13], and 85 years [14], respectively. Only the 61-year-old patient was HIV-positive, while the others were HIV-negative. The 47-year-old patient died shortly after the diagnosis, while the 85-year-old patient responded well to chemoradiotherapy and was alive after 19 months. The patient outcomes of the other two cases were not reported.

In our case, the histomorphology and immunophenotype were most consistent with the diagnosis of plasmablastic lymphoma. Important differential diagnoses included ALK-positive large B-cell lymphoma, HHV8-positive diffuse...
large B-cell lymphoma, diffuse large B-cell lymphoma associated with chronic inflammation (DLBCL-CI), and florid reactive lymphoid hyperplasia (lymphoma-like lesion or pseudolymphoma). ALK and HHV8 negativity on immunohistochemistry was not consistent with the diagnosis of ALK-positive large B-cell lymphoma and HHV8-positive diffuse large B-cell lymphoma, respectively. DLBCL-CI is an interesting consideration, especially considering that many cases arise in inflamed closed spaces such as pyothorax and pseudocysts and a subset has an excellent prognosis. Moreover, a case of DLBCL-CI with plasmacytic differentiation was recently reported [15]. On the other hand, anal fistula and skin abscess associated with plasmablastic lymphoma in the aforementioned case series [4] might also be considered as closed spaces with chronic inflammation. These cases and ours might represent a conceptual overlap between plasmablastic lymphoma and DLBCL-CI. Depending on how the disease is defined, an argument for the diagnosis of florid reactive lymphoid hyperplasia could also be made. The clinical course of a spontaneously regressing lymphoma and that of a pseudolymphoma would be indistinguishable. Reanalysis of cases that were retrospectively diagnosed as florid reactive lymphoid hyperplasia might reveal some cases that could also be interpreted as spontaneously regressed lymphoma. Although PCR analysis of immunoglobulin genes could have provided important information regarding the clonality of the proliferating plasmacytoid cells in our case, this investigation could not be done because the material from the second biopsy performed explicitly for this purpose did not contain the atypical cells seen in the first biopsy.

When atypical lymphoplasmacytic proliferation is encountered, the diagnosis and clinical decision making is often difficult. Hence, multidisciplinary discussion is crucial for the appropriate management of these patients.

Disclosure of conflict of interest

None.

Address correspondence to: Tomoyuki Otani, Department of Pathology, Kindai University Faculty of Medicine, 377-2 Ohno-Higashi, Osaka-Sayama, Osaka 589-8511, Japan. Tel: +81-72-366-0221; Fax: +81-72-360-2028; E-mail: tomoyu@gmail.com

References

[1] Geyer JT, Ferry JA, Harris NL, Young RH, Longtine JA and Zukerberg LR. Florid reactive lymphoid hyperplasia of the lower female genital tract (lymphoma-like lesion): a benign condition that frequently harbors clonal immunoglobulin heavy chain gene rearrangements. Am J Surg Pathol 2010; 34: 161-168.

[2] Colomo L, Loong F, Rives S, Pittaluga S, Martínez A, López-Guillermo A, Ojanguren J, Romagosa V, Jaffe ES and Campo E. Diffuse large B-cell lymphomas with plasmablastic differentiation represent a heterogeneous group of disease entities. Am J Surg Pathol 2004; 28: 736-747.

[3] Castillo JJ, Bibas M and Miranda RN. The biology and treatment of plasmablastic lymphoma. Blood 2015; 125: 2323-2330.

[4] Tchernonog E, Faurie P, Coppo P, Monjanel H, Bonnet A, Algarte Génin M, Mercier M, Dupuis J, Bijou F, Herbaux C, Delimer A, Fabiani B, Besson C, Le Gouill S, Gyan E, Laurent C, Ghesquieres H and Cartron G. Clinical characteristics and prognostic factors of plasmablastic lymphoma patients: analysis of 135 patients from the LYSA group. Ann Oncol 2017; 28: 843-848.

[5] Nasta SD, Carrum GM, Shahab I, Hanania NA and Udden MM. Regression of a plasmablastic lymphoma in a patient with HIV on highly active antiretroviral therapy. Leuk Lymphoma 2002; 43: 423-426.

[6] Armstrong R, Bradrick J and Liu YC. Spontaneous regression of an hiv-associated plasmablastic lymphoma in the oral cavity: a case report. J Oral Maxillofac Surg 2007; 65: 1361-1364.

[7] García-Noblejas A, Velasco A, Cannata-Ortiz J and Arranz R. Spontaneous regression of immunodeficiency associated plasmablastic lymphoma related to methotrexate after decrease of dosage. Med Clin (Barc) 2013; 140: 569-570.

[8] Yordanova K, Stilgenbauer S, Bohle RM, Lesan V, Thurner L, Kaddu-Mulindwa D, Bittenbring JT, Scharberger M, Aßmann G and Bewarder M. Spontaneous regression of a plasmablastic lymphoma with MYC rearrangement. Br J Haematol 2019; 186: e203-e207.

[9] Igawa T, Sato Y, Kawai H, Kondo E, Takeuchi M, Miyata-Takata T, Takata K and Yoshino T. Spontaneous regression of plasmablastic lymphoma in an elderly human immunodeficiency virus (HIV)-negative patient. Diagn Pathol 2015; 10: 1-5.

[10] Pather S, Philip V, Lakha AB, Wiggill TM, Suleman M and Patel M. An expanded spectrum of high-grade B-cell non-hodgkin lymphomas in-
Transient plasmablastic proliferation with pyometra involving the cervicovaginal region. Int J Gynecol Pathol 2015; 34: 564-569.

[11] Matsuki E, Miyakawa Y, Asakawa S, Tsukada Y, Yamada T, Yokoyama K, Kudoh J, Ikeda Y and Okamoto S. Identification of loss of p16 expression and upregulation of MDR-1 as genetic events resulting from two novel chromosomal translocations found in a plasmablastic lymphoma of the uterus. Clin Cancer Res 2011; 17: 2101-2109.

[12] Hwang JP, Jeong SH, Kim HK and Park JM. Human immunodeficiency virus (HIV)-negative uterine plasmablastic lymphoma on 18F-FDG PET/CT. BJR Case Rep 2017; 3: 20160124.

[13] Arce J, Broadway K, Somma J and Khader S. A case of plasmablastic lymphoma diagnosed on liquid-based pap test. Diagn Cytopathol 2014; 42: 956-958.

[14] Liu F, Asano N, Tatematsu A, Oyama T, Kitamura K, Suzuki K, Yamamoto K, Sakamoto N, Taniwaki M, Kinoshita T and Nakamura S. Plasmablastic lymphoma of the elderly: a clinicopathological comparison with age-related Epstein-Barr virus-associated B cell lymphoproliferative disorder. Histopathology 2012; 61: 1183-1197.

[15] Moreno EM, Ferrer-Gómez A, Arias HP, García IG and García-Cosío M. Fibrin-associated diffuse large B-cell lymphoma with plasmacytic differentiation: case report and literature review. Diagn Pathol 2020; 15: 117.