Transient Atypical Lymphoplasmacytic Proliferation in Endometrium Associated With Pyometra: a Case Report

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Case Report

Keywords: plasmablastic lymphoma, spontaneous regresseion, uterus, endometrium, case report

Posted Date: January 11th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-141432/v1

Abstract

Background 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 in the uterus is rare. Here we report a case of atypical lymphoplasmacytic proliferation resembling plasmablastic lymphoma associated with pyometra that disappeared completely as the pyometra resolved.

Case presentation 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 cytoplasms 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 histological 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.

Conclusions This case underscores the sometimes blurry distinction between benign inflammation and lymphomas.

Background

Distinguishing between lymphomas and benign lymphoma-like lesions can be difficult, in endometrium[1] and other organs. Further complicating the situation is the ever more 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 Presentation

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-tinged and malodorous purulent material, and transvaginal ultrasonography revealed a uterus filled with irregular echogenicity (Fig. 1A). Culture of the vaginal discharge grew *Escherichia coli* and, with 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 (Fig. 2). These findings were consistent with the diagnosis of pyometra.

Histopathological examination of the biopsy specimen from the endometrium revealed a dense cellular infiltrate expanding the endometrial stroma (Fig. 2A). Remarkably, among mixed inflammatory infiltrate were a significant population of large lymphoid or plasmablastoid cells with abundant cytoplasms and prominent nucleoli. Mitotic figures were scattered (Fig. 2B). 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 (Fig. 2C&D). Ki67 labelled at least 80% of the large cells. (Fig. 2E). 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 (Fig. 2F). Since the positive cells did not have obvious large nuclei, it could not be determined whether they belonged to the large proliferating cells or the admixed inflammatory cells. The histological picture was highly indicative of lymphoma, especially plasmablastic lymphoma or aggressive B-cell lymphoma, though the unusual clinical context was deemed problematic for a definite diagnosis.

After repeated irrigation with saline, the intrauterine echogenicity completely disappeared (Fig. 1B). Flow cytometry and PCR analysis for immunoglobulin heavy chain gene rearrangement, using an endometrial sample acquired days after the biopsy, did not reveal any significant findings. Further work-up with PET-CT and bone marrow biopsy did not reveal any lymphoproliferative lesions or plasma cell neoplasms. 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 And Conclusions

Lymphomas arising primarily in the female genital tract are rare, though secondary involvements are not uncommon.[2] Transient lesions mimicking lymphomas are known under the name of “florid reactive lymphoid hyperplasia,” “pseudolymphoma,” or “lymphoma-like lesion.”[1,3] 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 proved to be a monoclonal proliferation.[1] This underscores the sometimes blurry distinction between benign inflammation and lymphomas.

Plasmablastic lymphoma is a mature B-cell neoplasm with plasmablastic differentiation, often associated with HIV infection and other forms of immunosuppression.[4–6] A classic example is a tumor in the oral mucosa of an HIV-positive patient.[7] EBV is positive in 60–75% of cases.[4,8] In HIV-negative, non-transplant patients, Tchernonog et al[9] 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,[10,11] in patients with autoimmune disease after decreasing[12] or stopping[13] immunosuppressive therapy, and in an HIV-negative patient who had not undergone any intervention.[14]

Plasmablastic lymphoma in the uterus is very rarely reported. After excluding secondary involvement,[15] we identified four reported cases of patients aged 47 years[16], 54 years[17], 61 years[18], and 85 years, respectively.[19] 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 is of excellent prognosis. Moreover, a case of DLBCL-CI with plasmacytic differentiation was recently reported.[20] On the other hand, anal fistula and skin abscess associated with plasmablastic lymphoma in the aforementioned case series[9] 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, a case for the diagnosis of florid reactive lymphoid hyperplasia could also be made. The clinical course of lymphoma, which regresses spontaneously, and that of 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.

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.

List Of Abbreviations

HIV: human immunodeficiency virus; EBV: Epstein–Barr virus; EBER: EBV-encoded small RNA; DLBCL-CI: diffuse large B-cell lymphoma associated with chronic inflammation.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

none

Authors' contributions

TO drafted the manuscript. TO, MK, TS and AI conducted the histopathological study and diagnosis. KM and NM provided care for the patient. MM conducted the radiological study and diagnosis. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

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Figures

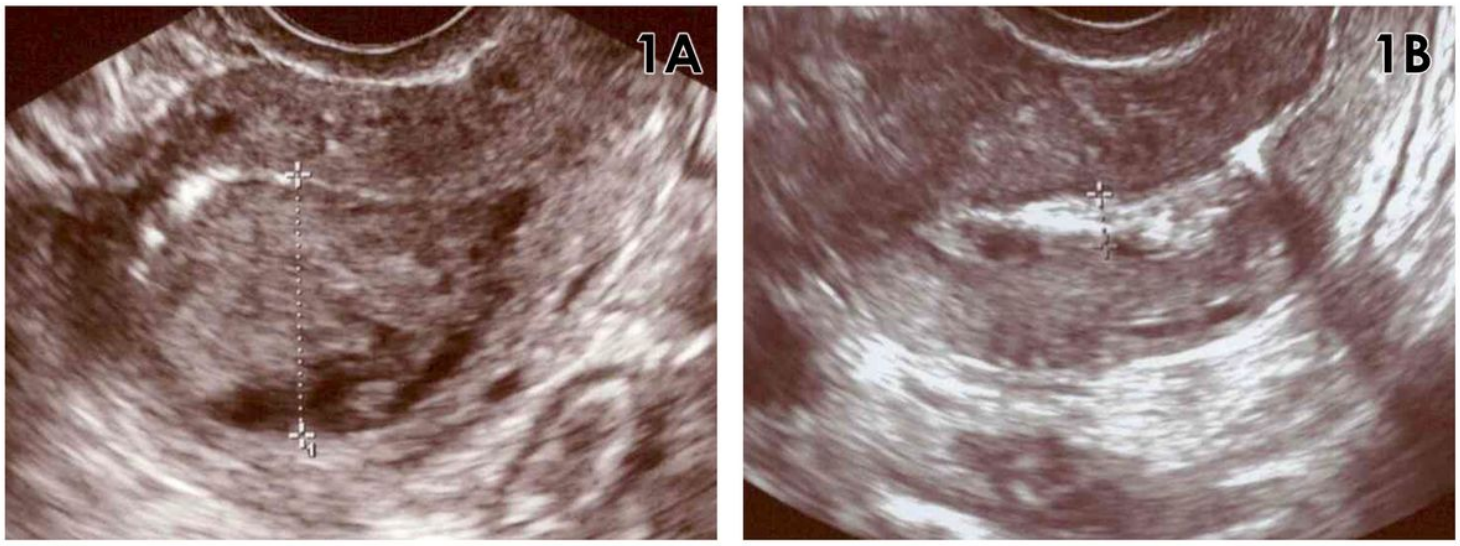

Figure 1

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

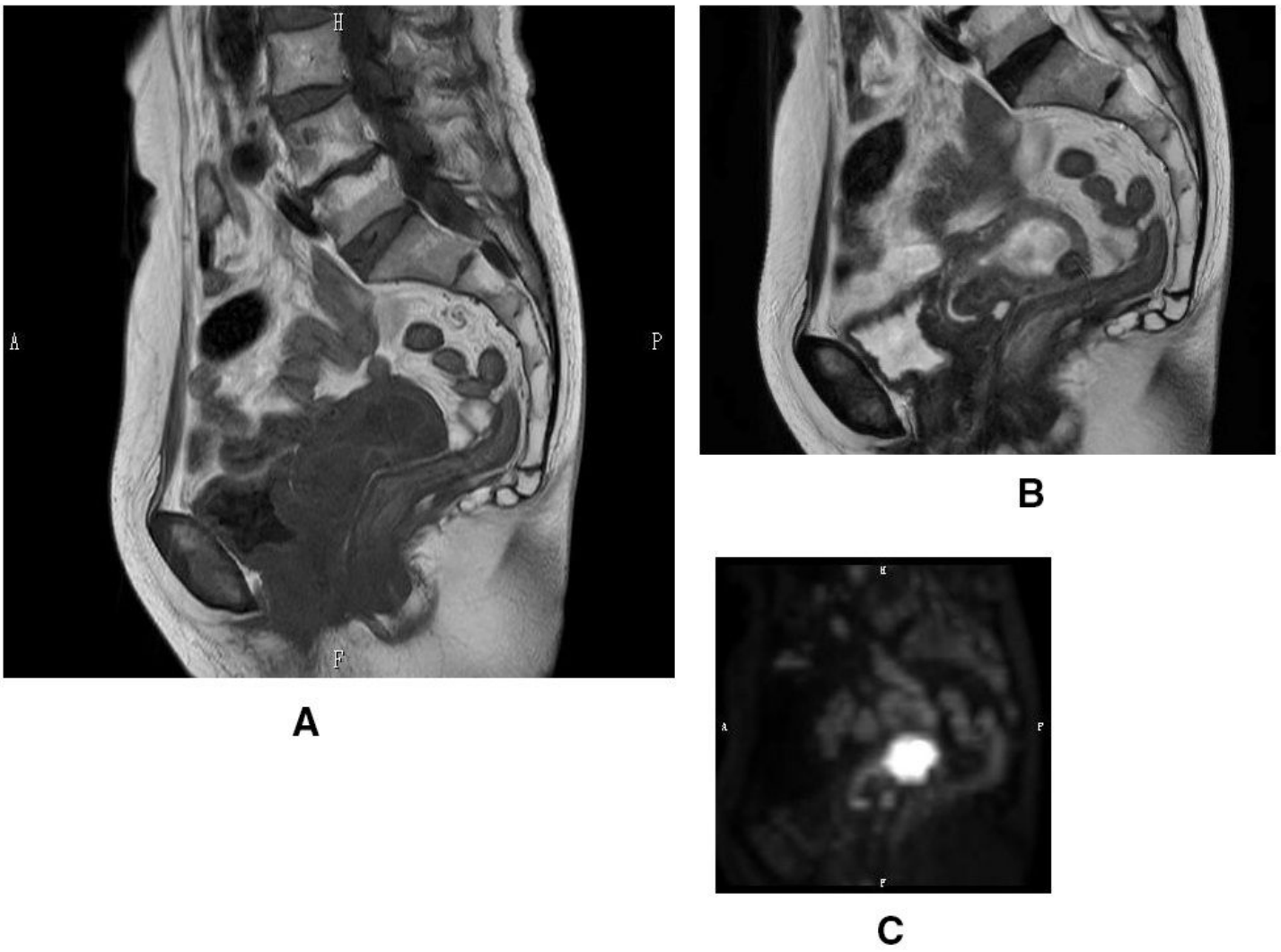

Figure 2

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

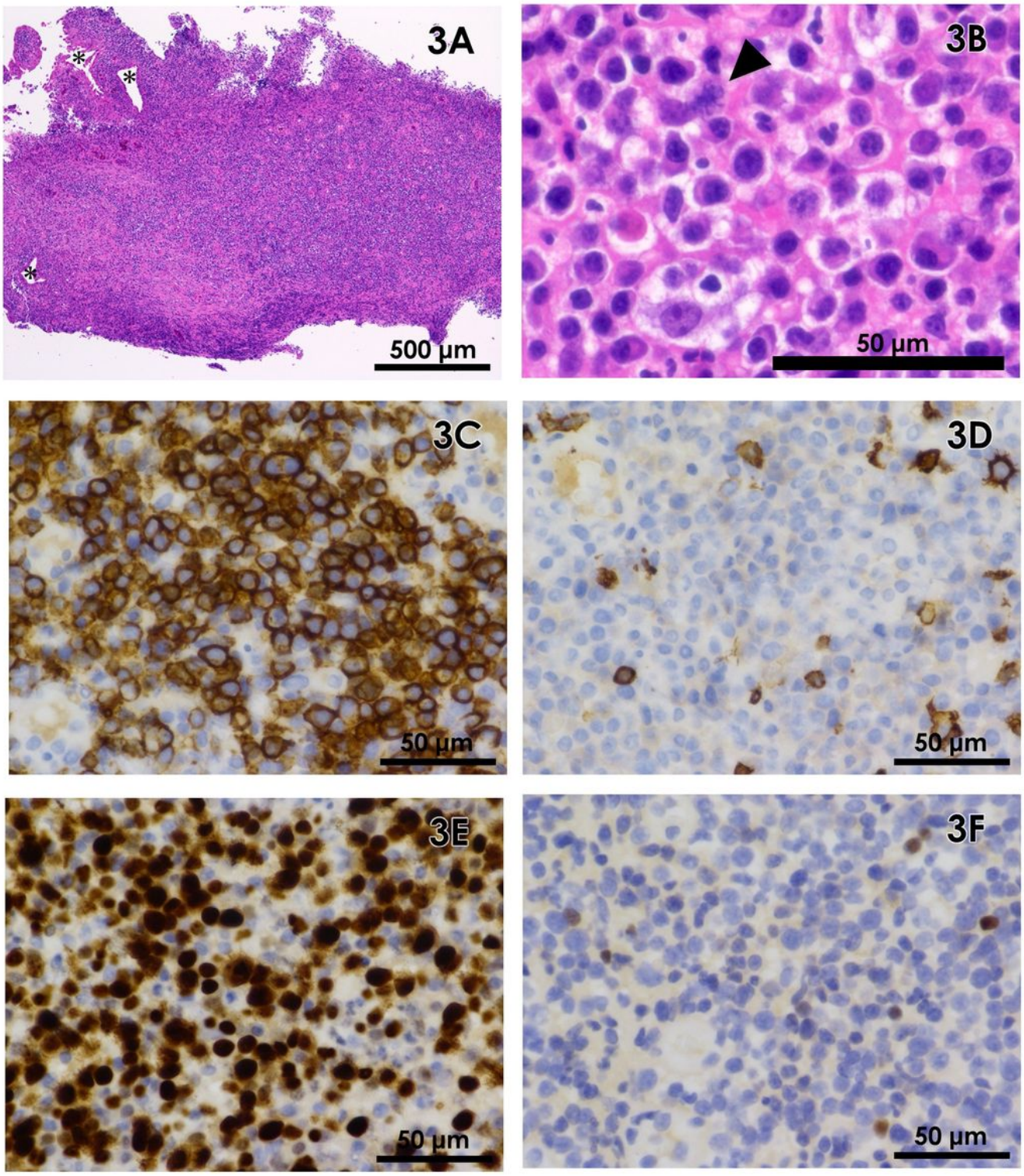

Figure 3

Atypical lymphoplasmacytic proliferation resembling plasmablastic lympohoma in the endometrium associated with pyometra. Large lymphoid or plasmablastic cells with prominent nucleoli and abundant cytoplasm proliferated in the endometrial stroma. Asterisks (*) indicate endometrial glands (A). Some mitotic figures (arrowhead) were scattered. Immunohistochemistry revealed that the large plasmablastic cells were CD138-positive (C) and CD20-negative (D). Ki67 labelled at least 80% of the large cells (E).

Scattered cells were positive for EBV by EBER in situ hybridization (F). (hematoxylin–eosin, original magnification X40, bar = 500 μm [A] and X400, bar = 50 μm [B]; original magnification X400, bar = 50 μm [C–F])

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