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Case Report

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

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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 regresseion, 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-tinged 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-

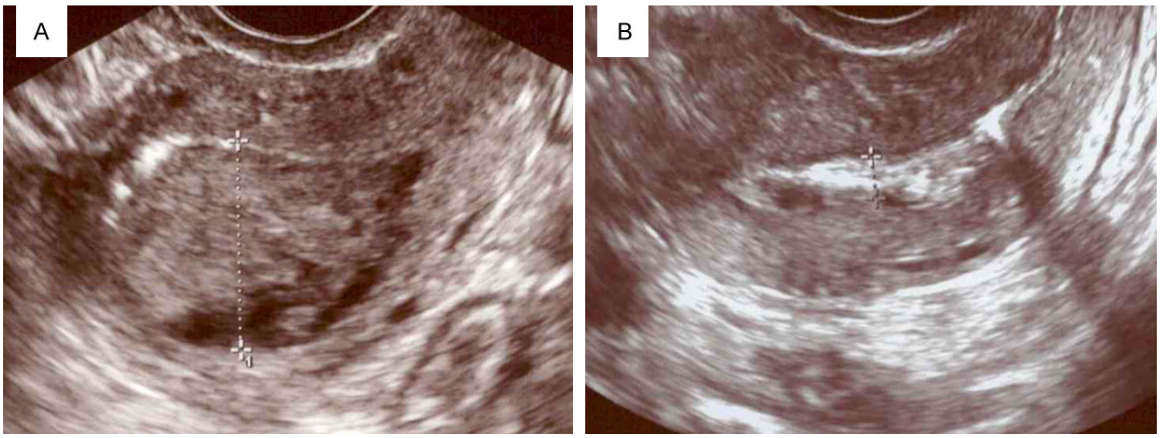

Figure 1. Ultrasonographic imaging. The uterus was filled with irregular echogenicity (A), which disappeared completely after repeated irrigation (B).

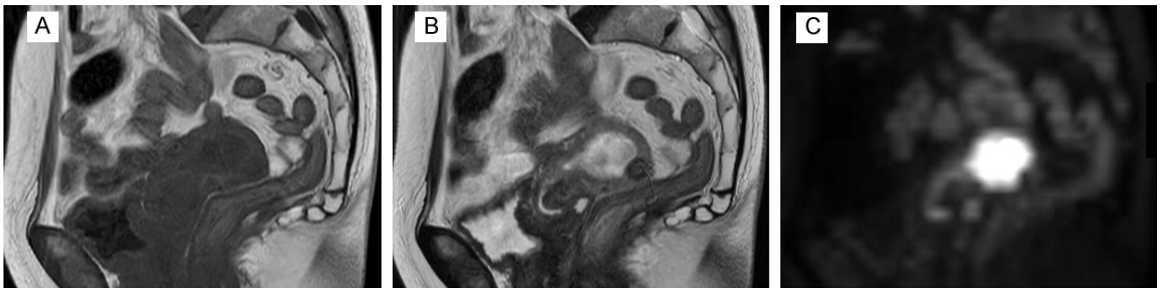

Figure 2. MRI. Inside of the uterine cavity was T1-hypointense (A), T2-hyperintense (B), and diffusion-restricted (C), consistent with pyometra.

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.

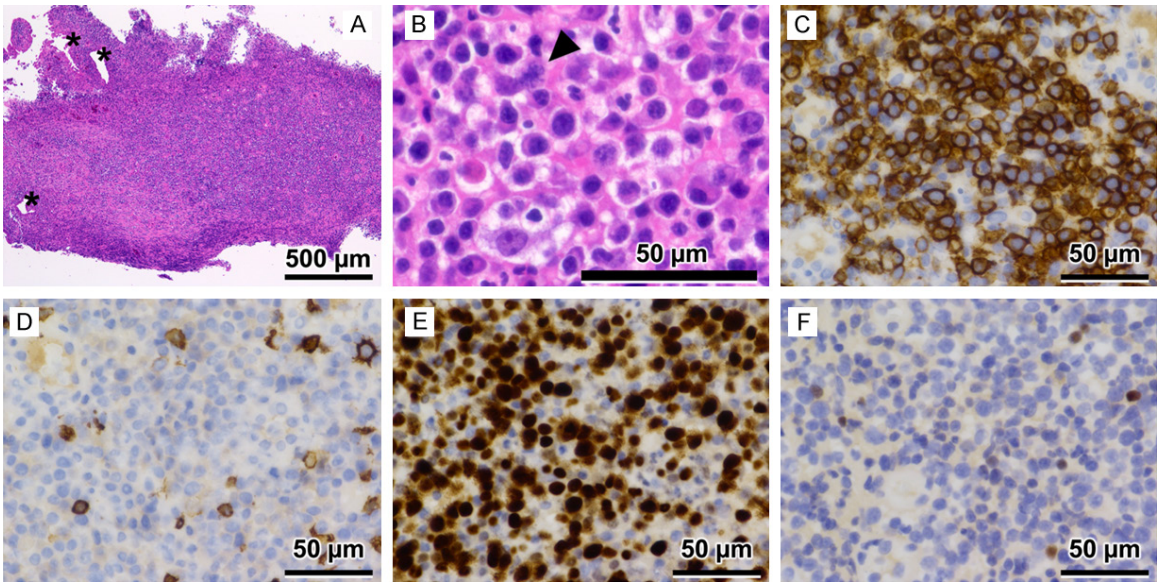

Figure 3. Atypical lymphoplasmacytic proliferation resembling plasmablastic lympohoma in the endometrium associated with pyometra. Large lymphoid or plasmablastic cells with prominent nucleoli and abundant cytoplasm proliferated in the endometrial stroma. Asterisks (*) indicate endometrial glands (A). Some mitotic figures (arrowhead) were scattered (B). 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]).

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 lymphoplasmacytoid 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.

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