A rare case of primary extranodal marginal zone B-cell lymphoma of the ovary, fallopian tube, and appendix in the setting of endometriosis

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Extranodal marginal zone B-cell lymphomas (MZL) of the female genital tract are exceedingly rare. We report the first case of a primary extranodal MZL of the ovary, fallopian tube, and appendix arising in the setting of chronic inflammation due to endometriosis.

Extranodal marginal zone B-cell lymphomas are uncommon. Most occur in the gastrointestinal tract. Marginal zone B-cell lymphomas of the female genital tract are rare, and few cases exist of marginal zone B-cell lymphomas of the uterus, cervix, and fallopian tubes. We report the first marginal zone B-cell lymphoma of the ovary, fallopian tube, and appendix arising in endometriosis.

Key words: endometriosis, extranodal marginal zone B-cell lymphoma, fallopian tube, ovary

Case Report

A 47-year-old woman, gravida 0, para 0, with severe dysmenorrhea was referred for evaluation and treatment. Her past medical history included polycystic ovarian syndrome. She had no prior surgical history. She had a family history of cancer, including her mother who had acute lymphoma, maternal and paternal grandmothers who had ovarian cancer, and a maternal cousin who had peritoneal cancer. Pelvic examination was significant for right adnexal and posterior cul-de-sac tenderness. Preoperative transvaginal ultrasound revealed small uterus and ovaries and laboratory tests including complete blood count, comprehensive metabolic panel, and hormone levels were within normal limits for a postmenopausal female.

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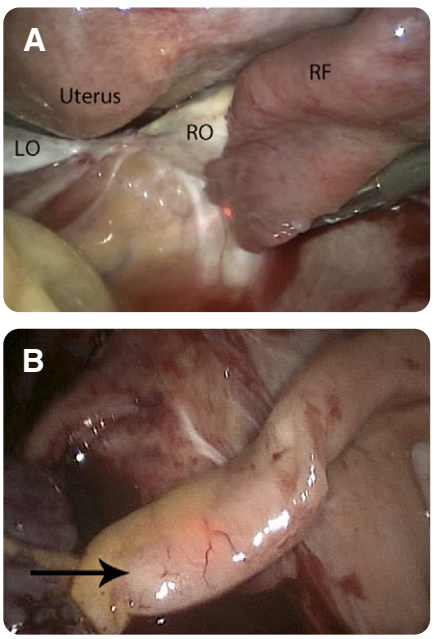
The patient underwent multipuncture operative laparoscopy as previously described,[1] with removal of the uterus, cervix, bilateral ovaries, appendix, and peritoneal biopsies. Findings during the procedure included severe endometriosis, thick adhesions of both ovaries and fallopian tubes to the pelvic sidewalls (Figure 1, A), and obliteration of the posterior cul-de-sac. The appendix appeared asymmetric and adherent to the pelvic sidewall (Figure 1, B). All visible lesions, adhesions, and scarring in the pelvis and abdomen were excised during the surgery.

The surgical pathology report described dense infiltrates of lymphocytes involving the right ovary (Figure 2, A), fallopian tube, appendix, and right pelvic sidewall consistent with a low-grade B-cell lymphoma. Endometriosis was present in the rectosigmoid biopsy, left ovary (Figure 2, C), and left fallopian tube. The uterus was unremarkable. The peritoneal washings performed were negative for malignant cells, but demonstrated numerous histocytes, mesothelial cells, and hemosiderin-laden macrophages indicative of endometriosis. Immunohistochemical staining of the lymphocytes was positive for the B-cell lineage marker, CD20 (Figure 2, B). These lymphocytes were also positive for BCL-2. The cells were negative for CD3, CD5, CD10, CD43, BCL-1 (cyclin D1), and BCL-6. A marker of proliferation Ki-67 was positive in 10% of the cells. The findings were consistent with a low-grade B-cell lymphoma with features of a marginal zone lymphoma.

After the surgery, a bone marrow biopsy with flow cytometry was performed. The results were negative for residual lym-

FIGURE 1
Laparoscopic images of the pelvis



A, Laparoscopic image of the right adnexa, the right ovary (RO), left ovary (LO), and right fallopian tube (RF) were normal appearing but densely adherent to the posterior cul-de-sac and pelvic sidewall. **B**, The appendix (*arrow*) was thickened at its tip and was adherent to the pelvic brim.

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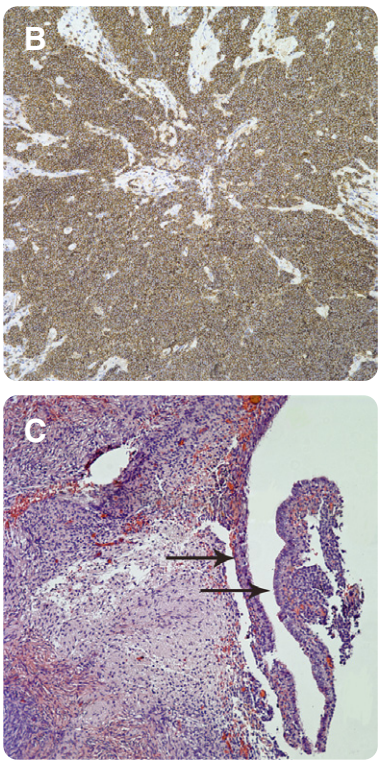
FIGURE 2
Histology



A, The right ovary (hematoxylin and eosin [H&E] stained) was densely infiltrated by lymphoid cells which appear on the left (*arrow*), contrasted by normal ovarian stroma on the right (magnification ×100). **B**, CD20 immunoperoxidase staining of the right ovary revealed dense aggregates of lymphoid cells, which are positively stained brown against the light blue background of ovarian stroma (magnification ×100). **C**, The left ovary (H&E stained), had endometrial glands and stroma (*double arrows*) adherent to the ovarian cortex. This finding is characteristic of endometriosis (magnification ×100).

Nezhat. Primary extranodal MZL of the ovary, fallopian tube, and appendix. Am J Obstet Gynecol 2013.

phoma. The patient underwent whole body positron emission tomography (PET) imaging at 1 week, 4 months, and 12 months after surgery; all studies showed no evidence of disease. The patient was Stage I A according to the Ann Arbor staging system modified for extranodal lymphomas.[2,3] Consultation with a hematologist/oncologist recommended close observation with PET imaging every 6 months, which could be extended to every 12 months if she had no progression of disease.

COMMENT

Marginal zone lymphomas are a subset of non-Hodgkin's lymphomas that originate from the marginal zone of B-cell follicles. The most common extranodal sites of occurrence are gastric mucosa,[4] small and large intestine,[5] salivary gland,[6] lung,[7] thyroid, orbit,[8] and skin.[9] Of the extranodal MZLs, only 2% originate in the female genital tract.[10] The most common site is the uterus.[11,12] Two case reports of fallopian tube MZLs exist in the literature.[13,14] No cases of ovarian MZLs have been reported to date. This is the first case of a primary extranodal MZL of the ovary, fallopian tube, and appendix, and the first case of a MZL associated with endometriosis.

MZLs of mucosa-associated lymphoid tissue (MALT)-type are associated with chronic infection and inflammation where antigens induce clonal B-cell proliferation. These lymphomas are most common in the gastrointestinal tract where they are linked with chronic gastritis and *Helicobacter pylori* infection.[15] MZLs also occur in patients with autoimmune diseases. Several case reports exist of MALTs arising in the thyroid glands of patients with Hashimoto's thyroiditis[16,17] and in the salivary glands of patients with Sjögren syndrome.[6]

In the female genital tract, endometriosis is a common and chronic inflammatory disorder. Inflammation because of endometriosis is theorized to lead to malignant transformation in some cases of uterine[18] and ovarian cancers.[19,20] This phenomenon has been well-documented[21] because Sampson reported the first case in 1925.[22] In fact, women with endometriosis have a 2-fold higher risk of developing ovarian cancer, 30% higher risk of developing breast cancer, and 40% higher risk of developing hematopoietic malignancies such as lymphoma.[23]

Endometriosis is known to stimulate a milieu of inflammatory mediators that promote angiogenesis, cell proliferation, and produce reactive oxygen species that cause DNA damage. This inflammatory environment is hypothesized to stimulate B-cell proliferation and neoplastic transformation. The significance of this case is the association between endometriosis and other inflammatory disorders. Endometriosis may share similar pathways as other established infectious and autoimmune diseases. In part, this finding could lead us to explore current therapies for other disorders for the treatment of endometriosis. ■

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