False-positive malignant peritoneal cytology associated with pelvic endometriosis

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The peritoneal washings obtained at diagnostic laparoscopy of two women with suspected endometriosis contained cells with cytologic features of adenocarcinoma. Exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic washings confirmed endometriosis with no evidence of cancer. At 1.5-year and 4.0-year follow-up, respectively, cancer had not developed in either patient. The authors report what they were able to find in the literature regarding false-positive assessments of malignancy obtained by cytologic examination. They also outline steps to be taken should a diagnosis of malignancy arise in a woman with endometriosis who desires pregnancy.

(Key words: Endometriosis, peritoneal cytology)

Fifteen percent of women aged 14 to 44 years have endometriosis, and 30% of all infertile women have that condition. Diagnosis requires laparoscopy or laparotomy for obtaining a biopsy specimen. In women with endometriosis, peritoneal washings have been obtained for diagnosis, and for determining CA-125 levels, prostaglandin level, leukocyte population, and the presence of autoantibodies. Seventeen percent of ovarian tumors are associated with endometriosis, and 1% of endometriotic lesions undergo malignant transformation. Also, 30% of early and 90% of advanced ovarian cancers produce findings of malignancy on peritoneal cytologic assessment. We describe two cases of endometriosis in which laparoscopic peritoneal cytologic examination was falsely positive for malignant cells.

Report of cases

Case 1
A 45-year-old woman, gravida 4, para 3, abortus 1, underwent diagnostic laparoscopy for probable endometriosis. Results of a preoperative cervical cytologic analysis were normal. Laparoscopy revealed a retroverted, slightly enlarged uterus; a smooth, unilocular 3-cm left ovarian cyst; a right ovary densely adherent to the posterior leaf of the broad ligament; and 20 mL of clear fluid in the cul-de-sac.

There was no visual evidence of cancer in the abdomen or pelvis. Peritoneal fluid contained cells with cytologic features of adenocarcinoma in cohesive groups with hyperchromatic, eccentrically placed nuclei; clumped nuclear chromatin; occasional macronuclei; and chaotic nuclear polarity (Figures 1 and 2).

Postoperative abdominal and pelvic computed tomography (CT) scans, a barium enema, an upper gastrointestinal tract examination, an intravenous pyelogram, and a mammogram showed no evidence of cancer. Exploratory laparotomy with total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic washings, and omentectomy revealed no visual or palpable evidence of cancer in the abdomen or pelvis.

Pathologic examination revealed endometriosis of...
the right ovary, right pelvic side wall, and bladder peritoneum but no adenocarcinoma. Cytologic washings of the pelvis showed benign glandular cells. At a 4.0-year follow-up examination, the patient had no evidence of cancer.

Case 2
A 35-year-old woman, gravida 2, para 2, underwent diagnostic laparoscopy for probable endometriosis. The findings of the preoperative cervical cytologic examination were normal. Laparoscopy revealed endometriosis on the uterosacral ligaments. Both ovaries appeared to be normal. There was no visual evidence of cancer in the abdomen or pelvis.

A biopsy specimen from the uterosacral ligaments showed endometriosis. Pelvic washings contained cells with cytologic features of adenocarcinoma with a high nucleocytoplasmic ratio, clumped nuclear chromatin, sharply angulated and irregular nuclear membranes, and occasional nuclear grooves (Figures 3 and 4). Psammoma bodies were also identified (Figure 5).

Exploratory laparotomy with total abdominal hysterectomy, bilateral salpingo-oophorectomy, resection of endometriotic tissue, pelvic washings, and a Papanicolaou smear of the diaphragm revealed no visual or palpable evidence of cancer in the abdomen or pelvis. Pathologic examination showed endometriosis of the left ovary and both uterosacral ligaments, but no evidence of carcinoma. Pelvic washings and a Papanicolaou smear of the diaphragm showed no atypia. At a 1.5-year follow-up examination, the patient had no evidence of cancer.

Discussion
Atypical cells in peritoneal washings have been associated with endometriosis and other benign gynecologic diseases. Zuna and Mitchell retrospectively examined peritoneal washings from 149 women with benign gynecologic disease. A false-positive determination of malignancy by cytologic assessment occurred in 2.7% of benign cases. One case of endometriosis associated with a false-positive determination of malignancy was reported, but there was no discussion of the surgical procedure undertaken and no follow-up information was given.

One additional case of a false-positive reading of malignancy attained by peritoneal cytologic analysis associated with endometriosis has been reported, but, again, the surgical procedure was not discussed nor was follow-up information given. To our knowledge, ours is the first detailed report of false-positive diagnoses of malignancy obtained by this method in association with endometriosis.
A false-positive cytologic diagnosis of malignancy in women with endometriosis is significant because of the association of endometriosis with ovarian cancer. In the two cases reported here, neither women desired fertility and, therefore, a hysterectomy and oophorectomy were performed, permitting a definite diagnosis. To detect common malignancies associated with a cytologic diagnosis (cancer of the ovary, uterus, fallopian tubes, cervix, colon, pancreas, and breast), further diagnostic information should be obtained preoperatively by cytologic examination of the cervix, assessment of the CA-125 and carcinomaembryonic antigen levels, CT of the abdomen and pelvis, barium enema films, and mammography.

A dilemma would arise if malignancy were diagnosed by cytologic analysis in a woman with endometriosis who was attempting pregnancy. We have no experience with this situation nor
LAPAROSCOPY
Malignant peritoneal cytology

PREOPERATIVE EVALUATION
Cervical cytology
CA-125 and CEA levels
CT of abdomen/pelvis
Barium enema
Mammography

Does not desire fertility
Laparotomy
Total abdominal hysterectomy
Bilateral salpingo-oophorectomy
Frozen section

Desires fertility
Laparotomy
Exploration of abdomen/pelvis
Biopsy of tissue suggestive of malignancy
Frozen section

FROZEN SECTION:
Ovarian cancer
Staging
Cytoreduction

FROZEN SECTION:
No cancer
No further treatment

FROZEN SECTION:
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Cytoreduction

FROZEN SECTION:
No cancer
No further treatment

Figure 6. Algorithm for diagnosis and treatment of women with positive peritoneal cytologic evidence and no obvious primary cancer.

has such a case been reported in the literature. However, because of the association of endometriosis with ovarian cancer and the possibility of malignant transformation of endometriosis, a laparotomy would be necessary following preoperative evaluation (Figure 6).

Visual and palpable exploration of the entire abdomen and pelvis should be performed with the assistance of a gynecologic oncologist. Biopsy specimens should be taken from all regions suggestive of malignancy. Biopsies should be performed on both ovaries, and all ovarian cysts should be excised. All biopsy specimens should be analyzed by frozen section.

If ovarian cancer is diagnosed, appropriate surgical staging and cytoreductive surgery should be performed by the gynecologic oncologist. If no ovarian cancer is diagnosed on frozen section and
if this diagnosis is confirmed by permanent section, the woman can retain her uterus and ovaries and continue to attempt pregnancy. Of course, all options and risks would need to be discussed with the patient preoperatively.

Comment
Pursuant to the two cases described here, we are currently performing a prospective study to evaluate the incidence of false-positive malignant peritoneal cytologic assessment in women with endometriosis.

References