Peritoneal Cytology in Gynecologic Cancer: an Essential Adjunct

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Accurate evaluation of the extent of disease is essential to accurately stage gynecologic cancers. Methods to assess the spread of such tumors include random biopsies of the serosal surfaces, lymph node sampling, and obtaining direct cytologic smears of large areas of the peritoneum (1). Peritoneal fluid cytology results play an important role in the staging and prognostication of gynecologic cancers.

The study of a large series of patients with gynecologic cancers reported by Zuna and Behrens (2) in this issue of the Journal documents the need for this type of evaluation. This study is important for several reasons. First, it evaluates peritoneal washings in patients with various types of gynecologic neoplasms, including endometrial and cervical cancers as well as ovarian tumors (2-4). Second, it details the method of obtaining the sample. Early in the surgical procedure, before manipulation of the peritoneal surfaces or of the serosal tumor, sterile saline is instilled into the peritoneal cavity, after which it is aspirated and sent to the cytology laboratory (2). This procedure reduces the risk of obtaining false-positive results. This technique, which is "second nature" to a well-trained gynecologic oncologist, may be virtually unknown to a general surgeon or a non-specialist gynecologic surgeon. Hence, if a general surgeon or a non-specialist gynecologic surgeon is performing the surgery, the inappropriate sampling technique may confuse the cytologic evaluation (5).

Zuna and Behrens (2) point out that the expertise in these situations must extend also to the pathologist. The study design indicates that surgeons treating different types of tumors of the female reproductive system collect variable numbers of peritoneal samples, ranging from an average of one for cervical cancer to five for ovarian tumors. No ancillary diagnostic techniques, such as ploidy analysis (6) or immunocytochemistry (6,7), were used by Zuna and Behrens to refine the results. Indeed, one value of the study by Zuna and Behrens is that it relied on standard cytologic and histologic correlation and hence can be utilized in virtually any pathologic practice setting. The pathologist, however, must be fully aware of the wide range of pathologic changes that can be seen in reactive mesothelial cells, unusual but benign inclusions of the peritoneum, effects of pharmacologic agents (especially hormones) on the histology of the mesothelium, and a variety of other benign inflammatory conditions that can interfere with the pathologist's interpretation of the peritoneal samples.

These conditions include florid mesothelial hyperplasia (8,9), endosalpingiosis (10), detached ciliary tufts (11), and endometriosis, decidual reaction, mesonephric remnants, squamous metaplasia, endocervicosis, and histiocytic inflammatory reactions (9). Obviously, interpreting any of these benign lesions as carcinoma will lead to overstaging, perhaps unneeded therapy, and spurious predictions regarding prognosis.

Florid mesothelial hyperplasia (8,9) is most often seen in patients with ovarian epithelial tumors. The pathologist may identify clusters or papillae of large cells mimicking a serous ovarian neoplasm; psammoma bodies may be seen. The experienced pathologist will recognize the plate-like edges of the mesothelial cells in the cluster and the uniform reactive appearance of the nuclei to aid in differentiating this mesothelial hyperplasia from carcinoma.

Detached ciliary tufts in peritoneal washings are predominately found in premenopausal women, who are usually in the secretory phase of the menstrual cycle. They are believed to represent a physiologic cyclical shedding of cilia from the fallopian tube epithelium. In cytologic preparations, the identification of cilia is a reassuring clue of a benign process (11).

Endometrial, tubal (endosalpineal), or mucinous (endocervical) epithelium may be identified in the mesothelium, which probably reflects multidirectional metaplasia along various müllerian-derived tissues (9). Recognition of the bland nuclear features, cellular uniformity, and ciliated cells in the tubal type of metaplasia should help in distinguishing such lesions from malignant cells in peritoneal fluid.

Decidual reactions of the submesothelial stroma can mimic both histologically and cytologically a squamous cell carcinoma. Even in women who are not pregnant, these reactions may be found in the peritoneum as a result of either intrinsic hormonal abnormalities or exogenous hormone ingestion. The bland cytologic features aid in differentiating such lesions from malignant lesions (8).

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Metaplasia of the surface mesothelium to squamous or even transitional (urothelial-like) cells can occur and can potentially cause diagnostic confusion. Here again, however, the experienced pathologist will use clues of bland nuclear features to distinguish benign from malignant lesions.

When the method of obtaining the specimen and the pathologic interpretation are correct, then the importance of the study by Zuna and Behrens (2) becomes obvious. In the setting of an adequate debulking procedure in a patient with an ovarian tumor or in the setting of extirpation for endometrial or cervical cancer (even if the lymph nodes sampled are negative for metastases), the presence of positive cytologic findings in peritoneal fluid and/or washings appears to be an important variable that predicts a poor prognosis. The exception is in low-malignant-potential tumors of the ovary, where positive cytologic findings do not appear to have an impact on prognosis; these lesions, often diagnosed in young women (<30 years old), are unusual in so many other respects that it is not surprising that, in the issue of peritoneal cytology findings, the low-malignant-potential tumors are "outliers" again.

It is rare for positive findings in peritoneal cytology to be the sole indicator of a high stage for gynecologic cancer. In the study by Zuna and Behrens (2), a case is cited in which, following identification of malignant cells in the washings, re-examination of the gross uterine specimen disclosed minute serosal seedings of tumor that had not been initially recognized.

The study by Zuna and Behrens specifically excluded evaluation of peritoneal washings from "second-look" surgical procedures. It would be interesting to examine such a series to assess the value of this test in predicting late recurrences of gynecologic cancers after "negative" second-look surgery.

If further studies of this type confirm the findings of Zuna and Behrens, oncologists should address new therapeutic strategies for these subgroups of patients with gynecologic cancers who appear to have optimal resections but whose peritoneal washings contain malignant cells.

References


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