**CASE**

Apprehension over a chance of cancer

She was frightened of the ovarian cyst that her gyn detected during an annual exam, thinking that he might find that she had ovarian cancer. She was only 45 years old, after all, dreaming of many more birthdays, desiring to be there to see her children marry, hoping to play with her grandchildren.

Now, she had to shoulder the anxiety of wondering what might be discovered at surgery. Did she have ovarian cancer? Was she going to die far, far too young?

According to the American Cancer Society, approximately 21,550 new cases of ovarian cancer were diagnosed last year and 14,600 women died of the disease. In fact, in the United States, ovarian cancer is the most common cause of death from a gynecologic malignancy.

To our frustration, ovarian cancer typically isn’t diagnosed until it has reached an advanced stage.

**Snapshot of the new test**

HE4 is expressed in normal male and female reproductive tract epithelium and in pulmonary epithelium. Its biologic function hasn’t been fully characterized, but it may be an inhibitor of trypsin.

A team of researchers led by Leroy Hood reported in 1999 that HE4 was over-expressed in ovarian cancer tissues. Their discovery translated to development* of an ELISA blood test for HE4 that has value in detecting and managing ovarian cancer.

HE4 is overexpressed in:
- approximately 90% of women who have serous ovarian cancer
- 99% of women who have endometrioid ovarian cancer
- 50% of women who have clear-cell cancer
- mucinous and germ-cell ovarian cancers do not over-express HE4

The normal range of circulating HE4 is ≤150 picomoles/L, or pico-molar (pM). In one study, the mean serum HE4 level in healthy control women was 41 pM; in those who had ovarian cancer, 1,125 pM.²

Recurrence and progression of ovarian Ca monitored with HE4

The assay for HE4 has been approved by the US Food and Drug Administration to aid in monitoring the recurrence and the progression of epithelial ovarian cancer. The test is not FDA-approved for making a diagnosis of ovarian cancer.

The National Comprehensive Cancer Network recommends that, for women who have ovarian cancer and an elevated level of CA 125 at the time of their diagnosis, the level of CA 125 be measured before each cycle of chemotherapy. This approach helps to ensure that disease activity is accurately monitored and progression is detected quickly—enabling the oncologist to switch as necessary to a more effective regimen.

Measuring both CA 125 and HE4 before each cycle of chemotherapy likely improves the accuracy of the determination of a patient’s true clinical status. An increase of 25% or more across sequential HE4 measurements suggests recurrence or...

*By Fujirebio Diagnostics. The test is available through Quest Diagnostics.
Preop studies of a pelvic mass
Pelvic ultrasonography is critical; the platelet count is valuable

Determining the presence of a malignancy is a major goal in the preoperative evaluation of a woman who has a pelvic mass. As I noted, referring a patient in whom you suspect ovarian cancer or pelvic malignancy to a specialty center for care increases her chance of survival.

Pelvic US is critical and the platelet count is useful in the preoperative evaluation of a pelvic mass. Here’s how to apply these studies.

Sonographic findings in an ovarian cyst that raise the risk of an ovarian malignancy include:
- solid tumor with irregular borders
- ascites
- detection of four or more papillary structures in the cyst or tumor
- ovarian cyst diameter greater than 10 cm
- Doppler demonstration of significant blood flow into the cyst or tumor

US findings that suggest the ovarian cyst is benign include:
- unicellular cyst
- no solid cyst component greater than 7 mm in diameter
- smooth cyst surface
- no significant blood flow into the cyst on Doppler imaging

The platelet count is routinely available to you preoperatively because it is automatically reported as part of a complete blood count.

In a woman who has a pelvic mass, a preop platelet count of >400 × 103/μL, signifying thrombocytosis, is associated with an increased risk of malignancy.2,3 A study of 102 patients who had a benign pelvic mass and 139 patients whose tumor was malignant or classified as borderline determined that thrombocytosis was present in 16% of women who had a benign pelvic mass and 56% of women who had a malignant or borderline tumor.2

Preoperative thrombocytosis has also been reported in children and adolescents who have a germ cell tumor.7

The lesson? Before you operate on a pelvic mass, check the platelet count!

References
5. Moore RG, McMeekin DS, Brown AK, et al. A major challenge for us is to accurately identify, before initial surgery, those women whose pelvic mass or ovarian cyst is most likely to be ovarian cancer. Proper identification would permit us, appropriately, to refer them to a specialty center.

MEASURING HE4 AND CA 125 IN COMBINATION may represent a significant advance in our ability to accurately identify and triage patients who are at high risk of serous and papillary ovarian cancer. In one study of postmenopausal women who had a pelvic mass,4 tandem measurement of HE4 and CA 125 resulted in:
- a greater chance of being cured of ovarian cancer that has been made available to us in 25 years.

Consider taking this step forward now
If you haven’t measured HE4 in your patients who have a pelvic mass or a complex ovarian cyst, consider evaluating the utility of this assay in your practice. There’s good reason to do so: HE4 is the first new marker for ovarian cancer that has been made available to us in 25 years.