Commentary (Seidman/Kurman): Update on Low Malignant Potential Ovarian Tumors

June 01, 2000
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The borderline category of ovarian tumors is one of the most controversial topics in gynecologic oncology and pathology, and is confusing to both clinicians and patients. Although numerous reviews have appeared in the literature, most of them rehash the prevailing views on borderline tumors without critically evaluating the published data that allegedly validate some rather puzzling and perplexing notions. For example, although these tumors are considered to be a subset of carcinoma, most patients are cured even when they have “metastatic” disease that has been inadequately treated. In addition, reports cite recurrence and death as late as 39 years after the diagnosis of tumors that appear histologically bland and noninvasive.

Dr. Menzin thoroughly examines commonly held views on these tumors. He also draws attention to several key problems that have obscured our understanding of these tumors. The borderline category of ovarian tumors has played an important role in the evolution of our understanding of ovarian carcinomas by segregating a group of tumors that, in contrast to typical ovarian carcinomas, do not invade the ovarian stroma and therefore are considered to be noninvasive. Most importantly, these noninvasive tumors have a superior prognosis when compared with ovarian carcinomas stage for stage.

Unfortunately, the category has also led to a clinical dilemma because many patients with borderline tumors are young and wish to preserve their fertility. However, because borderline tumors are regarded as a subset of carcinomas, their treatment has often been more aggressive than is necessary based on their behavior, which is usually benign. Recent critical evaluation of the published data has led to a reassessment of the entire concept of borderline tumors.

**Serous Borderline Tumors**

A recent review of over 2,000 published cases of stage I serous borderline tumors showed a survival rate of 99.5%. [1] It has therefore been proposed that, in the vast majority of cases, the “borderline” or “low malignant potential” designation be replaced by the term “atypical proliferative serous tumor,” which more accurately reflects the benign behavior of these tumors. Furthermore, stage II and III serous borderline tumors—ie, those with peritoneal “implants” involving the pelvic organs or abdominal cavity, respectively—can be subclassified into benign and malignant types based on their histologic appearance, and their outcome can be predicted based on the microscopic appearance of the implants. Atypical proliferative serous tumors with noninvasive implants are, for all practical purposes, benign, with survival rates of 95% to 100%. Serous tumors with invasive implants carry a 34% mortality and behave like low-grade invasive carcinomas. [1]

The vast majority of serous tumors with invasive implants have a characteristic micropapillary architecture that can be distinguished from atypical proliferative serous tumors; the former tumors have been designated “micropapillary serous carcinoma.” [2-4] Thus, although both atypical proliferative serous tumors and micropapillary serous tumors appear to be noninvasive histologically, the former tumor is benign, while the latter behaves like a low-grade carcinoma.

**Mucinous Borderline Tumors**

Mucinous borderline stage I tumors have a survival rate close to 100%. In contrast, stages II and III mucinous borderline tumors have a poor survival but are nearly always associated with the
syndrome of pseudomyxoma peritonei.[5] It is now generally acknowledged that pseudomyxoma peritonei is of gastrointestinal origin, usually stemming from a ruptured mucinous adenoma of the appendix that results in implantation of mucinous epithelium on peritoneal surfaces with production of copious amounts of mucin.[5-8] Therefore, apparent advanced-stage ovarian mucinous borderline tumors with pseudomyxoma peritonei represent secondary ovarian involvement from a gastrointestinal neoplasm and should not be classified as ovarian. When these tumors and a small group of deceptively bland metastatic mucinous carcinomas that have been misclassified as primary ovarian tumors are removed from the mucinous borderline tumors category, no advanced-stage mucinous borderline tumors remain. Hence, all properly classified mucinous borderline tumors are benign. Some investigators have recommended that these tumors be designated “atypical proliferative mucinous tumors.”

**Treatment Approaches**

In light of these considerations, treatment is straightforward. Stage I serous and mucinous tumors require no further treatment. Similarly, advanced-stage serous tumors with noninvasive implants require no further therapy, as long as the surgeon has performed a thorough exploration and removed as much of the extraovarian disease as is feasible, and the peritoneal implants have been well sampled.

Patients with bilateral serous tumors diagnosed as “borderline” at the time of frozen section should undergo careful exploration and staging since these tumors pose a substantially greater risk of extraovarian disease compared to unilateral tumors. It is important to emphasize that, for all apparent borderline tumors of the ovaries, thorough sampling of the available tissue is essential, as is examination by a pathologist who is familiar with these entities.

Tumors with invasive implants are nearly always micropapillary serous carcinomas and behave like low-grade carcinomas. These tumors probably should be treated with chemotherapy, although no prospective clinical trials have evaluated its effectiveness in these patients. Patients who have mucinous tumors with pseudomyxoma peritonei should undergo an appendectomy and cytoreductive surgery and be treated according to protocols specifically designed for this entity.

**Conclusions**

When the borderline category was first introduced in the early 1970s, it was viewed as provisional based on the data available at that time. However, longstanding usage led to its acceptance and entrenchment in the literature as an ostensibly specific and uniform group of tumors with an intermediate behavior. It is now clear that this intermediate behavior results from inclusion of both benign and low-grade malignant tumors in the borderline group. Once this fact is recognized, the basis of the “intermediate” behavior can be comprehended, and the need for the category disappears. Accordingly, “borderline” has outlived its utility as an appellation for a group of ovarian tumors with an intermediate and often enigmatic behavior, and the category should now be abandoned.

**References:**


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