OVARIAN TUMORS OF LOW MALIGNANT POTENTIAL

INTRODUCTION

Ovarian tumors of low malignant potential, also known as borderline tumors of the ovary, account for roughly 15% of all primary epithelial ovarian tumors. For years, experts held differing opinions as to whether these tumors are benign, semi-malignant or malignant. While there continues to be some controversy regarding these borderline tumors, most experts agree that borderline tumors are their own entity of ovarian tumors as their behavior is quite different from ovarian carcinoma. These tumors are now classified as having low malignant potential, as microinvasion and transformation to a true invasive ovarian cancer, especially at late stages, is possible but unlikely.

UNDERSTANDING THE CONDITION

Analogous to the term ovarian cancer, borderline tumors of the ovary are also a hypernym for a variety of histologic subgroups, the most common subgroups being the serous and mucinous borderline tumors. Similar to ovarian cancer, the affected cells show changes in cell size, changes in nucleus size and increased mitosis; and these cells can also spread to other parts of the body. But an important contrast to ovarian cancer is that these tumors are non-invasive. Neither the primary site nor the cells that spread show distinct invasion or destruction of surrounding tissue.

Ovarian tumors of low malignant potential are staged analogously to ovarian cancer, using the FIGO (International Federation of Gynecological Oncologists) system. This system describes

<table>
<thead>
<tr>
<th>FIGO stages</th>
<th>TNM categories</th>
<th>Description</th>
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<tbody>
<tr>
<td>Stage I</td>
<td>T1, N0, M0</td>
<td>Tumor confined to the ovaries</td>
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<tr>
<td>Stage II</td>
<td>T2, N0, M0</td>
<td>Tumor involves one or both ovaries with extension into pelvis</td>
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<tr>
<td>Stage III</td>
<td>T3, N0 or N1, M0</td>
<td>Tumor involves one or both ovaries with spread outside of the pelvis into the peritoneum and/or metastasis to retroperitoneal lymph nodes</td>
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<tr>
<td>Stage IV</td>
<td>Any T, Any N, M1</td>
<td>Distant metastasis</td>
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whether the tumor is confined to the ovaries or fallopian tubes (Stage I), whether the tumor cells have extended to the pelvis (Stage II) or beyond (Stages III and IV). (See Figure 1) Because of their indolent behavior, cells that spread to other parts of the body are often defined as “implants” as they do not carry the same adverse prognosis as an overt metastatic ovarian cancer.

The demographics for borderline ovarian tumors are also different than that of ovarian cancer. Unlike ovarian cancer, borderline tumors affect mostly younger women, with the highest incidence between 40 and 50 years of age. Approximately one-third of women are less than 40 years of age when diagnosed. Furthermore, the vast majority of borderline tumors are detected at an early stage of the disease, making their prognosis far better than that of invasive ovarian cancer.
Although recurrence can appear decades after the disease and subsequent malignant transformation is possible, only rarely is this the cause of death. The eventual cause of death is most often a benign complication of the disease, such as obstruction of organs due to implants.

Some studies have suggested a lower prevalence of BRCA mutations with borderline tumors of the ovary, but the significance of the BRCA mutation in relation to this entity remains unclear.

**DIAGNOSIS**

Most diagnoses of borderline ovarian tumors are incidental and found at early stages. Patients are mostly asymptomatic with a suspicious adnexal mass found incidentally during routine physical examination or on pelvic imaging (i.e., ultrasound) performed for other reasons. Symptoms such as abdominal or pelvic pain usually do not present until advanced stages. The tumor marker CA-125 does not appear to be useful for the diagnosis of borderline ovarian tumors. In fact, if CA-125 is found to be elevated significantly, then ovarian carcinoma should be highly suspected. The definite diagnosis is a histopathological one; therefore, surgery is necessary for diagnosis and proper staging.

**TREATMENT**

Surgery is the mainstay of treatment. Due to the excellent prognosis at early stages, stage I borderline tumors of the ovary can be treated with fertility-preserving surgery, i.e., unilateral salpingo-oophorectomy or ovarian cystectomy. This is important since often diagnosed at a younger age, some patients may not have completed their family planning when initially diagnosed. Bilateral tumors in this age group can be treated with a unilateral oophorectomy and contralateral cystectomy. Those for whom fertility-preserving surgery is being contemplated need to be informed about the elevated risk of progression or recurrence of the disease and the need to be monitored closely. For those women who are not planning further pregnancy, as well as those with advanced-stage disease, the standard of care is a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO), which can help minimize the risk of recurrence. Chemotherapy is not a standard component of therapy, although some experts may recommend its use in advanced, non-resectable disease.

**FOLLOW-UP**

Patients should be followed with routine ultrasound imaging and physical examinations. If the tumor marker CA-125 was elevated before initial surgery, then the CA-125 levels must also be monitored. Recurrence has been reported in up to 10% of patients for up to 20 years after initial diagnosis; therefore, long-term follow-up is of utmost importance. If recurrence does occur, then malignant transformation is also possible. Rates of malignant transformation are unclear and study figures vary between 0.5 and 2%. Whether or not these figures are all due to real transformation, or whether they include de novo cancers, is also unclear. Regardless, recurrence is infrequent and malignant transformation even more so.

**PROGNOSIS and MORTALITY RISK**

As with any tumor, the prognosis depends on the staging of the ovarian tumor. Noting that these are also known as ovarian tumors of low malignant potential, the prognosis for borderline ovarian tumors is generally favorable. Research based on the SEER (Surveillance Epidemiology, and End Results of the National Cancer Institute/USA) database with data from approximately 2800 women with borderline tumors of the ovary showed 10-year relative survival rates of 99% (Stage I), 98% (Stage II), 96% (Stage III) and 77% (Stage IV).

Despite the necessity for long follow-up in clinical medicine, from an insurance point of view the rates of recurrence and malignant transformation for early stages of these tumors are negligible. Stage IV disease, however, is associated with higher recurrence rates, possible complications due to implants and higher risk for malignant transformation.

**SUMMARY/CONCLUSIONS**

Ovarian tumors of low malignant potential account for roughly 15% of all primary epithelial ovarian tumors. While staged similarly to ovarian cancers, these tumors behave quite differently from ovarian carcinoma as these tumors are non-invasive, appear more frequently in younger women, and mostly present with Stage I disease. Surgery is the standard therapy and despite the necessity for long-term follow-up, prognosis is far better than that of invasive ovarian cancer.

**References**

About the Authors

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