Endometriosis and Risk of Ovarian Cancer: An update

May 01, 2012
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Emerging information on the link between ovarian cancer and endometriosis gives us an unprecedented opportunity to develop comprehensive screening plans for early detection and prevention of specific types of ovarian cancer.

Endometriosis - defined as the presence of endometrial-like glands and stroma in any extraterine site - is a common disease occurring in 7-10% of all women, and is often associated with chronic pelvic pain and infertility. Apart from these significant individual problems women with endometriosis and their families may face, this disease has a significant impact on our society due to its chronic nature

The symptoms of endometriosis are variable and its course is often unpredictable. While some women may be asymptomatic, the most common manifestations are pelvic pain, particularly with periods, dyspareunia, pain associated with bowel movements, and dysuria or hematuria in cases of bladder involvement. Despite significant improvements in understanding of this disease, the pathogenesis of endometriosis remains unclear. There are several theories that were suggested; most prominent includes theory of retrograde menstruation associated potentially with genetic susceptibility for the disease. Also theories of hematogeneous and/or lymphogenic spread, genetic link, or defects in immunocompetency have been suggested.

The link between endometriosis and ovarian cancer is well recognized and has perplexed physicians for a long time. Epidemiological studies have suggested a specific link with endometrioid and clear-cell ovarian cancers, but no firm evidence established endometriosis as an ovarian cancer precursor lesion. Several lines of clinical evidence have supported the observation that non-serous ovarian carcinomas such as endometrioid and clear-cell carcinomas arising from atypical endometriotic foci have a higher likelihood of early diagnosis, as the associated endometriosis can cause pelvic pain or infertility requiring specialized gynecologic care including diagnostic laparoscopy. Deligdisch et al. reported a series of 76 cases of stage I ovarian carcinomas and documented that non-serous carcinomas (54/76) were diagnosed because of the associated symptoms including pelvic pain associated with endometriosis or vaginal bleeding associated with hyperestrogenism and endometrial pathology. Interestingly they also found that serous carcinomas were frequently found in asymptomatic women with breast cancer diagnoses. These and similar observations support the emerging dual model of ovarian carcinogenesis. According to this model, Type I cancers are low grade, slowly developing ovarian carcinomas (including endometrioid, mucinous and low grade serous) associated with KRAS, BRAF, PTEN and B-catenin mutations and often associated with endometriosis. Type 2 is high-grade serous carcinomas associated with TP53 mutations that develop rapidly, are more aggressive and their origin is now thought to be tubal epithelium.

In the recent remarkable study reported in Lancet Oncology, the team of researchers from the Ovarian Cancer Association Consortium (OCAC) performed pooled analysis of 13 case-control studies and confirmed that women with self-reported history of endometriosis have significantly increased clear cell carcinoma (odds ratio 3.05) and endometrioid ovarian cancer (odds ratio 2.04). In addition the authors show, for the first time, that endometriosis is associated low-grade serous ovarian carcinomas, doubling its risk in women with endometriosis. However, there was no association between endometriosis and high-grade serous carcinomas or other subtypes of ovarian cancer in the study.

Taken together these findings will have considerable clinical implications and may affect the ways we think about strategies for ovarian cancer screening and prevention. In particular, the emerging knowledge of the link between ovarian cancer and endometriosis gives us an unprecedented opportunity to develop comprehensive screening plans to aid in the early detection and prevention of specific types of ovarian cancer in women with endometriosis. Such planning should include: 1) Identification of all women with endometriosis - either surgically documented or self-reported by
symptoms;
2) Careful follow up of ovarian presumed endometriomas by imaging studies, perhaps by MRI, for any characteristics changes such as mural formation;
3) Complete surgical resection of all endometriotic foci in women undergoing surgical treatment and tissue evaluation of ovarian endometriomas to rule out malignancy;
4) Hormonal treatment aimed at reducing the risk of cancer in high-risk women.
While it is well known that most women with endometriosis do not develop ovarian cancer, the women and their physicians should always discuss these new findings, carefully document and discuss any new symptoms and formulate plan for regular evaluations and treatment.

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