Prophylactic Surgery in Hereditary Breast/Ovarian Cancer Syndrome

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Drs. Levine and Gemignani have provided a comprehensive review of the literature regarding the management of patients with hereditary breast/ovarian cancer syndrome. As noted, over 200,000 new cases of breast cancer and 25,000 new cases of ovarian cancer are estimated for 2003.[1] Only a small portion of these cases will be hereditary; however, these are the cases that may benefit from preventive measures. The potential for risk-reducing strategies in these patients has become a critical issue over the past several years. This review highlights the salient features of identifying “at-risk” patients, as well as the benefits and limitations of surgical prophylaxis.

Prophylactic Mastectomy
Prophylactic mastectomy remains an option for certain patients. The literature reports a significant reduction in risk following prophylactic mastectomy among high-risk women with a family history or BRCA-affected disease and among those with a personal history of unilateral breast cancer. The authors point out that due to small amounts of breast tissue that remain following both subcutaneous and total mastectomy, the possibility of subsequent malignancy cannot be completely eradicated. The patient must have a clear understanding of this concept, and the fact that long-term, regular, follow-up exams are necessary after the prophylactic surgery. The follow-up method for these patients (physical exam, mammography, sonogram, magnetic resonance imaging) remains controversial and requires further evaluation. The authors allude to the concept of sentinel node biopsy at the time of prophylactic mastectomy. It should be noted that the incidence of occult breast cancer among these women is reported to be approximately 5%.[2] Performing a sentinel node biopsy at the time of prophylactic surgery would spare the patient a second surgical procedure (ie, complete axillary node dissection) should an occult malignancy be identified. Given that the risk-benefit ratio in this setting has not yet been clarified, the role of sentinel node evaluation accompanying prophylactic mastectomy remains investigational. The decision to proceed with prophylactic mastectomy is a complex process that is intricately tied to the patient's satisfaction with the procedure. The authors report that, likely due to anxiety, there is a propensity for women to overestimate their risk of breast cancer. It is also noted that 5% to 30% of patients express regret with their decision to undergo risk-reducing surgery. It is critical that patients be accurately counseled as to their risk of carrying a germ-line mutation, understand the associated risk of developing a malignancy, and undergo BRCA testing when indicated. Being equipped with appropriate information may alleviate unnecessary anxiety. Patients should be educated as to the risks and benefits of nonsurgical options such as increased surveillance and/or chemoprophylaxis with tamoxifen. Lastly, the authors point out that emotional readiness is critical to a successful outcome. Women who expressed regret were generally those who perceived the decision-making as being initiated by the physician rather than the patient herself. Adequate counseling, education, and psychosocial support by a multidisciplinary team in both the pre- and postoperative setting can lead to a more satisfying outcome for women faced with this difficult situation.

Prophylactic Oophorectomy
Prophylactic oophorectomy bears a different set of concerns. In ovarian cancer, the majority of patients are diagnosed at an advanced stage, when the chance for cure is slim. No effective strategy currently exists for earlier diagnosis via increased/intensive surveillance. Although prophylactic oophorectomy is associated with deprivation of natural estrogen in younger patients who are then...
faced with the controversies of hormone replacement therapy, most patients report a reduction in anxiety and improved quality of life. The procedure itself is generally performed on an outpatient basis and with significantly less physical disfiguration than is associated with prophylactic mastectomy. The benefit of the procedure in terms of reducing the risk of ovarian cancer (85% to 96%) and breast cancer (53% to 70%) is well documented. The incidence of occult malignancy identified at the time of prophylactic oophorectomy appears to be approximately 4%. Recent data suggest that performing peritoneal lavage during prophylactic oophorectomy may assist with the detection of occult disease. [3] The significance of positive cytology in the absence of histopathologic findings remains unclear, but certainly, the ease and minimal expense of obtaining cytology support its use. In addition, fallopian tube carcinoma has been associated with BRCA mutations. For this reason, the suggested prophylactic procedure would be a bilateral salpingo-oophorectomy with peritoneal cytology, unless future investigations suggest otherwise. Hysterectomy

The role of hysterectomy in high-risk patients remains controversial. There is little evidence to support an increased risk of endometrioid adenocarcinomas of the uterus in the presence of BRCA mutations. Uterine papillary serous carcinomas have recently been associated with BRCA mutations. [4,5] At present, the data are controversial and, therefore, this relationship cannot be stated with certainty. [6] The most definitive data linking endometrial adenocarcinomas with high-risk women appear to be those from women with breast cancer who are being treated with tamoxifen. Although the data suggest that the majority of tamoxifen-induced endometrial cancers are low grade, recent studies have indicated that tamoxifen users are at significantly increased risk of mixed mesodermal tumors or other uterine sarcomas compared to matched controls (15.4% vs 2.9%). [7] A review of all National Surgical Adjuvant Breast and Bowel Project trials reported the incidence of sarcoma to be 0.17/1,000 women-years in patients randomized to tamoxifen, compared to 0 in patients randomized to placebo. [8] Of the 12 sarcomas that were identified, 9 were mixed mesodermal tumors. These data, along with multiple case reports, have prompted the Food and Drug Administration to amend the warning label on tamoxifen packaging to include the risk of uterine sarcomas. Despite this finding, the significant benefit that tamoxifen affords breast cancer patients clearly outweighs the risks of uterine malignancies. However, it would be the patients who require tamoxifen therapy and plan to undergo risk-reducing surgery who would benefit most from the addition of hysterectomy to the prophylactic procedure. Similar to prophylactic mastectomy, risk-reducing salpingo-oophorectomy is not guaranteed to prevent papillary serous carcinoma of the peritoneum. This disease has been associated with BRCA germ-line mutations and, unfortunately, follows a clinical course that is indistinguishable from ovarian cancer. [9,10]

Conclusions

In conclusion, Levine and Gemignani have presented a thorough summary of the data available for counseling women who are at high-risk or carry a known BRCA germline mutation. Once these patients have been identified, they should be offered extensive multidisciplinary counseling through a recognized screening program. By doing so, patients will be better equipped to make educated and rational decisions in their own behalf.

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