Case 4: Health outcomes after risk-reducing salpingo-oophorectomy

Susan (see Case 3) has undergone a laparoscopic RRSO for a *BRCA1* mutation at age 40. She is concerned about health outcomes, including menopause and quality of life after surgery. She wonders what follow-up she should have after the surgery to manage her cancer risk.

Questions

What are the potential consequences of premature menopause due to the surgery?

The typical age for menopause in the U.S. is about 51 years. While removing tubes and ovaries in mutation carriers at a younger age is very important to prevent ovarian cancer, it does cause early menopause.

Premature menopause is associated with several health risks, including early onset of cardiovascular disease and osteoporosis. Other long-term health issues include an increased risk of cognitive impairment and dementia, particularly with younger age at oophorectomy. Parkinsonism, anxiety, and psychosexual dysfunction also constitute significant risks. The sudden menopause that occurs with oophorectomy can cause bothersome and persistent symptoms as well as a negative impact on long-term health. Non-hormonal prevention measures such as a healthy diet, appropriate calcium and vitamin D intake, and weight-bearing exercise can improve bone and cardiovascular health. Maintaining a healthy weight, limiting alcohol intake, avoiding tobacco, getting adequate sleep, and managing stress also improve overall health and decrease overall cancer risk.

Is hormone replacement therapy an option for Susan?

The results of the Women's Health Initiative and the Nurses' Health study have raised concern about whether hormone replacement therapy is an option after RRSO. However, the patients in the WHI were women who underwent spontaneous menopause in their 50s and then took additional hormone therapy in their 60s. These women in WHI are a vastly different population than *BRCA1* and *BRCA2* mutation carriers, who typically make the decision about RRSO a decade earlier, in their 30s and 40s, before they have entered natural menopause. Therefore, conclusions from the WHI are not applicable to early surgical menopause.

In women who have not had a hormone receptor-positive breast cancer, no study has shown an increased risk of breast cancer associated with hormone therapy in women who have undergone RRSO prior to menopause. In addition, one study conducted in patients with *BRCA1* and *BRCA2* mutations demonstrated that short-term use of hormone therapy did not negate the protective effect of RRSO on risk of subsequent breast cancer; the majority of these patients were receiving estrogen alone, not combined estrogen and progestin therapy.

Even if a woman chooses not to take systemic hormone therapy, local estrogen treatment to the vagina can help with dyspareunia (painful intercourse), vaginal dryness, and other urogenital symptoms. Vaginal estrogen has not been shown to increase the risk for breast cancer since its effect is largely limited to the local tissues. Such treatment, however, does not help with other menopausal effects, such as heart disease, osteoporosis, or hot flashes.

What can Susan do to address sexuality-related concerns?

Women who undergo RRSO are at risk of developing symptoms that affect sexual function, including decreased desire, vaginal atrophy, and dyspareunia. Body image may be particularly impacted in women who have undergone risk-reducing mastectomies. Hormone therapy, when appropriate, may help but may not necessarily alleviate all symptoms. It is important that both providers and patients are aware of this phenomenon, such that patients can receive realistic counseling about these outcomes and be prepared to address persistent symptoms. The references below provide resources available to women to improve menopausal symptoms.

What kind of post-RRSO surveillance might be used?

Clearly, RRSO substantially reduces the risk of pelvic serous cancer, with an approximate 80 to 90% reduction in risk. Additionally, premenopausal oophorectomy is associated with a 50% reduction in breast cancer risk in *BRCA1* and *BRCA2* mutation carriers. A small residual risk for peritoneal cancers remains after RRSO, with more recent estimates at 1 to 2% lifetime risk.

Risks may be somewhat higher for women who did not have complete serial sectioning done at the time of RRSO. Because we have no effective screening for peritoneal cancer, there is no clearly established recommendation for surveillance following risk-reducing surgery. It is important for the patient and her health care providers to consider

this risk for peritoneal cancer if she develops abdominal symptoms such as pain, bloating, early satiety, or nausea and vomiting.

Because of increased risk of cardiovascular disease and osteoporosis in women who undergo early menopause, surveillance with lipid profiles and bone density scans are recommended.

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