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Prophylactic bilateral Salpingo-oophorectomy and eventual development of endometrial cancer: Two individual case reports

Sophia Halassy [a,b,*], Katrina Au [c], Vinay Malviya [a], Janet Mullings-Britton [a]

[a] Ascension Providence Hospital, Department of Obstetrics & Gynecology, Southfield, MI, United States of America
[b] Michigan State University, East Lansing, MI, United States of America
[c] School of Medicine, St. George's University, True Blue, Grenada

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ABSTRACT

Prophylactic bilateral salpingo-oophorectomy (PBSO) is regularly performed when patients have a high risk of developing ovarian cancer (i.e. a personal or family history). Most commonly, PBSO is performed in premenopausal women who have completed childbearing. The major risk of uterine preservation is future development of endometrial cancer. We report two cases that highlight such occurrences in women who believed that the uterus was important for sexual function. The misunderstanding that the uterus is important for sexual satisfaction should be thoroughly discussed and rectified prior to initial surgery. This is especially important in patients who may eventually require hormone replacement therapy.

1. Introduction

In the general female population, it is estimated that there is a 1% lifetime risk of developing ovarian cancer [1]. However, this risk may be dramatically increased by a family history of such cancer: 23% of ovarian cancers are related to hereditary conditions [1]. Unfortunately, there is no effective screening test for ovarian cancer. Patients at high risk of developing it are recommended to undergo PBSO and hysterectomy upon completion of child-bearing [2]. However, some women decline prophylactic hysterectomy due to an erroneous belief that removal of the uterus will result in sexual dysfunction. Patients who choose to retain their uterus may be at increased risk of future endometrial cancer. We present two such cases that spotlight the development of endometrial cancer after PBSO whilst preserving the uterus.

2. Cases

The first case concerned a 59-year-old Caucasian woman with a history of BRCA1 tumor suppressor gene mutation. The patient had undergone a risk-reducing bilateral salpingo-oophorectomy 12 years prior to presentation. Presurgically, the patient was counseled on the potential risks of uterine preservation. Against advice, the patient opted to forego hysterectomy for fear that she would lose the ability to experience sexual stimulation and pleasure. The patient presented to the office with a primary complaint of breakthrough bleeding. Office endometrial biopsy confirmed a diagnosis of endometrial malignancy. The patient was referred to a gynecologic oncologist for further management.

Other than the BRCA1 positive status, the patient had no significant medical history. She underwent yearly breast cancer screening with magnetic resonance imaging (MRI). There was a family history of breast and colon cancer in her cousins. At presentation, the patient was gravida 4, para 2, and was sexually inactive. She had never used any form of birth control and pap smears had always been normal. She had not received hormone replacement therapy (HRT). She denied any history of tobacco, alcohol or illicit drug use.

The endometrial biopsy revealed a moderately differentiated adenocarcinoma. She underwent an exploratory laparotomy, extrafascial hysterectomy with partial vaginectomy, bilateral pelvic and selective para-aortic lymphadenectomy. During surgical intervention, the patient was found to have extensive lymphovascular invasion into the myometrium, with two-thirds of the myometrium involved. Pelvic lymphadenectomy included 7 lymph nodes in the right pelvis, 13 lymph nodes in the left pelvis and 3 lymph nodes in the para-aortic space. All were negative on final pathology. The dimensions of the tumor were 5.2 × 5.0 × 2.0 cm. The disease was histologically categorized as FIGO grade 2 with extension encompassing two-thirds of the thickness of the myometrium. All margins of resection were disease-free. Due to the aforementioned pathological disruption and pronouncements, the disease was classified as stage Ib, moderately differentiated endometrial cancer with extensive lymphovascular invasion.

* Corresponding author at: Ascension Providence Hospital, Department of Obstetrics & Gynecology, 16001 W Nine Mile Road, Southfield, MI 48075, United States of America.
E-mail address: sophia.halassy@ascension.org (S. Halassy).

Given the recurrence rate of 30% and BRCA1 status, she was subsequently prescribed 6 cycles of cytotoxic chemotherapy with carboplatin and taxol.

The second case concerns a 64-year-old Caucasian woman with a history of bilateral oophorectomy due to family history of ovarian cancer. She was referred to a gynecologic oncologist after undergoing intracavitary uterine hysteroscopic assessment and endometrial tissue sampling due to postmenopausal vaginal spotting. A working diagnosis of urinary tract infection was empirically arrived at; however, urine cultures were negative. Symptoms persisted so attention was turned to uterine cavity evaluation. As mentioned, hysteroscopic evaluation with concurrent biopsy was performed. Final histology of the biopsy was consistent with mixed endometrial adenocarcinoma, predominantly endometrioid with focal clear cell carcinoma and a rare component of serous carcinoma.

The patient was gravida 0, para 0 and had used oral contraceptive pills for 39 consecutive years. She had undergone risk-reducing bilateral oophorectomy 13 years previously following the demise of her mother secondary to ovarian cancer. Patient declined BRCA 1 and 2 investigative studies. On the other hand, the patient's sister tested negative for both oncogenic mutations. The patient opted to maintain her uterus due to fear of sexual dysfunction. She underwent iatrogenic menopause at age 51 after bilateral oophorectomy and did not receive hormone replacement therapy (HRT). Otherwise, she had no gynecological complaints. Her medical history was positive for asthma and she had up-to-date routine age-appropriate screening. She denied any current tobacco, alcohol or illicit drug use. Initial office physical examination revealed a stenotic cervix. She had a palpable 8-week-size uterus. There were no other significant findings.

Ultrasound imaging demonstrated a 5.4 × 3.9 × 4.3 cm uterus with a right-sided fibroid measuring 2.3 cm. There were complexed endometrial echoes and a thickened 12 mm endometrial stripe with a small amount of endometrial fluid. The endometrial cavity appeared irregular and lobulated. The right and left ovaries were surgically absent.

The patient underwent an exploratory laparotomy, extrafascial hysterectomy, bilateral pelvic and selective para-aortic lymphadenectomy, and partial omentectomy. The dimensions of the uterine specimen were 5.5 × 3.5 cm. Final histologic evaluation was positive for an endometrioid adenocarcinoma, FIGO grade 1. Less than one half of the myometrium was involved. The omentum and selected lymph nodes were all negative for metastases. There was no evidence of clear cell carcinoma. Additional DNA mismatch repair immunoassay for hereditary non-polyposis-related endometrial carcinoma was negative.

3. Discussion

The estimated risk of developing ovarian cancer in the general female population is 1% [1]. Family history plays a significant role in the risk, with 23% of ovarian cancers being related to hereditary conditions [1]. For example, the rate of developing ovarian cancer is significantly increased in BRCA positive women. By age 70, 39–46% of patients positive for BRCA1 and 11–12% of patients positive for BRCA2 develop ovarian cancer [1]. Syndromes which increase the risk of ovarian cancer development include Lynch syndrome and Li-Fraumeni [3]. Once a patient has been diagnosed with ovarian cancer, the five-year survival rate is estimated to be around 47%. However, most patients are diagnosed at stage III and stage IV and hence have lower survival rates: 41% and 20% respectively [4]. Currently, there is no effective screening test for ovarian cancer [2]. Consequently, patients at high risk of developing ovarian cancer are recommended to undergo a prophylactic bilateral salpingo-oophorectomy and hysterectomy after child-bearing [2]. For patients at average risk, a bilateral salpingo-oophorectomy is recommended if the patient is already undergoing a hysterectomy for another condition [2].

Patients may be adamant about preserving their uterus due to the belief that there is post-hysterectomy sexual dysfunction. In one study by Lonnée-Hoffman and Pinas, 20% of women reported deteriorated sexual function after a hysterectomy. Notwithstanding, other factors such as pre-operative sexual dysfunction and depression have been shown to play a role [5]. Furthermore, studies show that the removal of the ovaries, causing a significant decrease in estrogen, plays a far larger, deleterious role in sexual function post-operatively [5]. There have been some reports showing increased sexual function after hysterectomy. However, these patients usually suffer from benign uterine dysfunction before surgery [6,7]. Overall, studies are inconclusive and further investigation is required.

If the patient elects to undergo only a bilateral salpingo-oophorectomy, inspection of the peritoneal cavity, pelvic washings and removal of all adnexal tissue to the insertion point on the uterus should be executed, following both the American College of Obstetricians and Gynecologists (ACOG) and the Society of Gynecologic Oncology [8]. In pre-menopausal patients, this approach will result in surgical primary ovarian insufficiency. A discussion of hormone replacement therapy should be conducted [9].

The patients featured in the case reports developed post-bilateral salpingo-oophorectomy endometrial cancer. Whether a prophylactic hysterectomy should have been done to prevent endometrial cancer is therefore the question. In 2015, there was a 26.5% incidence rate of uterine cancer in the US [10]. 10% of uterine cancer cases are genetic. Only 5% of uterine cancers are related to a site-specific genetic disorder such as Lynch syndrome [11,12]. Few studies have investigated the incidence of uterine cancer after risk-reducing bilateral salpingo-oophorectomy. One study done by Shu et al. found that in BRCA-positive patients who chose to undergo only bilateral salpingo-oophorectomy, the rate of endometrial cancer was not elevated [13]. Interestingly, the incidence of the serous subtype of uterine cancer, the more deadly subtype, was elevated compared with the general population [13]. One of the presented patients developed a very rare subtype of endometrial cancer: clear cell. Both the serous and clear cell histological subtypes fall under type 2 uterine cancer, which comprise only 20% of all uterine cancers [14]. Type 1 uterine cancer is more common and histologically is only the endometrioid subtype [15]. A proposed model by Sherman suggests that an atrophic endometrium contributes to the development of type II uterine cancer [15]. This model could suggest that patients with bilateral salpingo-oophorectomy could be more susceptible to developing type II uterine cancer, especially those who have the procedure done before menopause. Inquiries into the effects of prophylactic bilateral salpingo-oophorectomy and the development of type 2 uterine cancer could be very enlightening. Nonetheless, it may be challenging to attain a statistically significant number of patients for participation in the study group, given the rarity of both type 2 uterine cancer and patients who opt for uterine preservation with a bilateral salpingo-oophorectomy. A study published by de Jonge et al. in 2019 demonstrated an increased risk of endometrial cancer in those with germline BRCA-associated hereditary breast and ovarian cancer (HBOC) syndrome. Their patients with loss-of-heterogeneity (LOH) germline BRCA mutations were more likely to be diagnosed with non-endometrioid and grade 3 histology, whereas those with negative LOH status mainly had grade 1 endometrioid endometrial cancer. While we do not know the LOH status fo the two patients reported here, just their individualized increased genetic risk may have been associated with the eventual development of a rare endometrial cancer [16].

4. Conclusion

When performing a risk-reducing, prophylactic bilateral salpingo-oophorectomy, it is of paramount importance to effectively and extensively counsel patients regarding the risks incurred with uterine preservation. Both genetic variants (BRCA1 and BRCA2) typically identified

with ovarian cancer are similarly associated with a high risk of endometrial cancer. Should the patient demonstrate hesitancy over or a fear losing sexual function with loss of her uterus, appropriate advice regarding the lack of evidence supporting this fallacy should be given. This could protect the patient against a future diagnosis of endometrial cancer. This applies primarily in the case of bilateral salpingo-oophorectomy in pre-menopausal women where hormone replacement therapy may be considered. Preoperative counseling from providers and healthcare practitioners is crucial in maintaining both the short- and the long-term health of our patients.

Contributors

Sophia Halassy was the primary author and drafted the manuscript.

Katrina Au performed the literature review.

Vinay Malviya provided case information and contributed to revision of the manuscript.

Janet Mullings-Britton contributed to revision of the manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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