



Case Report

Occult tubal carcinoma found at risk reducing salpingectomy in a *BRCA1* carrier[☆]Sarah H. Kim^a, Melissa K. Frey^b, Stephanie V. Blank^{b,*}^a Drexel University College of Medicine, Philadelphia, PA, USA^b New York University School of Medicine, Division of Gynecologic Oncology, New York City, NY, USA

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Introduction

Recent studies highlight the importance of the fallopian tube as a putative site of origin for serous ovarian carcinomas, previously felt to arise exclusively from ovarian tissue. The initial association emerged from the pathologic analysis of *BRCA* mutation carriers undergoing risk-reducing bilateral salpingo-oophorectomy (RRBSO), where a high percentage of incidentally diagnosed cancers and cancer precursor lesions were discovered in the distal fallopian tube (Herzog and Dinkelspiel, 2013; Crum et al., 2012; Kwon et al., 2013). These findings have enlivened the discussion on the appropriate management of women at high risk for ovarian cancer, proposing risk-reducing bilateral salpingectomy with delayed bilateral oophorectomy as a reasonable alternative to RRBSO and a means to diminish postoperative sequelae related to estrogen-deficiency. We searched MEDLINE using PubMed for all English language articles from 1980 to 2014, with search terms including “ovarian cancer,” “fallopian tube cancer,” “*BRCA*,” “risk reducing oophorectomy” and “risk-reducing salpingectomy.” To date, all reported cases of occult serous carcinoma found in the fallopian tube have been in women with known *BRCA* mutations who underwent RRBSO. Here, we report a case of invasive high-grade serous carcinoma found in the fallopian tube of a woman with a *BRCA1* mutation who underwent a risk-reducing salpingectomy with ovarian preservation.

Case

A 41-year-old (gravid 1, para 1) Ashkenazi Jewish woman presented for ovarian cancer risk assessment. Her personal history was significant for a deleterious *BRCA1* mutation, 187delAG. The patient's mother and maternal aunt were positive for the same mutation and her maternal aunt had bilateral premenopausal breast cancer. The patient underwent an endovaginal ultrasound and serum CA-125 measurement, both of which were normal. A pelvic exam performed at this visit was also within normal limits.

At the conclusion of the initial consultation, the patient was advised that the currently accepted guidelines recommend RRBSO for women with hereditary breast and ovarian cancer syndrome by age 40 or when childbearing is complete (American College of Obstetricians and Gynecologists, 2008, 2009). The patient was reluctant to have her ovaries removed due to anticipated health and quality of life consequences, and after extensive discussion, elected to undergo a risk-reducing salpingectomy nine months following the original consultation, with the intention of having her ovaries removed at a second surgery performed closer to initiation of natural menopause.

The patient underwent an uncomplicated minimally invasive salpingectomy. Intraoperatively, the uterus, ovaries and fallopian tubes were noted to be grossly normal. Histologic examination of the left fallopian tube revealed an in situ and invasive high-grade serous adenocarcinoma, measuring 2 mm in greatest dimension. Pelvic washings were negative for malignant cells.

The pathology results, along with the next steps in management, were reviewed with the patient at a follow-up visit. The patient underwent minimally invasive hysterectomy, bilateral oophorectomy, and staging, including pelvic and para-aortic lymph node dissection and omentectomy. The pathology from the second procedure was all negative for malignancy. The patient completed six cycles of platinum-based chemotherapy. She has no evidence of disease 7 months since diagnosis and is maintained on oral hormone replacement.

Discussion

The current standard of care for women with hereditary breast and ovarian cancer is RRBSO at 40 years of age or upon completion of childbearing (American College of Obstetricians and Gynecologists, 2008, 2009). The rationale behind this recommendation is that the risk of ovarian cancer increases significantly after age 40 in women with

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BRCA1 mutations, with 10–21% of these women being diagnosed with ovarian cancer by age 50 (American College of Obstetricians and Gynecologists, 2009). The risk of premenopausal ovarian cancer in *BRCA2* mutation carriers is considerably lower, with 3% of women in this group developing ovarian cancer by age 50, although the risk of developing breast cancer before the age of 50 is still quite high, at 26–34% (American College of Obstetricians and Gynecologists, 2009). Bilateral salpingo-oophorectomy has been shown to lessen the risk of ovarian and fallopian tube cancer by 80–90%, and the risk of breast cancer by 50% in *BRCA* mutation carriers (Rebbeck et al., 2009). Many women in this high-risk population are reluctant to undergo RRBSO due to potential effects of early menopause, including osteoporosis and cardiovascular disease (Kwon et al., 2013), as well as anticipated negative impact on quality of life, especially in women previously diagnosed with hormone receptor positive breast cancer, and therefore unable to take hormone replacement. Perhaps as a direct result of these concerns, only 60–70% of *BRCA* mutation carriers are estimated to have undergone RRBSO (Kwon et al., 2013), and only 43% of those less than age forty (Friebel et al., 2007).

With newfound insight that a significant percentage of serous carcinomas originate in the fallopian tube, salpingectomy with delayed oophorectomy has been proposed as an alternative risk reduction strategy for premenopausal women with deleterious *BRCA* mutations. In an effort to define the benefits associated with bilateral salpingectomy versus salpingo-oophorectomy, Kwon et al. (2013) developed a simulation model to compare different strategies for risk reduction in *BRCA* mutation carriers, evaluating incremental cost-effectiveness ratio. The investigators compared the following three strategies: 1) RRBSO, 2) bilateral salpingectomy, and 3) bilateral salpingectomy with delayed oophorectomy. They found RRBSO to be the superior strategy for *BRCA* mutation carriers, with associated lowest cost and highest life expectancy. Interestingly, salpingectomy at age 40 followed by delayed oophorectomy at age 50 had the highest life expectancy when quality-of-life measures were taken into account. In this study, risk-reducing salpingectomy was associated with a 60% reduction in *BRCA*-associated mullerian cancer risk, compared to an 80% decrease with RRBSO. While the investigators maintained that the standard of care remains RRBSO by age 40, they concluded that salpingectomy with delayed oophorectomy might be a reasonable option for premenopausal women who are reluctant to undergo RRBSO. They emphasize that this strategy would reduce the risk of *BRCA*-associated mullerian cancer in this high-risk population without increasing the risk of death from cardiovascular disease, and with the least negative impact on the patients' quality of life (Kwon et al., 2013). There are several ongoing clinical trials investigating the efficacy of salpingectomy in reducing the risk of pelvic cancer in *BRCA* carriers (Centre Oscar Lambret, 2011), and comparing the rates and safety of RRBSO with those of prophylactic salpingectomy with delayed oophorectomy (PSDO) (M.D. Anderson Cancer Center, 2013). These studies, in addition to British Columbia's OVCARE initiative to remove fallopian tubes at every hysterectomy (Finlayson, 2011), will play an integral role in providing the data needed to appropriately counsel premenopausal high-risk patients.

While some experts have cautioned that it is “premature” to offer salpingectomy as a risk reduction strategy prior to evaluation of “comprehensive comparative data (Vaughan et al., 2011)” and “prospective cohort studies[s] (Narod, 2013)”, offering salpingectomy to this 41 year-old woman resulted in a diagnosis of a Stage IA grade 3 fallopian tube cancer. Had salpingectomy not been proposed as an option, no risk reducing sur-

gery would have been performed as yet, and the cancer would have had the potential to metastasize, increasing the stage of her disease, and negatively impacting her survival.

While recent literature reports a significant rate of occult cancer found at the time of risk-reducing salpingo-oophorectomy (Manchanda et al., 2011; Powell et al., 2011), this is the first report of occult cancer diagnosed at risk reducing salpingectomy, and illustrates the importance of flexibility and compromise in counseling women at increased genetic risk of ovarian cancer. While it is critical to stress the importance of risk-reducing surgery in this high risk population, management must be individualized for each patient, as a rigid approach which alienates young mutation carriers could result in missed opportunities to reduce cancer risk. When proposed, risk-reducing salpingectomy is offered as the first step in a two-part risk reduction strategy, with plan for delayed oophorectomy, and not as a substitute for RRBSO.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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