Case report

A rectovaginal septum mass in a BRCA1 positive patient years after risk reducing surgery: A case report

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1. Introduction

Ovarian cancer accounts for 1.3% of all incident cancers in US women. Ovarian, fallopian tube and primary peritoneal cancers have the highest proportion of heritable germline mutations. Women with BRCA1 have a lifetime risk through age 70 of pelvic cancer of 39–46%. With BRCA2 mutation the lifetime risk through age 70 is approximately 12–20% (King, 2003), (Chen and Parmigiani, 2007). A 2009 meta-analysis reported that risk reducing bilateral salpingo-oophorectomy (RRBSO) was associated with 79% reduction in risk of BRCA-associated gynecologic cancer (Rebbeck et al., 2009).

Despite the significant risk reduction with RRBSO for BRCA positive patients, there remains an approximately 4% risk of primary peritoneal cancer after risk reducing surgery (Finch et al., 2006). To our knowledge, based on review of Pubmed, Medline, and Cochrane databases as well as institutional library database encompassing most scientific journals, using search terms rectovaginal septal mass, BRCA, and papillary serous carcinoma, there are no reported cases of adenocarcinoma developing in a Mullerian remnant in the rectovaginal septum in a BRCA1 patient.

2. Case

This is the case of a 46-year-old Caucasian female, G2P2002, with a known BRCA1 germline mutation who presented to the gynecologic oncology department initially in 2012 and underwent a risk reducing robotic assisted total laparoscopic hysterectomy, bilateral salpingo-oophorectomy and cystoscopy. Final pathology showed atypia of the fallopian tube but no carcinoma or serous tubal intraepithelial carcinoma (STIC) lesions were noted. (Fig. 1). All other uterine and ovarian tissue was without carcinoma or atypia and pelvic washings were negative for malignant cells.

She re-presented to gynecologic oncology in November 2020 with significant vaginal bleeding for several weeks. Her last pap smear, in 2015 was negative and she had no history of abnormal pap smears prior to her hysterectomy. Pelvic exam at the initial visit showed serosanguinous fluid, gross blood and a 3 cm raised lesion on the vaginal floor approximately 3 cm from the vaginal cuff. Exam under anesthesia confirmed a 7 cm rectovaginal septum mass and biopsies revealed a high grade serous carcinoma. Magnetic Resonance Imaging showed a heterogeneous mass in the pelvis measuring 6.3 × 5.5 × 6.2 cm in size likely arising from the posterior vaginal wall extending into the rectovaginal space with loss of fat plane with the anterior wall of the rectum. Imaging was also notable for prominent pelvic lymph nodes along the left pelvic sidewall. (Fig. 2) Gastroenterology evaluation of the rectum with flexible sigmoidoscopy noted compression of the anterior wall of the rectum with an 8 mm area of ulceration. This mass effect was 5–8 cm from the anal verge. Final pathology from the ulcerated area within the rectum showed high grade serous carcinoma.

Five days after her positive biopsies she underwent exploratory laparotomy, ureteral stent placement, tumor debulking with radical parametrectomy with partial vaginectomy, omentectomy, lower anterior rectal resection with coloanal pull-through anastomosis with diverting loop ileostomy, bilateral ureterolysis, bilateral pelvic...
lymphadenectomy, and vaginal reconstruction. She was cytoreduced to no visible disease. She recovered well post-operatively and was discharged home on postoperative day 5. Pathology was notable for a left obturator node that was positive for malignancy. The vagina, rectum, and sigmoid colon en-bloc resection was notable for poorly differentiated carcinoma of Mullerian origin arising in the recto vaginal septum with direct extension through the vaginal mucosa and the rectal mucosa. Mullerian origin was demonstrated by immunohistochemistry staining with WT1 which was diffusely positive. Foundation One testing of the tumor showed a loss of heterozygosity score of 31.6% and BRCA1 R10726fs*3 mutation. One perirectal lymph node was also positive for microscopic metastatic carcinoma. Previous pathology from risk

Fig. 1. Histology from primary risk reducing BSO. A) Focal epithelial stratification and mild cytological atypia in the fallopian tube from the RRBSO; B) Immunostaining for Ki 67 increased in this area which was p53 negative, thus falling short of a definite diagnosis of serous tubal intraepithelial lesion (STIL).

Fig. 2. Pre-operative MRI. (a) MRI pelvis showing 6.3 × 5.5 × 6.2 cm posterior vaginal/rectovaginal septum mass (b). Enlarged pelvic lymph nodes noted on MRI prior to surgery.
reducing surgery was again reviewed at time of tumor debulking and findings were consistent with mild atypia without STIC lesions. (Fig. 3)

The case was presented at our multi-disciplinary tumor board with the recommendation for adjuvant chemotherapy with carboplatin, paclitaxel and bevacizumab, followed by maintenance therapy with PARP inhibitor and bevacizumab. She has completed cycle 5 of adjuvant therapy with carboplatin, paclitaxel and bevacizumab (Ray-Coquard et al., 2019).

3. Discussion

Approximately 1 in 345 to 1 in 800 women have a BRCA1 or BRCA2 mutation. ([6]) The risk of ovarian cancer in BRCA 1 and 2 mutation carriers ranges from 12 to 46% (King, 2003). This risk can be decreased by approximately 71–89% if risk reducing bilateral salpingo-oophorectomy is performed prior to age 50 or immediately after child-bearing is completed (Rebbeck et al., 2009; Finch et al., 2006) (Kauff et al., 2002; Hartmann and Lindor, 2016).

Despite receiving prophylactic surgery in 2012 at the age of 38, our patient was found to have a Mullerian origin tumor arising in the rectovaginal septum. Though peritoneal cancer is the most likely pelvic cancer to arise after a prophylactic RRBSO in BRCA mutation carriers, this patient’s peritoneal lining was found to be uninvolved by her tumor. Based on review of the current literature, there are only 4 reported cases of Mullerian type carcinoma arising from the rectovaginal septum, unassociated with endometriosis (Lopez, 2016). The most common malignancies not related to endometriosis in this location are gastrointestinal stromal tumors (GIST). Our patient’s histology was of high grade papillary serous Mullerian type, consistent with her known BRCA1 status. Lopez et al. reported a case of a recto-vaginal septum tumor with papillary serous histology, however there was also peritoneal and ovarian involvement with primary peritoneal carcinoma (Leteurtre et al., 1999). Our patient had a single solid tumor of the recto-vaginal septum without any disease noted within the peritoneal cavity.

Her histology is high grade papillary serous with Foundation One tumor testing confirming a BRCA1 mutation and loss of heterozygosity at 31% consistent with her known germline BRCA1 mutation. In summary, we report the first case of a BRCA1 associated, high grade serous carcinoma, arising in Mullerian remnants in the recto-vaginal septum.

Primary therapy for a rectovaginal septum mass commonly consists of surgery, radiation therapy, and chemotherapy. BRCA1 positive, high grade serous, ovarian cancer patients typically have excellent responses to platinum based multi-agent chemotherapy. Due to the extensive surgical procedure including coloanal anastomosis, and an expected excellent response to chemotherapy, we elected to reserve radiation therapy for treatment of recurrent or progressive disease. The role of maintenance therapy is crucial in this patient. Extrapolating from the experience with BRCA1 positive ovarian cancer patients in the PAOLA-1 trial, the decision was made to treat with maintenance bevacizumab and PARP inhibitor. Dual maintenance therapy with bevacizumab and PARP inhibitor showed a prolonged disease-free interval vs. bevacizumab alone in the PAOLA-1 trial (Ray-Coquard et al., 2019).

CRediT authorship contribution statement

Logan Blankenship: Conceptualization, data curation, writing-original draft, writing-review & editing. Yasmin A. Lyons: Writing-review & editing. Haisar Dao Campi: Data curation, Validation. Philip T. Valente: Data curation, writing-review & editing. Philip T. Valente: Data curation, writing-review & editing. Edward R. Kost: Conceptualization, data curation, supervision, writing-review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Informed consent has been obtained in writing and is on file if needed at any time.
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