Clinical Oncology: Case Reports

Case Report

A SCITECHNOL JOURNAL

Ovarian Remnant Syndrome and its Implications in a *Brca1* Positive Patient

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Abstract

Presentation: A 44-year-old Caucasian female with a BRCA1 variant c.3598C>T (p.Q1200X) mutation carrier was referred to the cancer genetics services to discuss risk reduction.

Treatment: She opted for risk reducing prophylactic bilateral salpingo-oophorectomy. Despite the initial procedure she continued to menstruate and underwent two further procedures to remove remnant ovarian tissue.

Diagnosis: Ovarian remnant syndrome.

Discussion: Despite risk reducing salpingo-oophorectomy some patients still develop ovarian cancer. In BRCA1 mutation carriers, bilateral salpingo-oophorectomy is associated with a 70% reduction in risk of ovarian cancer in women without a prior breast cancer and 85% in those with a prior breast cancer. It is possible that remnant ovarian tissue could account for some of these cases of ovarian cancer after risk reducing surgery.

Keywords

BRCA1; Ovarian remnant syndrome; Risk reduction

Introduction

Ovarian Remnant Syndrome (ORS), is characterized by the presence of ovarian tissue post Bilateral Salpingo-Oophorectomy (BSO), and can present as a pelvic mass, pain at the operative site or failure to achieve menopause [1,2]. The incidence of ORS is difficult to determine as most of the available literature is limited to case reports or retrospective cases [3,4]. Prevention of ORS is recommended through meticulous surgical technique [5].

BRCA1 and *BRCA2* genes are tumour-suppressor genes that encode proteins required for the repair of DNA double-stranded breaks by homologous recombination [6]. The presence of mutations in *BRCA1* or *BRCA2* significantly increases the risk of developing cancers such as breast and High-Grade Serous Cancer (HGSC) of ovarian origin. An increased incidence of tumours of other organs such as tubal, primary peritoneal, prostate, male breast, and pancreas is also noted in BRCA gene mutation carriers [6]. Studies have shown that the cumulative ovarian cancer risk to age 80 years was 44% for *BRCA1* and 17% for *BRCA2* carriers [7]. The NCCN guidelines suggest a combination of cancer surveillance and risk reducing surgery for management of patients who carry BRCA mutations. Risk-reducing salpingo-oophorectomy is the cornerstone of ovarian cancer prevention in *BRCA1/2* mutation carriers typically between 35 and 40 years [8].

A risk of malignancy in ORS tissue has been described in women with a history of BSO [9]. One series reviewed histological samples of 20 women with ORS, two of whom had evidence of malignancy on histology upon resection of the remnant tissue [9].

Case report

A 44 year old Caucasian female, para 4, who is a known *BRCA1* mutation carrier was referred to the cancer genetics services. The patient received genetic counseling regarding management options for her significantly increased risk of both breast and ovarian cancer, and chose breast screening according to the NICE guidelines with annual MRI between the ages of 30-49 years and annual mammography between the ages of 40-69 years. She was counseled about her lifetime risk of developing ovarian cancer and opted for risk reducing BSO. She had a BSO at the time of caesarean section for her fourth child in October 2016 while living in Brazil. However several months after her surgery she failed to achieve menopause and experienced ongoing menstruation.

She returned for follow up with ultrasound imaging and was noted to have persistent follicle producing ovarian tissue on her right side. She opted for further operative management and returned for resection of the remnant ovarian tissue in August 2017. Intraoperatively it was noted that she had remnant ovarian tissue bilaterally and this was resected.

The patient then returned to another hospital in Ireland and continued to menstruate for several months. She presented for investigation initially with a transvaginal ultrasound which showed a normal anteverted uterus with endometrial thickeness of 5 mm. A right ovary with a follicle was visualised. The left ovary was not visualized but a slight thickened tissue was visualised which raised the possibility of persistent ovarian tissue. Magnetic Resonance imaging was arranged and identified a right ovary with a 25 mm cyst. The left ovary was not identified. No adnexal mass or cyst was seen.

She had a third risk reducing surgery on the 20th of January 2019. Intra-operatively on the left no ovary was identified but the infundibulopelvic ligament was removed to ensure no residual ovarian tissue. The right ovary was identified and removed.

Histology was consistent with right ovarian tissue showing physiologic cysts, and a benign simple cyst. No atypia was seen. The specimen labelled left infundibulopelvic ligament specimen showed fibroadipose tissue only. A follow up hormonal panel in September 2019 was consistent with menopause with estradiol levels of <37pMol/L, FSH level at 53.55 IU/L and LH levels were 28.32 IU/L.

Discussion

ORS remains a rare and poorly understood entity. Further research is needed to evaluate the incidence and accurate diagnosis of ORS in patients who undergo risk reductive surgery for *BRCA1/2* gene mutations. In patients with persistent symptoms and negative imaging administration of clomiphene has been shown to demonstrate

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Received: December 07, 2020 **Accepted:** February 25, 2021 **Published:** March 10, 2021

the presence of a cystic mass on repeated imaging [10]. Treatment options include further surgery, and pharmacological therapy with medications that suppress ovulation [10]. Biochemical panels including anti-mullerian hormone have been investigated to assess volume of ovarian tissue following BSO malignancy [9]. This has been evaluated in animal studies looking at anti-mullerian hormone as a diagnostic tool for ovarian remnant syndrome in bitches and although false negatives may arise a positive result has been shown to be a beneficial method for the diagnosis of ORS in bitches [11]. In patients who are symptomatic or as in this case desire complete removal of ovarian tissue further surgical evaluation is warranted [10].

Conclusion

Despite risk reducing salpingo-oophorectomy some patients still develop ovarian cancer. In *BRCA1* mutation carriers, bilateral salpingo-oophorectomy is associated with a 70% reduction in risk of ovarian cancer in women without a prior breast cancer and 85% in those with a prior breast cancer. It is possible that remnant ovarian tissue could account for some of these cases of ovarian cancer after risk reducing surgery.

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