Fertility Preserving Surgery in A Woman with Synchronous Endometrial and Ovarian Cancer Followed by Successful Pregnancy Outcome: Case Report and Review of Literature

Vanita Suri

Post Graduate Institute of Medical Education and Research

Ramandeep Bansal (✉ raman.bansal1120@gmail.com)

Post Graduate Institute of Medical Education and Research

Neelam Aggarwal

PGIMER, Chandigarh

Pooja Sikka

PGIMER, Chandigarh

Seema Chopra

PGIMER, Chandigarh

Subhash Chandra Saha

PGIMER, Chandigarh

Nalini Gupta

PGIMER, Chandigarh

Bhavana Rai

PGIMER, Chandigarh

Case report

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Abstract

Background: Successful pregnancy outcome in women with synchronous ovarian and endometrial cancers is very rare. We report successful pregnancy outcome in a young woman managed conservatively for synchronous endometrial and ovarian cancer.

Case presentation: 30 years old nulliparous lady presented following exploratory laparotomy, left salpingo-oophorectomy and hysteroscopic polypectomy for left adnexal mass. Histology revealed endometrioid carcinoma of left ovary and moderately differentiated adenocarcinoma in the resected polyp. She underwent staging laparotomy along with hysteroscopy which confirmed above findings without any evidence of further tumor spread. She was treated conservatively with high dose oral progestin (megestrol acetate, 160mg) and leuprolide acetate 3.75mg monthly injections for three months along with four cycles of carboplatin and paclitaxel based chemotherapy followed by monthly injection of leuprolide for further three months. After failure of spontaneous conception, she underwent ovulation induction for six cycles along with intrauterine insemination which failed. She underwent in vitro fertilization with donor egg followed by elective cesarean section at 37weeks of gestation. She delivered a healthy baby of weight 2.7 Kg. Intraoperatively 5×6cm right ovarian cyst was found which drained chocolate coloured fluid on puncture and cystectomy was carried out. Histological examination revealed endometrioid cyst of right ovary. Uterus was spared as she wanted to preserve her fertility. She is being followed periodically and is normal nine months following delivery. She is on injection Depot medroxy progesterone acetate once every three months.

Background

Synchronous ovarian and endometrial cancer defined as simultaneous occurrence of cancers in ovary and uterine endometrium, though not uncommon, is encountered only rarely in clinical practice [1]. We report a young woman with synchronous endometrial and ovarian cancer who was managed conservatively and had a successful pregnancy outcome.

Case Presentation

30 years old nulliparous lady presented three and a half years back (November 2016) to our tertiary care hospital. She had already been evaluated at another center for abnormal vaginal bleeding and found to have left adnexal mass. Subsequently she underwent exploratory laparotomy, left salpingo-oophorectomy and hysteroscopic polypectomy. Postoperative histopathological examination revealed endometrioid carcinoma of left ovary and moderately differentiated adenocarcinoma in the resected polyp. Omental and peritoneal biopsies did not reveal evidence of tumor deposits. Two weeks after surgery, she presented to our tertiary care hospital for further evaluation. Histopathological review of slides confirmed the previous findings. She was diagnosed as a case of synchronous endometrioid carcinoma of ovary and adenocarcinoma of uterus and was further evaluated. Detailed general physical, systemic and gynecological examinations were normal. Routine hematological (hemoglobin, total and

differential leucocyte counts, platelet counts) and biochemical (fasting and random blood sugars, liver, renal and thyroid function tests, serum calcium and phosphorus and serum electrolytes) investigations were normal. CA-125 levels were 15.2IU/ml (normal: <46U/ml) Gadolinium enhanced magnetic resonance imaging of pelvis revealed two tiny hemorrhagic cysts in right ovary. There was no focal lesion in the uterine cavity and endometrial thickness was 5mm. She underwent staging laparotomy along with hysteroscopy. Intra-operatively right ovary and fallopian tube were found to be normal while left ovary and fallopian tube were absent. No metastatic deposits were found in any abdominal or pelvic organs. Biopsies were taken from right ovary, omentum and lymph nodes along with peritoneal washing. Hysteroscopy guided uterine curetting was done in the same setting. Frozen sections obtained during the procedure did not reveal any evidence of tumor. Histopathological examination of uterine curetting revealed moderately differentiated adenocarcinoma. She was planned for conservative management as she desired preservation of fertility. She was given high dose oral progestin (megestrol acetate, 160mg) and leuprolide acetate 3.75mg monthly injections for three months along with four cycles of carboplatin and paclitaxel based chemotherapy. After three months she underwent hysteroscopy guided endometrial biopsy which was normal. She was given monthly injection of leuprolide for further three months. Repeat CA-125 levels were normal.

Six months later, she was allowed for spontaneous conception. Her cycles were monitored along with ovulation study. A repeat hysteroscopy guided endometrial biopsy was normal. However she did not conceive spontaneously and was planned for assisted reproduction one year after last cycle of chemotherapy. Routine ultrasonography revealed right ovarian endometriotic cyst. Prior to assisted reproduction she was planned for diagnostic hystero-laparoscopy, but she did not agree for the same. Hysteroscopy guided endometrial biopsy did not reveal any abnormality. As she wanted conception despite explaining the risks, she underwent ovulation induction for six cycles along with intrauterine insemination. However she still did not conceive. She was planned for right sided oophorectomy followed by in vitro fertilization (IVF) with donor egg subject to absence of any abnormality in right ovary. However she did not agree for procedure and underwent IVF with donor egg at another center. She again presented to us at 27 weeks of gestation along with cholestasis of pregnancy for which she was managed conservatively. She underwent elective cesarean section at 37weeks of gestation and delivered a healthy baby of weight 2.7 Kg. Intraoperatively, 5×6cm right ovarian cyst was found which drained chocolate coloured fluid on puncture and cystectomy was carried out. Histological examination revealed endometriotic cyst of right ovary. Uterus was spared as she wanted to preserve her fertility. She is being followed periodically and is normal nine months following delivery. She is being administered injection depot medroxy progesterone acetate once every three months.

Discussion And Conclusion

Simultaneous occurrence of ovarian and uterine endometrial cancer is relatively uncommon. According to previous estimates, approximately 3-10% of women with cancer of ovary have simultaneous presence of endometrial cancer while 3-5% of women with cancer of uterine endometrium have simultaneous presence of cancer of ovary [1-4].

In one landmark study [5] (n=235,454 women with endometrial carcinoma), synchronous ovarian cancer was found in 1.7% of women with endometrial carcinoma, the incidence being highest (3.1-5%) in women between 29-47 years of age. The women with synchronous endometrial carcinoma and ovarian cancer were more often young black women with grade 1-2 tumors of endometrioid or serous histology type and stage I-II disease [5]. Most common histological combination was endometrioid cancer in both ovary and uterus (45.6%) followed by endometrioid cancer in uterus and non-endometrioid cancer in ovary (33%) and non-endometrioid cancer in both ovary and uterus (16.1%). Women with synchronous endometrioid cancer in both ovary and uterus were younger and had better 10 year survival rate (88.7%) compared to women with endometrioid carcinoma of uterus and non-endometrioid cancer of ovary (74.2%), non endometrioid cancer in both ovary and uterus (62.9%) and women with only endometrial carcinoma (80.7%) [5]. In another study [6], 3.3% of women with endometrial cancer and 2.7% of women with cancer of ovary had evidence of synchronous cancer of ovary or uterus respectively.

The exact mechanisms for this association remain to be determined. One possible explanation may be related to the fact that molecular receptors present in epithelial lining of ovaries and uterus are shared. Their concurrent response to a common carcinogenic insult in an index patient may lead to development of synchronous cancers in uterus and ovary [6].

The common clinical symptoms of synchronous ovarian and uterine cancer include abnormal vaginal bleeding (41%), pain (21%) or fullness (18%) in abdomen [6]. The symptoms which can be attributed to uterine carcinoma usually dominate the symptoms. In fact presence of abnormal vascular bleeding in setting of endometrioid ovarian cancer suggests coexistent endometrial pathology as was the case in our patient. In one study [7], 10/11 (90.9%) of women with abnormal vaginal bleeding in setting of endometrioid ovarian tumor had coexistent pathology which is much higher than that of general population (1.3% of premenopausal [8] and 17.1% of menopausal women [9] with abnormal vaginal bleeding harbor endometrial cancer or atypical hyperplasia). In fact women with abnormal vaginal bleeding may be detected and treated as they seek medical help earlier. The median survival of women with synchronous ovarian and uterine cancer was 60 months in presence of abnormal vaginal bleeding compared to 54 months in its absence in one study [6], likely related to early detection and treatment of women with abnormal vaginal bleeding.

Synchronous ovarian and uterine carcinomas are usually characterized by low histological grade and early disease stage [6]. Staging of disease in women with synchronous cancers of ovary and uterus poses difficulties more so in women with similar histology at both sites. In conveyance with cancer staging, such a situation may qualify either for stage III uterine cancer or stage IIA ovarian cancer, instead of qualifying for synchronous primarily independent cancers. However the prognosis of patients with synchronous ovarian and uterine cancers is better than either of stage III endometrial or stage IIA ovarian cancer, suggesting synchronous cancers to be an independent entity [6].

Recommended treatment for management of endometrial adenocarcinoma is total abdominal hysterectomy with bilateral salpingo-oophorectomy $\pm$ pelvic and para-aortic lymphadenectomy [10].

However, such an approach may not be feasible in women desiring future fertility. The universally accepted indications for fertility preserving treatment include strong desire for preserving fertility, nulliparous status, endometrioid carcinoma, stage I disease, reliable follow up, normal serum CA125 and grade I (grade II in some studies) histology [10]. Our patients qualified for all these criteria and were chosen for fertility preserving treatment with high dose progesterone therapy as reported in another study [11].

Similar to endometrial carcinoma, management of endometrioid ovarian tumors requires several important considerations in women with strong desire for future fertility. Though radical surgery (bilateral salpingo-oophorectomy with hysterectomy and staging surgery) remains the treatment of choice for ovarian malignancies, it may not be possible in women who desire to preserve their fertility. Accordingly, conservative approach has to be adopted sometimes especially in younger women with desire for future pregnancy [4]. In one review [12] including 507 women undergoing fertility sparing surgery for women with early stage ovarian cancer, risk of recurrence was 10.3% and risk of death from disease was 5.5%. These values were similar to those reported for historical controls. 36.7% of these women had full term deliveries. However other series have reported recurrence rate of 4-6% in preserved ovary [13, 14]. Morice et al [15] concluded that stage IA grade 1 and possibly grade 2 tumors (serous, mucinous or endometrioid subtypes) can be considered for fertility sparing surgery. They also suggested that even women with Grade 1 stage 1C disease can be considered for surgery.

The fact that only close to 1/3rd of women with cancers of ovary are able to achieve full term pregnancy following fertility sparing treatment [12] raises concerns. The reasons for poor fertility outcomes in these women are not clear but may be related to coexistent endometrial pathology and adhesions and alteration of ovarian function after surgery. Our patient also did not conceive spontaneously and even after treatment for infertility. However she did conceive following in vitro fertilization and had successful pregnancy outcome.

While fertility sparing treatment is well documented in patients with both endometrial and ovarian carcinomas, the reports of fertility sparing treatment are sparse in literature with regards to synchronous cancers of ovary and uterus [16]. Atallah et al [16] reported a lady with synchronous ovarian and uterine cancer who conceived spontaneously and had a successful pregnancy outcome following fertility sparing treatment. However unlike their report, our patient could not conceive spontaneously and needed in vitro fertilization.

Conclusion

Above review and our report throw further light on some of the diagnostic and therapeutic aspects related to synchronous endometrioid tumors of ovary and uterus. A rational therapeutic approach, close follow up and careful planning taking into account requirements of the patient remain keys to successful management of these rare tumors. A conservative management followed by active fertility planning may be required for women who desire fertility.

Declarations

Ethics approval and consent to participate

The study was approved by institutional ethics committee and written informed consent was obtained from patient before participation in the study

Consent for publication

Written informed consent was obtained from patient before sending the manuscript for publication

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

Authors declare that we do not have any competing interests

Ramandeep Bansal

Writing of manuscript, collection of data

Neelam Aggarwal

Collection of data, revision of manuscript

Pooja Sikka

Collection of data, revision of manuscript

Seema Chopra

Collection of data, revision of manuscript

S C Saha

Collection of data, revision of manuscript

Nalini Gupta

Collection of data, revision of manuscript

Bhavana Rai

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Authors' contributions:

Vanita Suri: Collection of data, review of manuscript

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References

1. Zaino R, Whitney C, Brady MF, DeGeest K, Burger RA, Buller RE. Simultaneously detected endometrial and ovarian carcinomas—a prospective clinicopathologic study of 74 cases: a gynecologic oncology group study. *Gynecol Oncol*. 2001;83:355–62.
2. Chiang YC, Chen CA, Huang CY, Hsieh CY, Cheng WF. Synchronous primary cancers of the endometrium and ovary. *Int J Gynecol Cancer*. 2008;18:159–643.
3. Williams MG, Bandera EV, Demissie K, Rodriguez-Rodriguez L. Synchronous primary ovarian and endometrial cancers: a population-based assessment of survival. *Obstet Gynecol*. 2009;113:783–94.
4. AlHilli MM, Dowdy SC, Weaver AL, St Sauver JL, Keeney GL, Mariani A, et al. Incidence and factors associated with synchronous ovarian and endometrial cancer: a population-based case-control study. *Gynecol Oncol*. 2012;125:109–13.
5. Matsuo K, Machida H, Blake EA, Holman LL, Rimel BJ, Roman LD, et al. Trends and outcomes of women with synchronous endometrial and ovarian cancer. *Oncotarget*. 2018;9(47):28757–71.
6. Chiang Y-C, Chen C-A, Huang C-Y, Hsieh C-Y, Cheng W-F. Synchronous primary cancers of the endometrium and ovary. *Int J Gynecol Cancer*. 2008;18:159–64.
7. Jia S, Zhang J, Yang J, Xiang Y, Liang Z, Leng J. Risk of synchronous endometrial disorders in women with endometrioid borderline tumors of the ovary. *J Ovarian Res*. 2018;11:30.
8. Ozdemir S, Celik C, Gezginc K, Kiresi D, Esen H. Evaluation of endometrial thickness with transvaginal ultrasonography and histopathology in premenopausal women with abnormal vaginal bleeding. *Arch Gynecol Obstet*. 2010;282:395–9.
9. Katke RD. Successful treatment of pregnancy in borderline malignant ovarian tumor. *J Case Rep*. 2014;4(2):391–94.

10. Lai CH, Wang CJ, Chao A. The clinical management of endometrial cancer in young women. *Current Obstet Gynecol Rep.* 2013;2:26–31.
11. Patil M, Mahajan N. Fertility preservation in endometrial carcinoma: case series of 11 patients. *Onco Fertil J.* 2018;1:36–43.
12. Vitobello D, Siesto G, Bulletti C, Accardi A, Levi Setti PE. Gynecological fertility-sparing surgery. *Placenta.* 2011;32(Suppl 3):224–31.
13. Kajiyama H, Shibata K, Suzuki S, Ino K, Nawa A, Kawai M. Fertility-sparing surgery in young women with invasive epithelial ovarian cancer. *Eur J Surg Oncol.* 2010;36:404–8.
14. DePriest PD, Ueland FR, Cibull ML, Kryscio RJ, Cibull ML, Kryscio RJ, et al. Outcome of reproductive age women with stage IA or IC invasive epithelial ovarian cancer treated with fertility-sparing therapy. *Gynecol Oncol.* 2002;87:1–7.
15. Morice P, Denschlag D, Rodolakis A, Reed N, Schneider A, Kesic V, et al. Fertility Task Force of the European Society of Gynecologic Oncology. Recommendations of the Fertility Task Force of the European Society of Gynecologic Oncology about the conservative management of ovarian malignant tumors. *Int J Gynecol Cancer.* 2011;21:951–63.
16. Atallah D, Safi J, El Kassis N, Rouzier R, Chahine G. Simultaneous early ovarian and endometrial cancer treated conservatively with spontaneous pregnancy. *J Ovarian Res.* 2013 Aug;21:6:59.
17. **Legend to Fig. 1.**
18. a. An endometrioid adenocarcinoma of the ovary showing complex glandular pattern and desmoplastic stroma (H&E x20X).
19. b. The individual glands are lined by tall columnar lining epithelial cells showing moderate pleomorphism and prominent nucleoli (H&E x40X).

Figures

Figure 1

a: An endometrioid adenocarcinoma of the ovary showing complex glandular pattern and desmoplastic stroma (H&E x20X)