

In vitro fertilization in a patient with ovarian cancer (Stage IC) following conservative surgery and chemotherapy: a case report

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Summary

A 30-year-old female underwent left salpingo-oophorectomy followed by chemotherapy for Stage IC adenocarcinoma of the ovary. Three years later she had ovarian hyperstimulation and in vitro fertilization (OH-IVF) resulting in a singleton pregnancy. During cesarean section peritoneal washings and biopsies were negative for recurrence. Seven years after the initial diagnosis, the patient is still free of any disease. In conclusion, OH-IVF may be considered in young patients with early ovarian cancer treated with conservative surgery and chemotherapy.

Key words: Ovarian cancer; Chemotherapy; IVF.

Introduction

The rate of ovarian tumor diagnoses in reproductive age woman has increased parallel to the improvements in diagnostic methods and regular gynecological visits. Because of this, conservative surgeries for the preservation of reproductive function have gained more interest. Data on the role of in vitro fertilization (IVF) and ovarian stimulation in patients with established diagnoses of ovarian cancer and who want to get pregnant are still limited. Most of the reported cases are described in patients with low malignant potential (LMP) ovarian tumors and have shown encouraging fertility outcome [1, 2]. However, the situation seems to be more complicated for IVF treatment in patients with early-stage invasive cancer needing chemotherapy. The role and safety of IVF and ovarian stimulation in these patients are still controversial [3, 4]. This lack of consensus is attributed to the complex interactive nature of infertility, the potential effects of the medications, and other inherent risk factors in this patient population. This has left little guidance for women who have an established diagnosis of ovarian cancer and who want to conceive through fertility drugs. The problem becomes more complex in patients with invasive metastatic implants who require adjuvant chemotherapy.

We report a case of a young woman with a borderline epithelial ovarian tumor and invasive implants (Stage IC adenocarcinoma of the ovary) who underwent conservative surgery and chemotherapy followed by one successful IVF pregnancy, and another spontaneous pregnancy thereafter.

Case Report

The patient was a 30-year-old woman when she had surgery in another hospital for a persistent left complex ovarian cyst. She underwent open ovarian cystectomy (with intraoperative rupture of the cyst) in May 2000 and the pathology was consistent with a borderline mucinous ovarian tumor with negative peritoneal washings. No tumor markers were taken at that time. She was seen in our hospital in July 2000 for a recurrence of the cyst with an elevated CA125 of 742 with normal CA19-9 and CEA. CT scan of the abdomen and pelvis was unremarkable except for a 5 x 3 cm left ovarian complex cyst.

In August 2000, she underwent an exploratory ovarian staging laparotomy, peritoneal washing, left salpingo-oophorectomy, and appendectomy. There was now evidence of a residual adenocarcinoma (grade 1) limited to the left ovary. All the other specimens were negative. Following surgery and because of prior manipulation of the left ovary which now contained an invasive cancer (thus staged as IC), she received four adjuvant chemotherapy cycles of paclitaxel and carboplatin. She had amenorrhea during and three months following the chemotherapy. She then spontaneously had resumption of her menses. She has been followed since then with examinations, vaginal ultrasonography (US), and CA125 monitoring as well as a yearly computed tomography (CT) scan of the abdomen and pelvis with no recurrence of the tumor.

The patient got married in December 2003 and wanted to conceive. Her baseline day 3 FSH was 12.6 IU/ml and estradiol was 13 pg/ml. Hysterosalpingography showed a right patent tube and her husband had a normal semen analysis. She was unable to conceive spontaneously for seven months so a repeat day 3 FSH was done resulting as 18.6 IU/ml with estradiol of 32 pg/ml. After counseling she was referred to our IVF Unit. Controlled ovarian hyperstimulation was performed by a long standard protocol with GnRH agonist. In brief, GnRH agonist was started in the mid-luteal phase at a daily dose of 0.05 mg until the day of hCG injection. Recombinant FSH (200 U/day) was started on the third day of her cycle. Oocyte aspiration was performed approximately 36 hours after hCG administration. A total of six metaphase II oocytes were aspirated. Four embryos were transferred two days after oocyte pickup resulting in a singleton pregnancy. The patient had a smooth antenatal course. In

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August 2005, at term, she delivered by cesarean section for a breech presentation a live healthy female newborn weighing 3,200 g. She also had washing of the peritoneum in addition to biopsy of the right periovarian adhesion, remnant of left the infundibulopelvic ligament, anterior and posterior cul-de-sac peritoneum, peri-colic gutters, and remnants of the omentum. All were unremarkable.

One year later she had a spontaneous singleton pregnancy and again had a term repeat cesarean section and delivered a live female newborn weighing 3,100 g. Peritoneal washings and biopsies were again unremarkable.

Discussion

The role of IVF in patients with ovarian cancer has been described in few reports, mostly in patients with LMP tumors [1, 2, 5, 6]. In addition, spontaneous pregnancies following chemotherapy for ovarian cancer have been reported in several patients [3, 7]. However, the use of IVF in patients with established ovarian cancer treated with conservative surgery and adjuvant chemotherapy has been reported recently in only one patient, making our patient the second case to be reported in the literature [4]. Our patient was diagnosed initially as a case of LMP ovarian tumor and underwent conservative surgery. Unlike their invasive counterparts, LMP ovarian tumors tend to occur more frequently during a woman's reproductive years. Because the prognosis for patients with borderline ovarian tumors is excellent, particularly in patients with the most common stage - Stage I - there has been a trend over the past several years toward fertility sparing surgery in women of reproductive age who have not completed childbearing. The reproductive performance of women who underwent conservative surgery for borderline ovarian tumors was found to be adequate, and spontaneous pregnancies with good outcomes have been reported. Moreover, no relationship between pregnancy and recurrence has been demonstrated [1, 2].

Following her second surgery, our patient was discovered to have a frankly invasive mucinous ovarian adenocarcinoma rather than just a borderline tumor as previously diagnosed. Review of the original pathology confirmed the borderline nature, although the diagnosis of borderline versus malignant mucinous tumor is more difficult than the rest of the borderline epithelial tumors. Moreover, because of prior manipulation of the ovary and intraoperative rupture with her first surgery she was staged as Stage IC. During her second surgery, she wanted to preserve her fertility potential so a unilateral salpingo-oophorectomy with full staging was done. This was followed with four cycles of chemotherapy because of prior intraoperative spillage and the short time interval between the original diagnosis of the borderline and the diagnosis of the frankly malignant tumor. She underwent IVF with ovarian stimulation because of an increase in her day 3 FSH and her inability to conceive after a seven month trial. Data in the literature, mainly based on case reports, are not sufficient to argue about the safety of the

use of induction of ovulation or IVF in patients with advanced borderline tumors or those which are malignant. Several studies that examined the role of ovulation induction in the development of borderline ovarian tumors reported a possible positive association [8]. However, more recent data have provided reassuring evidence on the absence of a strong association between fertility drugs and subsequent risk of developing invasive epithelial ovarian cancer [9].

Data on the efficacy and safety of IVF procedures in patients with advanced LMP ovarian tumor or early frank ovarian cancer are still limited. Most of the cases reported did not have any significant progression of the disease [1, 2]. However, Attar *et al.* reported a rapid progression of peritoneal disease in a patient with a Stage IIIC serous tumour with a micropapillary pattern [10]. Thus, it does not seem possible to give guidelines concerning hyperstimulation and IVF in patients with advanced stage disease and/or micropapillary patterns. Although no definite conclusions can be drawn regarding the safety of infertility treatment in this group of patients, mainly because of the retrospective character of the studies and the small number of patients included, the results show that IVF after the diagnosis of a borderline ovarian tumor does not appear to affect survival. The recurrence rate after IVF treatment is reported to be 20%, similar to the rate reported for patients who underwent conservative treatment without any subsequent fertility therapy [6, 9]. Our patient has been disease free for seven years since her initial diagnosis and treatment, during which she had two successful pregnancies one of them a product of IVF.

Spontaneous pregnancy following chemotherapy for ovarian cancer has been reported in several patients [7]. The return of ovarian function and subsequently the fertility potential following chemotherapy varies with the patient's age, type of chemotherapy used, and her ovarian reserve. It is expected that most young patients who receive chemotherapy for ovarian cancer resume ovarian function and can expect normal fertility rate. Our patient took four cycles of chemotherapy that caused transient amenorrhea. Six months after finishing chemotherapy her menstrual cycles resumed. However, three years later, despite having regular ovulatory cycles, her FSH was increasing reflecting a decrease in her ovarian reserve. This could be due to chemotherapy and/or having only one ovary. Despite this she had adequate response to ovulation induction and successful IVF treatment, and had a spontaneous pregnancy one year after the delivery of her first child. One of the main concerns of patients who received chemotherapy is the effect of toxic chemotherapy in their offspring. The data available so far have not shown any significant increase in the frequency of congenital anomalies in the offspring [3].

In conclusion, IVF with ovarian stimulation may be considered in young patients with early ovarian cancer treated with conservative surgery and chemotherapy, and who fail to conceive spontaneously.

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