J Assist Reprod Genet (2011) 28:771–772
DOI 10.1007/s10815-011-9596-7

FERTILITY PRESERVATION

Successful extracorporeal mature oocyte harvesting after laparoscopic oophorectomy following controlled ovarian hyperstimulation for the purpose of fertility preservation in a patient with borderline ovarian tumor

Silvina Bocca · Daynelle Dedmond · Estella Jones · Laurel Stadtmauer · Sergio Oehninger

Received: 3 May 2011 / Accepted: 31 May 2011 / Published online: 9 June 2011

Abstract
Purpose To report the successful extracorporeal recovery of mature oocytes after laparoscopic oophorectomy following ovarian hyperstimulation for the purpose of fertility preservation in a patient with recurrent serous borderline ovarian tumor.
Methods A 25-year-old nulligravida woman presented with recurrence of a borderline serous adenocarcinoma in the right ovary after been treated conservatively with left oophorectomy for the same.
Result(s) The patient underwent ovarian stimulation followed by a laparoscopic oophorectomy and ex-vivo retrieval of oocytes. Twenty two oocytes were recovered: fourteen metaphases II, two metaphases I, five prophases I and one degenerate.
Conclusion(s) Mature oocytes were successfully retrieved *ex-vivo* from the hyperstimulated ovary recovered via laparoscopy. The procedure can be performed in a quick manner, with standard equipment, without damaging the ovary, the follicles or the oocytes, and without the risk of cancer cell spillage associated with the standard trans-vaginal oocyte retrieval if there is concern of ovarian surface/peritoneal metastatic disease.

Keywords Borderline ovarian tumor · Laparoscopy · *ex-vivo* oocyte retrieval · Fertility preservation

Capsule We report on extracorporeal oocyte retrieval after laparoscopic oophorectomy following ovarian hyperstimulation for fertility preservation in a young woman with a borderline serous ovarian tumor.

S. Bocca (✉) · E. Jones · L. Stadtmauer · S. Oehninger
The Jones Institute for Reproductive Medicine, Department of Obstetrics and Gynecology, Eastern Virginia Medical School,
605 Colley Ave.,
Norfolk, VA, USA
e-mail: boccas@evms.edu

D. Dedmond
Sentara Surgery Specialists,
Williamsburg, VA, USA

Borderline ovarian tumors generally have an excellent prognosis and can be treated conservatively in women who wish to preserve their fertility or are pregnant at the time of diagnosis [1].

Fatemi et al. [2] were the first ones to report on *ex-vivo* retrieval of mature oocytes after ovarian stimulation via laparotomy due to concerns of difficulty removing an enlarged, stimulated and fragile ovary via laparoscopy.

Here, we report the successful laparoscopic removal of a hyperstimulated ovary in a patient with a recurrent borderline tumor, with excellent intact oocyte recovery, accomplished with simultaneous cancer staging, and performed in an outpatient setting.

A 25-year-old nulligravida woman was referred by her Gyn Oncologist on January of 2011 for an emergency consult for fertility preservation due to history of a fast recurrent ovarian borderline serous tumor. She had undergone a laparoscopic left salpingo-oophorectomy for a 10 cm complex cystic adnexal mass with capsular projections and a CA 125 of 428 U/ml. Staging was performed due to frozen pathology showing a serous borderline tumor (Final pathology: borderline serous tumor, negative peritoneal washings and negative lymph nodes; FIGO stage 1c).

She started to experience cyclic right lower quadrant pain 2–3 months post op. A normal CT of the abdomen and pelvis was obtained on September of 2010 as well as a normal CA 125 of 14.4 U/ml on November of 2010. The

right lower pain intensified and she underwent a diagnostic laparoscopy with excision of a 6 cm cystic neoplasm with capsular implants on December of 2010 with frozen pathology revealing an atypical papillary borderline ovarian malignancy. Definitive treatment was delayed until consulting with a Reproductive Endocrinologist for fertility preservation. Initial evaluation revealed a right ovary with 10 small antral follicles as well as a trilobular cystic structure, each lobe measuring 13, 7 and 14 mm, respectively, with peripheral blood flow and normal hormonal levels (FSH 5 mIU/ml, LH 2 mIU/ml, and estradiol 51 pg/ml).

Due to the patient not having a partner and the risk of transplanting tumor cells back, neither ovarian tissue freezing nor transvaginal or laparoscopic follicular aspiration were considered good options. Instead, oocyte retrieval via *ex-vivo* follicular aspiration was considered to be the safest option. Patient signed IRB-approved consent for oocyte vitrification for fertility preservation.

She underwent controlled ovarian hyperstimulation following menses with 7 days of 200 u of Follistim in the evening, Ganirelix from d7-d10 in the morning, Ovidrel on cycle day 10 with peak estradiol of 1,977 pg/ml and a right ovary measuring 6.5×3.1×3.2 cm with 7 follicles 16 mm or large on the day of hCG.

The laparoscopic right salpingo-oophorectomy was performed with three 5 mm trocars (umbilical, left and right lower quadrants) and one 15 mm trocar in the suprapubic region. The specimen with no visible surface tumor implants was placed into an endobag inserted via the 15 mm trocar. The suprapubic incision was extended to approximately 6 cm (minilaparotomy) to accommodate an atraumatic removal of the stimulated ovary with follicles.

The endobag containing the removed ovary was placed in a pre-warmed stainless bowl. The ovary was removed from the endobag (10 min maximum ischemia time) and placed in a large Petri dish containing warm Quinn's Advantage Medium with HEPES supplemented with heparin. The oocyte retrieval was performed with the standard equipment for transvaginal oocyte aspiration for IVF [3]. The follicular fluid was immediately given in tubes to the embryologist who proceeded to identification of the cumulus-corona complexes under a dissecting microscope in the same operating room. No oocytes or cumulus cells were present in the fluid used to rinse the endobag. The oocytes were transported to the IVF laboratory (approximately 200 m away from the OR) in a 37^0 C portable incubator (K-Systems, MidAtlantic Diagnostics, Marlton, NJ, USA) in Quinn's Advantage Medium with HEPES supplemented with 10% Quinn's Advantage Serum Protein Substitute. Twenty two oocytes were aspirated and their cumulus cells were removed with 0.1% hyaluronidase yielding fourteen mature (metaphase II), two metaphases I, five prophases I and one degenerated oocytes. The mature oocytes were vitrified an hour later using a modified oocyte vitrification method as previously described by Kuwayama et al. [4].

The final pathology revealed a 27 g right ovary measuring 6×4.5×2.7 cm with a 0.9 cm in greatest dimension tan-brown, firm nodule at the periphery of the ovary attached to a 6.8×1.2×2.5 cm fimbriated tube with a serous borderline tumor, ovary with focal microscopic involvement of surface, and negative lymph nodes, fallopian tube and biopsies.

In conclusion, we described that mature oocytes can be successfully retrieved *ex-vivo* from a laparoscopically retrieved hyperstimulated ovary, followed by oocyte vitrification for fertility preservation. Performing the staging via laparoscopy with final extension of one incision for specimen removal allows for faster recovery then via laparotomy since there is minimal manipulation of the intestines with no need for packing. Despite initial concerns about the use of laparoscopy in gynecologic oncology [5], several case series, retrospective reviews, and case–control studies have demonstrated it to be both safe and effective for the staging of borderline ovarian tumors [6]. The procedure can be performed in a quick manner, with standard equipment, without damaging the ovary, the follicles or the oocytes, and importantly, without the risk of cancer cell spillage associated with the standard transvaginal oocyte retrieval.

Acknowledgements The authors would like to thank Mrs. Valerie Warsof, RN for her dedication to the patient's care as well as to Ms. Carnai Simpson for reviewing the manuscript.

Disclosures Dr S. Bocca is a speaker for Merck (Schering-Plough). Other authors have no disclosures.

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