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REVIEW

Live birth using vitrified–warmed oocytes in invasive ovarian cancer: case report and literature review

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Abstract This article reports the live birth of a healthy newborn using vitrified–warmed oocytes in a young patient with invasive mucinous ovarian carcinoma (stage Ic). Diagnosis was performed after a laparoscopic left adnexectomy. She underwent two cycles of ovarian stimulation, and 14 oocytes were vitrified before fertility-sparing surgery with uterus preservation went ahead. One year later, a transfer of two embryos was performed after insemination of warmed oocytes. Eighteen days after the transfer, she underwent a laparotomy because of abdominal pain, vaginal bleeding and haemoperitoneum. A right cornual ectopic pregnancy in the uterus was diagnosed and a wedge resection was performed to resolve it. One week later, a viable intrauterine pregnancy was confirmed under ultrasound. An elective Caesarean section was performed at week 38 of gestation, resulting in the birth of a healthy boy weighing 2650 g. As far as is known, this is the first live birth reported through vitrified–warmed oocytes in a patient with invasive ovarian cancer. Although oocyte vitrification is an alternative to be considered for fertility preservation in highly selected cases of ovarian cancer, controversial issues are discussed.

KEYWORDS: fertility preservation, fertility-sparing surgery, heterotopic pregnancy, ivf in cancer patients, ovarian cancer, oocyte vitrification

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Introduction

Cancer continues to be a major problem in Western countries not only in terms of survival but also in terms of loss in childbearing potential. Fortunately prospects have improved with the arrival of new techniques for oocyte cryopreservation and new approaches to therapeutic strategies for oncological patients. These advances have raised the possibility of seeking pregnancy in oncological patients. Nowadays, there is no evidence that fertility preservation techniques lead to reduced success rates in the treatment of cancer (Jeruss and Woodruff, 2009). Also, fertility preservation would be of psychological benefit to these patients (Letourneau et al., 2012) with the fertility preservation consultation providing a useful source of information. According to Kim et al. (2013), 73% of patients made up their mind about treatment after this consultation.

Published results using vitrified–warmed oocytes in young infertility patients and oocyte donors (Cobo et al., 2011; Rienzi et al., 2012) have made oocyte vitrification one of the strategies of choice for fertility preservation, although there is a trend towards combining several strategies in order to maximize chances of success (González et al., 2011; Martínez et al., 2013). Fertilization and pregnancy rates are similar to IVF/intracytoplasmic sperm injection with fresh oocytes, and no increase in chromosomal abnormalities, birth defects or developmental deficits have been described in children born from cryopreserved oocytes (Chian et al., 2008). So, the Practice Committee of the American Society for Reproductive Medicine (2013) recommends oocyte preservation as one of the options, with appropriate counselling, in patients with cancer and high risk for infertility and says that 'evidence indicates that oocyte vitrification should no longer be considered experimental'. Unfortunately referrals of oncological patients to fertility specialists are below 50% according to Quinn et al. (2009), despite the recommendations of scientific societies and committees (Kim et al., 2012; Lee et al., 2006; Martínez et al., 2013; Practice Committee of the American Society for Reproductive Medicine, 2013).

As far as is known, no case of a live birth has been described using oocyte vitrification as a strategy for fertility preservation prior to oncological surgery for invasive ovarian cancer, although there is a recommendation for fertility-sparing surgery in early stages of ovarian cancer (Kashima et al., 2013; Morice et al., 2011). This report describes a live birth using vitrified–warmed oocytes and fertility-sparing surgery in a woman with invasive ovarian cancer (stage Ic). Controversial issues are subsequently reviewed and discussed.

Case report

A 28-year-old patient attended this study centre for a second opinion in January 2010. She had a laparoscopic left adnexectomy in another centre because of a 17-cm adnexal cystic mass under ultrasound scan. Tumour markers were negative at that time. Pathology was consistent with an invasive mucinous carcinoma with foci of borderline mucinous carcinoma.

Fertility preservation was authorized by the Committee of Gynecological Oncology according to patient's desire, age, the histological diagnosis and the prognosis of the disease (surgical stage Ic of ovarian cancer). The patient was immediately referred to the Service of Reproductive Medicine for oocyte vitrification prior to completing surgery. The patient's ovarian reserve was assessed by antral follicle count on ultrasound (eight follicles) and anti-Müllerian hormone (2.1 ng/ml).

Ovarian stimulation was started under a multiple dose flexible gonadotrophin-releasing hormone antagonist protocol (cetrorelix 0.25 mg/ml; Cetrotide; Merck-Serono, Spain) and 225 IU/day recombinant FSH (Gonal F; Merck-Serono). Ovulation was triggered with 250 μg recombinant human chorionic gonadotrophin (Ovitrelle; Merck-Serono) when the two leading follicles were ≥17 mm. Follicular aspiration took place after 36 h and five oocytes were retrieved. Four MII oocytes were immediately vitrified as previously described by Kuwayama et al. (2005). A second ovarian stimulation cycle was performed 1 month later with an initial dose of 300 IU/day of recombinant FSH due to the low number of vitrified oocytes. Fourteen oocytes were retrieved and 10 MII were vitrified as previously described.

Patient underwent surgical treatment in the study centre in July 2010 by means of laparoscopic right adnexectomy, appendectomy and pelvic and aortic lymphadenectomy as well as omentectomy. Thus the uterus was preserved in this surgery. The histopathological study was normal and with no metastatic invasion in 26 lymph nodes. The patient did not require subsequent treatment with radio- or chemotherapy.

Fertility preservation and the later use of the oocytes for IVF were both approved by the Committee of Gynecological Oncology (reference no. CGOM27012010/2.4, approved 27 January 2010) and the Institutional Review Board (reference no. CIOG01092010/03, approved 1 September 2010) of University Hospital Quirón Dexeus. The patient gave her written consent for these processes.

One year later, tumour markers were negative and the Committee of Gynecological Oncology authorized the use of vitrified oocytes. Hormonal replacement therapy for endometrial preparation was prescribed according to the protocol described previously (Martínez et al., 2006). Warming of eight oocytes was performed in accordance with the protocol described by Kuwayama et al. (2005). Seven oocytes survived and were inseminated with the partner's semen using intracytoplasmic sperm injection after 2 h of culture in IVF medium (Vitrolife, Sweden). Normal fertilization of seven oocytes was assessed at 18 ± 2 h. On the following day (day 2), two optimal-quality embryos were transferred under ultrasound guidance (Coroleu et al., 2002). On day 3 of development (68 ± 2 h), two optimal-quality embryos were cryopreserved for future attempts.

Serum β-human chorionic gonadotrophin assayed 12 days after embryo transfer was 218 IU/l. The patient presented at her home hospital 8 days later with abdominal pain and vaginal bleeding. A laparotomy was performed with the clinical suspicion of heterotopic pregnancy since the patient's haemoglobin concentrations had decreased from 14 g/dl to 10.7 g/dl and an ultrasound scan demonstrated the presence of haemoperitoneum and an intrauterine gestational sac. The review of the abdominal cavity showed a right cornual ectopic pregnancy in the uterus. A wedge