Case Report

Inadvertent premature human chorionic gonadotropin administration does not prevent folliculogenesis and *in vitro* fertilization

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Abstract

A 41.9-year-old patient, G 10101 was referred to fertility preservation 2 weeks before chemotherapy, due to metastatic liver malignancy. Her past history was positive for laparoscopic sigmoidectomy, 5 years ago due to the stage I colon carcinoma. She has undergone a normal vaginal delivery in her previous marriage, 15 years ago and a septic abortion, 2 days after amniocentesis, a year ago, in her current marriage. Despite high follicle-stimulating hormone (FSH), she started ovarian stimulation with high dose recombinant gonadotropins and gonadotropin-releasing hormone antagonist, on the 6th day of her cycle, in the presence of two antral follicles. By mistake, she injected 250 μg of human chorionic gonadotropin (hCG), in addition to 450 units FSH/luteinizing hormone (Pergoveris, Merck Serono) on the 1st day of stimulation. The Controlled Ovarian Stimulation (COS) continued and on the 18th cycle day, 250 μg of hCG was administered and 35.5 h afterward, two metaphase II ova were retrieved by vaginal follicular aspiration. The ova have undergone intracytoplasmic sperm injection, and fertilization was documented after 20 h, and two embryos were cryopreserved on the 2nd day. This unusual case suggests that premature exposure to supraphysiologic concentrations of hCG and progesterone, may not interfere with normal folliculogenesis, oocyte maturation, and *in vitro* fertilization.

Key words: Cryopreservation, fertility preservation, human chorionic gonadotropin, *in vitro* fertilization, premature, random start ovarian stimulation

INTRODUCTION

The increase in cancer incidence in the young age and the significant increase in the long-term survival have brought about a ubiquitous interest in the attempts to preserve fertility in young patients exposed to gonadotoxic chemo- and radiotherapy.[1-5] Indeed, malignancy is estimated to occur in 1:49 women under the age of 40 in the US.[1,2] It has been previously estimated, that at present, one in every 250–715 people in the adult population will be a cancer survivor.[1,2] Therefore, the late effects of cancer treatment have recently gained a worldwide interest not only among reproductive endocrinologists but also among hematologists, oncologists, gynecologists, endocrinologists, rheumatologists, family physicians, and all healthcare providers,[1-5] and the protection against iatrogenic infertility caused by chemotherapy assumes a high priority.

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Several options have been put forward for preserving female fertility: Ovarian transposition, cryopreservation of embryos, unfertilized metaphase-II (M-II) oocytes, and ovarian tissue, and administration of gonadotropin-releasing hormone (GnRH)-agonistic analogs in an attempt to decrease the gonadotoxic effects of chemotherapy by simulating a prepubertal hormonal milieu.[1-5] Indeed, in the last decade a dramatic increase in the number of publications regarding fertility preservation has been experienced. Unfortunately, none of the suggested methods is ideal, and none guarantees future fertility in survivors. *In vitro* fertilization (IVF) and embryo cryopreservation, the only noninvestigational, clinically established method, used to necessitate postponing chemotherapy for at least 10–14 days, and is frequently not applicable to the very young patient without a partner. The following case report, similar to other recent publications suggests that premature exposure to supraphysiologic concentrations of human chorionic gonadotropin (hCG) and progesterone, may not interfere with normal folliculogenesis, oocyte maturation, and IVF.

CASE REPORT

A 41.9-year-old patient, gravida 2, para 1, abortion 1 was referred for fertility preservation 2 weeks before chemotherapy, due to metastatic liver malignancy. Her past history was positive for laparoscopic sigmoidectomy, 5 years ago due to the stage I colon carcinoma. She did not receive any previous chemo- or radiotherapy. In her infancy, she has undergone surgery due to congenital disclocation of the hip. She has undergone a normal vaginal delivery in her previous marriage 15 years ago, and a septic abortion in the 19th week of a spontaneous pregnancy, 2 days after amniocentesis, in another hospital, a year ago, in her current marriage. Her menstrual periods were irregular, ranging between 17 and 40 days and the last menses started 6 days before referral. The follicle-stimulating hormone (FSH) = 20.9 U/L, estradiol 80 picomolar, progesterone 2.5 nanomolar, CA19-9 = 618.2 U/mL (NR <39 U/mL), carcinoembryonic antigen = 39.1 ng/mL (NR <5.5 ng/mL), lactic dehydrogenase = 878 U/L (NR = 230–480 U/L), gamma glutamyl transpeptidase = 105 U/L (NR = 5–38 U/L), and alkaline phosphatase 178 U/L (NR = 30–120 U/L). The imaging methods and positron emission tomography/computed tomography were compatible with metastatic space occupying lesions in the right lobe of the liver and retroperitoneal lymph nodes. Due to the high FSH levels, she was advised against GnRH agonist co-treatment and ovarian tissue cryopreservation. However, despite the high FSH, due to the presence of two antral follicles she insisted on an attempt to try COS for IVF and cryopreservation of embryo.

Despite high FSH, she started ovarian stimulation with high dose recombinant gonadotropins and GnRH antagonist, on the 6th day of her cycle, in the presence of two antral follicles. By mistake, she injected 250 μg of hCG, in addition to 450 units FSH/luteinizing hormone (Pergoveris, Merck Serono) on the 1st day of stimulation. The COS continued and on the 18th cycle day, 250 μg of hCG was administered and 35.5 h afterward, two M-II ova were retrieved by vaginal follicular aspiration. The ova have undergone intracytoplasmic sperm injection and fertilization was documented after 20 h, and two embryos were cryopreserved on the 2nd day. This unusual case suggests that premature exposure to supraphysiologic concentrations of hCG and progesterone, may not interfere with normal folliculogenesis, oocyte maturation, and IVF.

CONCLUSIONS

The implication of all the presented.

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Conflicts of interest

There are no conflicts of interest.

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