

A 51-MONTH FOLLOW-UP OF FRESH AUTOLOGOUS HEMI-OVARY TRANSPLANTATION AT THE PFANNENSTIEL INCISION SITE AFTER HYSTERECTOMY AND ACCIDENTAL BILATERAL SALPINGO-OOPHORECTOMY IN A PREMENOPAUSAL WOMAN

Chang-Sheng Yin*, Kuei-Chen Huang, Hsiao-Ming Chiu

Department of Obstetrics and Gynecology, Kong-Ning General Hospital, Taipei, Taiwan.

SUMMARY

Objective: This case report evaluates a 51-month follow-up of the hormonal profiles and the menopausal status after fresh autologous hemi-ovary transplantation to the Pfannenstiel incision site in a woman aged 32 years after a total hysterectomy and accidental bilateral salpingo-oophorectomy.

Case Report: A 32-year-old, unmarried woman without sexual experience had undergone a total hysterectomy and accidental bilateral salpingo-oophorectomy for huge uterine fibroids and dense pelvic adhesion. A fresh autologous right normal hemi-ovary was transplanted into the adipose tissue on the right side of the Pfannenstiel incision site. During the 51-month follow-up after transplantation, a series of hormonal profiles for serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and progesterone were carried out, together with ultrasound detection of the presence of subcutaneous follicles and an analysis of menopausal symptoms. Postoperative hormone levels at months 14, 18, 22, 30 and 51 were as follows: (1) FSH, 17.06, 11.33, 51.44, 28.6 and 61.41 mIU/mL, respectively; (2) LH, 15.1, 6.7, 20.1, 15.7 and 28.9 mIU/mL, respectively; (3) E2, 79.7, 128, 55.9, 18.6 and <10 pg/mL, respectively; and (4) progesterone, 4.52, 9.51, 0.67, 0.45 and 0.25 ng/mL, respectively. The hormonal levels after month 22 indicated a menopausal status. Ultrasound evidence of follicles was present until 30 months after transplantation.

Conclusion: This case study showed a subcutaneous fresh autologous hemi-ovary transplant survived for at least 18 months after transplantation. [*Taiwan J Obstet Gynecol* 2009;48(1):69–71]

Key Words: autologous hemi-ovary, Pfannenstiel incision site, premature menopause, transplantation

Introduction

Premature menopause may be induced by the surgical removal of both ovaries owing to malignant or benign disease, and by chemotherapy and radiotherapy treatments for cancer [1]. Subcutaneous ovarian

transplantation is a promising approach which has the aim of preventing fertility loss and restoring hormone secretion in these patients. Early successful reports of heterotopic ovarian tissue transplantation, both fresh and cryopreserved, to the forearm and abdominal wall, have shown that the longest surviving graft was functional for at least 2 years after transplantation [2–5]. In this report, we present a 51-month follow-up of a woman aged 32 years who underwent a hysterectomy and accidental bilateral salpingo-oophorectomy for huge myomas whose normal right hemi-ovary was immediately transplanted into the adipose tissue at the Pfannenstiel incision site.



*Correspondence to: Dr Chang-Sheng Yin, Department of Obstetrics and Gynecology, Kong-Ning General Hospital, No. 26, Lane 420, Section 5, Cheng-Kung Road, Taipei 114, Taiwan.
E-mail: khivf@mail.knh.org.tw
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Case Report

A 32-year-old, unmarried woman without sexual experience and with a huge multiple uterine myoma was scheduled for a hysterectomy in May 2003. The operation was performed under spinal anesthesia with a low abdominal Pfannenstiel incision. During the operation, the huge size of the uterus resulted in a distortion of the pelvic structures. Unfortunately, both ovarian vessels were injured during the dissection; therefore, a hysterectomy plus a bilateral salpingo-oophorectomy were required to safely remove the tumor. The unexpected removal of both normal ovaries resulted in a suggestion to the patient of a fresh autologous ovarian transplantation in order to maintain her hormone levels. After counseling the patient and her family, an immediate written informed consent was obtained from her mother. We then selected the morphologically normal right hemi-ovary to be the graft. After thoroughly washing the ovary with saline solution, the graft was implanted into the right side subcutaneous tissue of the Pfannenstiel incision site. The early postoperative course was uneventful.

The patient was absent from follow-up examinations until 14 months after the transplant. At that time, a physical examination revealed a palpable lump at the transplant site. An ultrasound examination showed a 2.21×1.70 cm follicle (Figure). The hormonal profiles for follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and progesterone were evaluated at months 14, 18, 22, 30 and 51 and were as follows: (1) FSH, 17.06, 11.33, 51.44, 28.6 and 61.41 mIU/mL, respectively; (2) LH, 15.1, 6.7, 20.1, 15.7 and 28.9 mIU/mL, respectively; (3) E2, 79.7, 128, 55.9, 18.6 and < 10 pg/mL, respectively; and (4) progesterone, 4.52, 9.51, 0.67, 0.45 and 0.25 ng/mL, respectively. A slightly elevated level of FSH, but normal ranges of LH, E2 and progesterone were observed at months 14 and 18. The hormonal profiles at 22 months showed

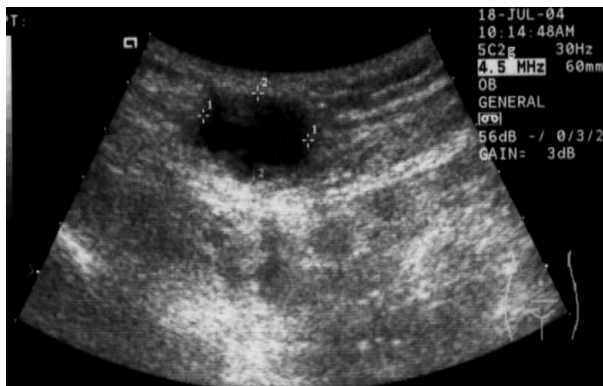


Figure. A subcutaneous follicle 2.21×1.70 cm present at 14 months following transplantation.

a menopausal state. The ultrasound evidence of a follicle was present until 30 months after transplantation. At 51 months after the transplantation, the patient denied having any menopausal symptoms.

Discussion

During the 51-month follow-up, we observed that the fresh autologous hemi-ovary transplanted into the Pfannenstiel incision site after accidental bilateral salpingo-oophorectomy in a woman aged 32 years was functioning hormonally for at least 18 months following the transplant. Leporrier et al [2] first reported heterotopic ovarian transplantation in a Hodgkin's patient. The patient's left ovary was transplanted to the subcutaneous tissue of the arm with vessel anastomosis. One year after the procedure, a postmature oocyte was aspirated. Accidental subcutaneous transplantation of normal ovarian tissue in the umbilical area during laparoscopic surgery has also been reported by Marconi et al [3]. Oktay et al [4] reported transplantation of fresh ovarian tissue into the forearm in two patients. The grafts survived for 18 months and 10 months after transplantation. Kiran et al [5] reported a similar case to ours in which they used fresh ovarian cortical strips and transplanted them into a 44-year-old woman. This graft still survived at the 6-month follow-up. Previous studies have confirmed that ovarian tissue grafts, either fresh or cryopreserved, with or without vascular anastomosis, can form functional tissue in a heterotopic site in women. Usually, 3 or 4 months are needed before graft activity is detected [2-5].

The key factor in ovarian autograft survival is rapid revascularization, which is influenced by the following angiogenic factors: basic fibroblast growth factor, transforming growth factor, and the levels of gonadotropins and ovarian steroids [6]. Several methods have been proposed by Oktay et al [4] to enhance the survival of grafts, and include subcuticular skin sutures with a non-pressure dressing, 75 IU/day of FSH directly injected into the subcutaneous tissue above the grafts, and 80 mg/day of oral aspirin for 7 days. They also recommended transdermal estradiol 0.1 mg within 48 hours after transplantation. Careful handling of grafts is also important; Nugent et al [7] administered an antioxidant, vitamin E, with the aim of improving the survival of the follicles and to reduce ischemic damage by reactive oxygen species. Salle et al [8], in 2003, reported a 2-year functionality of hemi-ovary autografts in ewes. They also emphasized that revascularization is the crucial step in graft survival.

Our patient had relatively elevated FSH levels but normal E2 and progesterone levels within 18 months after the transplant. Callejo et al [9] also observed an elevated FSH level after recovery of the secretion of E2 at 28 days in female syngeneic Lewis rats with heterotopically transplanted nonvascularized ovarian grafts. They proposed that ischemia in the nonvascularized ovarian grafts may bring about an inhibin deficit in the stroma that results in the increased levels of FSH and hyperplasia of granulosa cells.

Although the effect of estrogen on women's health has been debated in recent years, early observational studies and the report by Rocca et al [10] in 2008 have shown that women who have had their ovaries removed at a young age are at an increased risk of cognitive decline. It is not uncommon for a gynecologist to encounter a young woman with benign pelvic disease that may require removal or destruction of the ovarian tissue; this will lead to early menopause and a loss of fertility. For young surgically castrated women reluctant to receive hormone therapy, autologous ovarian transplantation may be one alternative. From this case report and others, the longevity of ovarian grafts is uncertain. Thus, sequential transplantations of cryopreserved grafts have been suggested for these women in the future. The principal obstacle to the success of transplantation is poor oocyte viability, which is affected by the cryopreservation method used and ischemic damage. Therefore, the excision of an intact ovary with its vascular pedicle for cryopreservation has been proposed. Vascular reanastomosis can then be carried out at a later date [11]. In some women, oocyte donation at a later time may still be an option. Other research that may play a role in the future includes research on nuclear or cytoplasmic transfer [12] and that looking at a process involving deriving oocytes from embryonic stem cells [13]. Case studies have a number of methodologic constraints; while they often provide a first insight into a specific phenomenon, further research is obviously needed in this area.

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