Two Ovarian Transplants Result in Normal Births

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Two recent births that were made possible by maternal ovarian transplants procedures were achieved with markedly different techniques and approaches.

U.S. expert Sherman Silber, M.D., of St. Luke’s Hospital, St. Louis, performed an ovarian allotransplant between 24-year-old identical twins, one of whom had premature ovarian failure. The procedure reversed the patient’s fertility and her ability to conceive normally (N. Engl. J. Med. 2005;353:58–63).

In Israel, the transplant performed by Dror Meirov, M.D., of Chaim Sheba Medical Center in Tel Hashomer, and colleagues was an autotransplant of a 28-year-old cancer patient’s previously frozen healthy ovarian tissue. Conception was achieved through in vitro fertilization (N. Engl. J. Med. 2005;353:318–21).

In the U.S. patient—a woman who had experienced premature ovarian failure at age 14—laparoscopic examination revealed no evidence of ovarian tissue. She underwent autotransplantation with atrophic, elongated (“streak”) gonads with no follicles and a small uterus with an otherwise normal reproductive tract. Her donor sister had three children who had been conceived naturally, and she had been using oral contraception in the year preceding the procedure.

The donor’s ovary was laparoscopically removed and the cortical tissue dissected ex vivo. Meanwhile, the recipient underwent a minilaparotomy during which the cortex of each streak ovary was resected, exposing the raw surface of the medulla.

Hemostasis was meticulously controlled with the use of pinpoint microcliporial forceps and continuous irrigation with heparin-treated saline to prevent the formation of a hematoma under the graft. The amount of cautery was also minimized to avoid impairing revascularization.

One-third of the donor ovary was sutured to each ovary of the recipient twin in the U.S. case. One-third of the donor twin’s ovary was sutured to the left ovary, and small fragments were injected into the right ovary. Menstruation resumed spontaneously 8 months later, and baseline levels of antimüllerian hormone, which were previously undetectable (consistent with ovarian failure), were high—consistent with the presence of active follicles in an early stage of growth.

This was followed by a rise in inhibin B to levels reported in ovulatory women. At this time, ultrasonography revealed a pre-ovulatory follicle in the left ovary, and small fragments were injected into the right ovary. Menstruation resumed spontaneously 8 months later, and baseline levels of antimüllerian hormone, which were previously undetectable (consistent with ovarian failure), were high—consistent with the presence of active follicles in an early stage of growth.

The Israeli transplant patient had experienced ovarian failure after high-dose chemotherapy for non-Hodgkin’s lymphoma. Ovarian tissue containing many primordial follicles was harvested and frozen before she underwent high-dose chemotherapy but after she had undergone a second-line conventional chemotherapy regimen.

The patient remained free of disease 24 months after undergoing chemotherapy, at which point she requested autotransplantation of the thawed ovarian tissue. Strips of the tissue were transplanted to the left ovary, and small fragments were injected into the right ovary. Menstruation resumed spontaneously 8 months later, and baseline levels of antimüllerian hormone, which were previously undetectable (consistent with ovarian failure), were high—consistent with the presence of active follicles in an early stage of growth.

The time from transplantation to recovery was compatible with the time needed for the growth and maturation of primordial follicles.” Dr. Meirov and colleagues wrote. The next month, another spontaneous menstrual period occurred, after which modified natural cycle in vitro fertilization was performed. A single egg was retrieved and fertilized, and a four-cell embryo was transferred to the uterus. A healthy infant was delivered by cesarean section at 38 weeks’ gestation.}

Drugs, Pregnancy, and Lactation

Antihyperlipidemic Agents

The large antihyperlipidemic class of drugs can be subdivided into three subgroups: HMG-CoA reductase inhibitors, fibric acid derivatives, ezetimibe, and niacin. With the possible exception of familial hypercholesterolemia, there appears to be no maternal benefit for the treatment of hyperlipidemia during gestation.

Nearly all reported pregnancy exposures have occurred accidentally. If treatment is required, only bile acid sequestrants are considered compatible in pregnancy and lactation.

Ezetimibe (Zetia) also appears to be low risk in gestation, but not in lactation. Because most drug-induced adverse effects (about two-thirds) in nursing infants have been reported during the first month after birth, delaying treatment of a nursing mother until after this period appears to be the best course.

Cholesterol is the precursor of bile acids that are excreted from the liver and gallbladder into the intestine to aid in the digestion of fat in food. Bile acid sequestrants—cholestyramine (Questran and other generic names), colestipol (Colestid), and colesevelam (WelChol)—are anion exchange resins that form insoluble complexes with bile acids in the intestine. The complexes are then excreted in the feces, removing cholesterol from the system.

Cholestryramine has been used as a treatment for intrahepatic cholestasis of pregnancy (both are risk factor C). Although there are no data, the drugs are probably excreted into milk, and women on these agents should not breast-feed because of the potential toxicity, such as tumors, in their infants. Ezetimibe (risk factor C) selectively inhibits the intestinal absorption of cholesterol and related phytosterols. At doses up to 10 times the human dose, the drug is teratogenic in rats but not in rabbits. Human pregnancy exposures have not been reported. If therapy during pregnancy is mandated, ezetimibe appears to be a better choice than statins. There are no data on use during lactation, but the drug is probably excreted into milk. Toxicity is a potential concern, and nursing infants should be monitored for jaundice, diarrhea, rash, pruritus, and other adverse effects observed in adults.

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