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ROLLINS COLLEGE

A Source of Human Ovarian Cortical Tissue from Sex Assignment Surgery

BIO 115 Term Paper

Quynh Nguyen

Thesis

Cryopreservation of ovarian cortical tissue is an innovative method for the preservation of primordial follicles for the purpose of restoring fertility. This technique was developed for young female cancer patients enduring chemotherapy. However, there is a limited source of donors, which confines the research on follicular growth after grafting. Research shows that young female-to-male transsexuals, having been on androgen therapy for prolonged periods of time, can be potential donors. This paper explores transsexuality and the options available for making the transition to the opposite gender. Then it will examine the process and effects of patients on androgen therapy and the effects it may or may not have on the primordial follicle pool. Finally, a thorough examination will look at the possibility of using ovaries from those undergoing sex-reversal operations as a source of tissue for research and possible oocyte donation in the future.

What is transsexuality?

Transsexualism is viewed as an extreme form of gender dysphoria, where individuals feel that they belong to the gender opposite to their own gender. A distinction should be made between gender, which is formed by society, and sex, a person's biological make up. Transsexualism was previously thought of as a mental disorder but the diagnosis was then removed from the Diagnostic and Statistical Manual of Mental Disorders and replaced by the term 'gender identity disorder' (Sutter, 2001). To reach the desired gender, transsexual people are treated by advanced hormonal and surgical therapy. Both possibilities take place after psychiatric evaluation, and surgery is only performed after the individual has successfully lived a specified amount of time in the desired gender role. The aim of cross-gender hormone therapy is an adjustment to the opposite sex via secondary sex characteristics. Specific hormones are administered in decreasing doses in consecutive time intervals. When secondary sex characteristics have fully developed, the high-dose regime is switched to a lifelong low-dose procedure.

Endocrine Therapy

Male to Female

An important component in treating transsexual people is cross-sex endocrine regimes. Feminizing endocrine treatment regimes of male to female transsexual people include various forms of estrogen, progestin and/or antiandrogens. Estrogen is crucial for feminizing M→F people. The typical dosage is two to three times higher than that of hormone replacement therapy in postmenopausal women. Antiandrogens are used to lower serum levels of testosterone or completely block its binding to the androgen receptor. This decreases masculine secondary sexual characteristics. Progesterone boost breast growth and decrease irritability and breast sensitivity. The risk of combining estrogen and progesterone includes increase risk of coronary heart disease, stroke and pulmonary embolism. Some studies report a decrease in hemoglobin in estrogen treated M→F transsexuals. In some cases, depression is increased in comparison to the general population. The risk is correlated to the dose and is similar to the side effects/risk in contraceptives.

Female to Male

Testosterone is the key hormone in F→M masculinizing endocrine treatment. This hormone is used for the development of secondary sexual characteristics and is given via injections. Oral testosterone is only available outside of the United States and contains lower serum testosterone levels. Typical testosterone doses range from 150-400 mg per month (Moore, 2003). Menstruation may not be sufficiently suppressed without the addition of progestin. GH-releasing hormone agonists are used in adolescent transsexual people to suspend puberty. This allows “cross-sex hormones to be postponed until adulthood” and creates “less psychological stress for the individual” (Moore, 2003). Menstruation is usually eliminated within several months. When evaluating the risks associated with androgen administration, it is important to consider that there have been limited studies conducted due to the small population of test subjects. From all the studies done, there were no reports of mortality. For patients with

extremely high levels of testosterone, there have been cases of cerebral vascular accidents in addition to weight gain, “decreased insulin sensitivity, poor lipid profile and an increase in hematocrit” raising concerns for cardiac issues (Moore, 2003). Testosterone treatment induces an increase of hemoglobin compared to the levels in biological men (Schlatterer, 2004). For both M→F and F→M transitions, “endocrinopathies and psychiatric problems are the most frequent disorders, followed by disease affecting the cardiovascular system, dermatological disorders, and chronic infectious diseases” (Schlatterer, 2004).

Sex Reassignment Surgery

Hysterectomy and Oophorectomy

In addition to hormonal therapy, transsexuals seeking a complete transition to the opposite sex will have sex reassignment surgery (also known as genital reconstruction surgery, sex affirmation surgery or sex-change operation). There are three processes for F→M transsexuals: hysterectomy, oophorectomy and metoidioplasty. Hysterectomy is the removal of the whole or part of the uterus and oophorectomy is the removal of the ovaries. There are several types of hysterectomy: (1) partial or supracervical in which only the upper part of the uterus is removed and the cervix is left in place (2) total removal of the uterus and cervix (3) radical which removes the whole uterus, the tissue on both sides of the cervix and the upper part of the vagina. This last option is done when cancer present. After a hysterectomy, menstruation ceases and patients are unable to become pregnant. The surgery requires a 5 to 7 inch incision in the lower part of the stomach or a cut in the vagina through which the uterus is taken out. Laparoscopic hysterectomy is an advanced version in which a thin, lighted tube and small camera is inserted into the belly's incision. The uterus is cut into smaller pieces and removed through the incision. Risks of having a hysterectomy include damage to close by organs (bowel, urinary tract, bladder, rectum, or blood vessels), pain during sexual intercourse, premature menopause (if the ovaries are removed) and anesthesia problems (breathing or heart problems).

Metoidioplasty

Metoidioplasty requires testosterone treatment to stimulate clitoris growth. After substantial augmentation of the clitoris, a surgical procedure constructs the new penis. Surgeons form an undersized phallus from the elongated clitoris by “cutting the ligament that holds the clitoris in place under the pubic bone as well as cutting away some of the surrounding tissue” (Perovic, 2003). The surgery may also involve scrotoplasty, which is the creation of a scrotum by “insertion of testicular implants inside the labia majora and then joining the two labia to create the scrotal sac” (Perovic, 2003). The procedure involves pain and discomfort, requires a significant amount of time for recovery and may leave large sections of visible scarring. Due to the temperament of the skin grafts, there is always a risk of tissue death. Potential complications include the extrusion of testicular or penile implants, the formation of a stricture (an abnormal narrowing; blockage) or fistula (an abnormal connection; leakage) in the urethral passage. In some cases there is damage to the nerves resulting in numbness or loss of function (Perovic, 2003).

Effects on Reproduction

All hormonal and surgical treatment options permanently remove the ability to reproduce in transsexual people. More and more people are diagnosed with transsexuality early in their life when they do not want children. Recently developed reproductive techniques make it possible for germ cells to be preserved for future use. In theory, transsexual people can use these germ cells after their transition. For male to female transsexual patients, sperm preservation occurs by freezing a substantial amount of sperm samples before starting hormone therapy. Feminizing hormonal therapy will induce hypspermatogenesis in transsexual women that leads to azoospermia. Irrevocable sterility will occur after a lengthened period of hormone therapy and the addition of gender reassignment surgery (the removal of the testes). For transsexual men (female to male transsexual patient), masculinizing hormonal therapy leads to irreversible amenorrhea. Ovarian follicles will remain in place unless castration occurs, at which point there will be irreparable ovarian failure. To allow for future procreation, oocyte and embryo banking are

viable options. Oocyte banking entails hormonal stimulation, oocyte retrieval and subsequent freezing of the oocytes. Studies have shown that developed oocytes are very vulnerable to chromosomal damage throughout the freezing and thawing process. Embryo banking requires hormonal stimulation, oocyte retrieval, spermatozoa from a male donor and subsequent freezing of the embryos.

Cortical Ovarian Tissue

New treatments increase the success rate of healing many young patients with cancer. But the aggressive treatments come with the cost of losing ovarian function and fertility. With the improved rate for long-term survival of young women with malignancies undergoing chemotherapy, the preservation of future fertility is pulling in great interest. Chemotherapy uses antimetabolites, specifically the administration of doxyruicine, mitoxantrone or platinum that induces ovarian failure. High-dose chemotherapy and total body irradiation induces menopause in about 92% of all patients (Fabbri, 2006). Cryopreservation of ovarian cortical tissue allows for the preservation of primordial follicles, which can be used to restore fertility in young female cancer patients after chemotherapy. Young patients have the option of preserving their ovarian tissue before chemotherapy but there are several important points to address before preservation is done. A patient's age is an influential factor since ovarian tissues gathered after 38 years of age have a lower follicular population. Loss of early follicles is strictly related to patient's age and follicular depletion is accelerated around 37 to 38 years (Fabbri, 2006). It is also known that "follicles are not homogeneously distributed within the ovarian cortex" (Fabbri, 2006). Therefore, it is recommended that a full ovary be removed. The quantity of tissue to cryopreserve is related to how chemotherapy influences the ovarian function. To reach optimal results, "healthy fresh ovarian tissue should be collected before anticancer treatment" (Fabbri, 2006). Therefore, young F→M transsexual patient are excellent potential voluntary donors of ovarian cortical tissue. Studies show that follicular growth can be obtained in ovarian cortical grafts from transsexual donors who have been on androgen therapy because primordial follicles can recommence early growth after the hormonal treatment period.

Cryopreservation and Grafting

To obtain ovarian tissue, the ovaries are bisected immediately after removal during reassignment surgery. “The medulla is removed and the cortex is scraped until all the medullary fragments are removed and only a 1 mm thick cortical slice remains. Fragments of the ovarian cortex are preserved in phosphate-buffered formaldehyde” (Soleimani, 2006). Grafting is done by making an incision in the dorsal region and dissecting the skin free from the underlying muscles. The thawed ovarian cortical grafts are inserted deep in the subcutaneous space. To recover the graft, the dorsal skin is re-opened; the grafts are “dissected from the surrounding tissues and immediately placed in phosphate-buffered formaldehyde” (Soleimani, 2006).

Source of primordial follicles

Studies have shown in individuals who have received androgens, there was no “increased activation or depletion of primordial follicles” (Soleimani, 2006). The patients’ ovaries contained similar amounts of primordial and primary follicles and women who have not received androgens. In all experiments conducted, results showed that there are no negative effects on the capability of ovarian follicles to resume growth from patients undergoing androgen therapy. All conclusive results support F→M transsexuals as a source of follicles for experimental use and donor oocytes in the future (Broecke, 2001).

Rising Issues

While the ability to locate a new resource of donations for research provides tremendous amounts of benefits for young female cancer survivors and the science community, there are oppositions regarding the source of the donation. There is a debate regarding the rights of ‘trannies’ to be legally recognized for their gender orientation and ‘moral conflicts’ of sex reassignment surgery. To some, the ability to change the nature of human beings with regards to the primary sexual organs is viewed as playing the power of God. We are fundamentally different because of our biological sex mechanisms and these features make us distinctly human. Many activists against transsexuals wonder where humanity will go if reassignment

surgery becomes the new phenomenon. These groups argue that the use of transsexual people's tissues for donation will only promote the growth of the transsexual community and provide an 'incentive' for changing what humans were destined to have. On a scientific standpoint, some opponents argue that increasing numbers of transsexuals will create an unbalance population because of reproduction limitations.

On the other hand, human rights activist groups are fighting for equal rights given to people of all nature, disregarding their sexual orientation or self-identification. Several scientists and surgeons from the studies used in this paper point out the greater strides made in follicular tissue research due to the new source of donors. All studies point out that recipients of the donations were informed about their donors and gave their consent before any further steps were taken. In this regard, some people argue that if there is agreement and safety in the procedure, there should not be an issue with transsexuals being a donor of primordial follicles.

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