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선천성 질결여증 여성에서 신생질을 통한 난자채취에 의한 성공적인 대리모임신 1예

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=ABSTRACT=

A Successful Uterine Surrogate Pregnancy Via Oocyte Retrieval Through the Neovagina in a Patient with Mayer-Rokitansky-Küster-Hauser Syndrome

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Congenital absence of vagina (Mayer-Rokitansky-Küster-Hauser Syndrome) is the second most common etiology of primary amenorrhea and also cause of primary infertility. Management for these women comprise of construction of neovagina for sexual life and screening for associated congenital anomalies and planning of getting her own genetic offspring. As associated assisted reproductive technologies involving in vitro fertilization and embryos transfer to surrogate mother become realizing, it is being possible for these women to have new opportunity of getting her own genetic baby. In most cases, oocyte retrieval for uterine surrogate program have been performed laparoscopically because of difficulty of oocyte retrieval via neovagina.

But we have experienced a case of successful surrogate pregnancy via oocyte retrieval through the neovagina in a patient with congenital absence of vagina, so report it after following observation of the babies for 3 years.

Key Words : Mayer-Rokitansky-Küster-Hauser Syndrome, Neovaginoplasty, IVF-ET, Surrogate pregnancy

Until recently, management of Congenital absence of vagina (Mayer-Rokitansky-Küster-Hauser Syndrome) have centered on creation of a functional vagina for adequate coital function and screening of associated congenital anomalies. As assisted reproductive technologies has been developed, women with these pathologic condition are able to reproduce her own genetic offspring. Although ovulation induction in uterine surrogate program is similar to any other IVF program, oocyte retrieval through the neovagina is not easy, sometimes impossible because of high lateral placement of ovaries and shortened, thickened vagina.

But we have experienced a case of successful surrogate pregnancy via oocyte retrieval through the neovagina in patient with congenital absence of vagina, so report it after following observation of the babies for 3 years.

CASE

Patient : ○○, Kim, 26 years old woman

Chief Complaint : To have her own genetic baby

Obstetrical History : 0-0-0-0

Menstrual History : Primary amenorrhea due to Mayer- Rokitansky-Küster-Hauser syndrome

Family History : Unremarkable

Past History : At age 19 years old, she had been transferred to our hospital from private OB & GY clinic for evaluation of primary amenorrhea, and diagnosed as Mayer-

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Rokitansky-Küster-Hauser syndrome, ie, normal female karyotype and phenotype with vaginal aplasia, rudimentary cornua uteri, and morphologically normal fallopian tubes and ovaries sited on the pelvic side wall.

We had decided to perform the Abbe-Wharton-McIndoe operation for creating the neovagina : (a) dissection of the adequate space between the rectum and bladder, (b) inlay human amnion to line the new vaginal space, obtained from very recently delivered placenta from full term primiparous woman who had been screened for hepatitis B and C, sexually transmitted disease, HIV infection, (c) continuous and prolonged dilation of neovagina during the contractile phase of healing. On regular follow up examination, neovaginal cavity was intact and 6 cm in length, she reported us satisfactory sexual intercourse.

Procedures of uterine surrogate program : Seven years after Abbe-Wharton-McIndoe operation for creating the neovagina, she married and wanted to have her own genetic baby in 26 years old. She had normal ovarian cycles demonstrated by ultrasonic assessment and hormonal profile, ie, normal levels of lutenizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, prolactin, thyroid-stimulating hormone (TSH), testosterone, dehydroepiandrosterone sulfate (DHEAS). Semen analysis of her husband showed normal results, and her sister-in-law, 32 years old married woman having two children agreed to be surrogate mother. Preliminary study was done in potential surrogate mother including hysterosalpingography and baseline hormone study (LH, FSH, estradiol, TSH, prolactin, DHEAS) and laboratory tests for hepatitis B and C, sexually transmitted disease, HIV infection for evaluation of adequacy as uterine surrogate. Hysterosalpingography showed normal uterine cavity and patent fallopian tubes, results of baseline hormone study was within normal limit and the screening test of hepatitis B and C, sexually transmitted disease, HIV infection were negative.

Informed consent form was signed by the woman with Mayer-Rokitansky-Küster-Hauser syndrome and her husband, and by the surrogate woman and her husband. Pituitary down regulation started with GnRH agonist (Goserelin, Zoladex®, 3.6 mg, Astra Zeneca) simultaneously for shut down of ovulatory cycle and synchronization in donor and recipient. After 3 consecutive subcutaneous injection of 3.6 mg, Zoladex® monthly, hormonal medication was started for endometrial preparation in potential surrogate mother, ie, oral estradiol valerate was administrated as following method, 1 mg for 5 days, 2 mg for 4 days, 6 mg for 4 days, 2 mg for 4 days, then continuously 4 mg till pregnancy test. Progesterone in oil was injected from oocyte retrieval day, 25 mg for 2 days, then 50 mg till pregnancy test. After confirmation of elevated β-hCG on embryo transfer 14 days, oral estradiol valerate 4 mg and progesterone 50 mg was continuously medicated till pregnancy 12 weeks. After 3 consecutive subcutaneous injection of 3.6 mg, Zoladex® monthly, controlled ovarian hyperstimulation was performed in the woman with Mayer-Rokitansky-Küster-Hauser syndrome with pure FSH and hMG (Metrodin® and Pergonal®, Serono), we used Metrodin® 6 vials and Pergonal® 36 vials for 12 days. The woman's ovaries with Mayer-Rokitansky-Küster-Hauser syndrome were accessible by the neovagina, so we decided to monitor the follicle growth and retrieve the oocyte by transvaginal ultrasound-guided technique. Follicle growth was monitored 3 days interval from gonadotropin day 5. On reaching the follicular size 18 mm more in diameter, human chorionic gonadotropin (Profasi®, Serono) 10,000 IU was injected, 35 hours later, oocyte aspiration was performed. Twenty seven mature oocytes were retrieved and inseminated with her husband's prepared spermatozoa. Of developed 22 embryos, 5 high graded 4-cell embryos were transfered to the sister-in-law's uterus. Measurement of β-hCG was performed 14 days after embryo transfer, the result revealed 1623.2 mIU/ml. Subsequently 2 viable fetuses and one fetal demise were identified at 5 weeks from the embryos transfer.

Then the surrogate mother received routine obstetrical care and was diagnosed as pregnancy induced hypertension and gestational diabetes at 24 weeks of gestation. During the close observation and management, she delivered prematurely at 28 weeks and first day. The twin babies were male and male, 1,150 gm and 1,150 gm, the Apgar score were 5/4 at 1 minute, 6/5 at 5 minutes. The premature twin babies were managed in neonatal intensive care unit, thereafter discharged. They are 3 year-old now and healthy without any handicap.

DISCUSSION

Mayer-Rokitansky-Küster-Hauser syndrome (M-R-K-H syndrome) is characterized by absence of apparent vagina and/or uterus, normal secondary sexual characteristics, normal reproductive hormonal profile, and a relatively common cause of primary amenorrhea (about 1 in 4,000

female births), more frequent than complete androgen insensitivity syndrome and second only to gonadal dysgenesis. Two important associated abnormalities, urinary tract abnormalities and skeletal anomalies, are identified in approximately one-thirds and 12% or more of these patients. Almost all patients have a 46,XX normal female karyotype, only a few chromosomal abnormalities have been reported in patients with congenital absence of the uterus and vagina.[1] The recent study suggests congenital absence of the uterus and vagina is not inherited commonly in a dominant fashion and it is likely a polygenic, multifactorial or possibly a recessive trait.[2]

Until recently, treatment for patient with M-R-K-H syndrome has centered on the creation of a functional neovagina to provide for adequate coital function. The non-surgical Frank technique, McIndoe's vaginoneoplasty using split-thickness skin graft and Ingram bicycle seat technique can be used and overall success rate is approximately 95% for these procedures.[3,4]

In 1985, the first report of a successful pregnancy through the uterine surrogacy was made.[5] Slowly afterwards, IVF-surrogacy have been tried for couples who would be unable to produce a genetic child because of absence of functioning uterus, life threatening medical risk associated with pregnancy, or due to multiple failed attempts at conception with standard treatment options.[6-8]

Since ovarian activity is completely preserved in patients with M-R-K-H syndrome, controlled ovarian hyperstimulation is similar to any other IVF case that is with urinary or recombinant gonadotropins following GnRH agonist down regulation. But the lack of menstruation due to absence of uterus precludes the identification of menstrual day. Ben-Rafael et al. suggested pituitary down-regulation with GnRH agonist once ovulation is determined by progesterone concentration >6 nmol/L through weekly measurement of progesterone plasma concentration.[9]

IVF-surrogacy delivery rate per embryo transfer reported by the ASRM/SART in the U.S. and Canada was 37.1%.[10] And patients with congenital absence of the uterus responded to ovulation induction better than patients who underwent a hysterectomy and overall pregnancy rate per cycle after IVF-surrogacy was 24%, with a live birth rate of 15.8%.[11]

The perinatal outcome of pregnancies established after IVF-surrogacy is better than after standard IVF program. The incidence of low birth weight infants is lower in the IVF-surrogacy than in the standard IVF program, and the occurrence of the pregnancy induced hypertension and bleeding in the third trimester (placenta previa, placental abruption) was four to five times lower in the IVF-surrogates, independently of whether they were carrying multiples.[12] But it was not true in our case.

While the neovagina could provide the adequate coital function, such an artificial vagina may not allow the usual vaginal elasticity and relaxation. In addition, it tend to be fibrotic and far remoted from the position of the ovaries. The high lateral placement of the ovaries in these patients makes transvaginal ultrasound guided oocyte retrieval uncomfortable, difficult, or impossible, so laparoscopic retrieval may be the route of choice for adequate oocyte harvesting in the majority of these patients.

In this case, we were able to retrieve the oocyte under the transvaginal ultrasound guidance through the neovagina created by Abbe-Wharton-McIndoe operation without difficulty and experienced successful IVF-surrogate pregnancy.

We hope this procedure offers the possibility of acquiring their own genetic children, not only to women with congenital absence of the uterus and vagina but also to hysterectomized women and women with other indications.

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=국문초록=

뮬러관형성부전증은 원발성 무월경의 원인 질환 중 비교적 흔한 경우로 그 빈도는 4,000 여아 출생 당 1명 정도로 보고된다. 이러한 환자의 해부학적 특성은 맹관 형태의 질을 보이고 자궁은 없거나 흔적 기관만 존재하나, 정상 난소를 가지며 정상 여성의 표현형과 핵형을 갖는다. 이러한 환자에서의 최근까지의 치료는 정상 성교가 가능한 기능적인 질을 만들어 주는 것에 촛점이 맞추어졌으나, 1985년 대리모를 통한 임신이 보고된 이후 뮬러관형성부전증 환자도 체외수정술을 통한 대리모임신을 이용하여 자신의 유전적인 자녀를 가지는 것이 가능해졌다. 뮬러관형성부전증 환자의 배란유도시 난소의 반응은 정상 여성과 유사하나 월경을 확인할 수 없으므로 성선자극호르몬 유리호르몬 효능제를 장기간 투여하여 완전한 뇌하수체 탈감작이 일어난 후에 과배란유도를 시작하든지, 매주 황체호르몬을 측정하여 배란을 확인한 후 황체기 중기 장기요법을 통한 과배란유도 방법을 이용하는 것이 일반적 방법이다. 난자채취는 난소가 외측으로 편위되거나 신생질이 짧고 섬유화로 비후된 경우가 많아 질을 통한 채취가 어려운 경우가 많아 복강경을 통한 난자채취가 일반적인 방법으로 알려져 있다.

저자들은 19세에 뮬러관 형성부전증으로 진단 받고 질형성술을 시행한 7년 후 신생질을 통한 난자채취에 의한 체외수정술과 대리모에 의한 성공적인 쌍태임신과 생존아의 분만을 경험하여 문헌 고찰과 함께 보고하고자 한다.

중심단어 : 뮬러관 형성부전증, 질형성술, 체외수정, 대리모임신