CASE REPORT

Successful pregnancy by transmyometrial and transtubal embryo transfer after IVF in a patient with congenital cervical atresia who underwent uterovaginal canalization during Caesarean section

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Successful pregnancy in a patient with congenital cervical atresia is a great challenge for assisted reproductive techniques and reproductive medicine. We report a case of successful pregnancy by transmyometrial and transtubal embryo transfer simultaneously after in-vitro fertilization (IVF) in a 33 year-old patient with congenital cervical atresia diagnosed at the age of 18 years. The patient had experienced cyclic abdominal pain and amenorrhoea since she was 13 years old. She had had two unsuccessful attempts to create a new uterovaginal canal in another hospital. At the age of 32 years, she was referred to our unit and had a successful pregnancy after transmyometrial and transtubal embryo transfer. Caesarean section was performed at 36 weeks gestation due to progressive pre-eclampsia and gestational diabetes. A healthy male baby weighing 2812 g was safely delivered. Uterovaginal canalization with amniotic membrane for the covering of the neo-endocervical wall was performed during Caesarean section. Normal menstrual outflow and symptomatic relief have continued for 5 months after the operation. To the best of our knowledge, this is the first reported case of successful pregnancy by transmyometrial and transtubal embryo transfer as well as uterovaginal canalization performed during Caesarean section in a patient with congenital cervical atresia.

Key words: cervix/congenital cervical atresia/embryo transfer/IVF/uterovaginal canalization

Introduction

Congenital cervical atresia is a rare anomaly caused by abnormal development of the Müllerian system (Faber and Marchant, 1975). Why the cervix alone would undergo atresia remains unknown. Primary amenorrhoea and cyclic abdominal pain related to haematometra and retrograde menstruation are the most common clinical presentations, usually occurring after menarche. Subsequently, endometriosis usually develops. The aims of treatment in this condition are mainly to relieve the symptoms, and to restore fertility and regular menstruation (Rock et al., 1984). Many reconstruction procedures have been performed to relieve the symptoms. However, due to severe complications, such as intra-abdominal infection or re-stenosis of the neo-canal, hysterectomy eventually cannot be avoided in most cases (Jacob and Griffin, 1989). It seems that pregnancy is a dream for patients with partial or complete cervical atresia. However, with the progress of artificial reproductive techniques (ART), pregnancy becomes possible in this group of patients.

We report here a case of successful pregnancy by transmyometrial and transtubal embryo transfer (TET) after in-vitro fertilization (IVF) followed by uterovaginal canalization during Caesarean section in a patient with complete cervical atresia in the presence of a normal vagina. To our best knowledge, this is the first reported case in which pregnancy was achieved by two ART methods simultaneously. In addition, uterovaginal canalization with amniotic membrane for the covering of the neo-endocervical wall was undertaken during Caesarean section to allow the patient to resume normal regular menstruation.

Case report

In 1998, a 32 year old woman was referred to the outpatient clinic of the reproductive endocrinology unit at National Cheng Chung University Hospital with the complaints of primary amenorrhoea and cyclic abdominal pain for 19 years. Tracing
Back her past history, there had been a normal onset of thelarche and pubarche at 12 years old. The patient had experienced cyclic abdominal pain since the age of 13 years. She had been treated with long courses of oral contraceptives at other clinics. Cyclic abdominal pain improved during therapy but recurred rapidly when treatment ceased. Complete cervical atresia with normal vagina was diagnosed at another hospital when she was 18 years old. At the age of 20 and 22 years, she experienced cyclic abdominal pain since the age of 13 years. The patient underwent two reconstructive operations of her cervix in order to build a functional uterovaginal passage, but these failed. Because repeat stenosis of the neocervix developed after reconstructive operations, cyclic abdominal pain had subsided for months but recurred subsequently. Hysterectomy had been suggested, but the patient refused. Medication for relief of her symptoms had been ongoing for a long time.

The patient got married at 32 years old. She first visited our reproductive endocrinology unit because she wished to have a child. Pelvic examination demonstrated that a small fibrotic mass could be palpated in a normal vaginal vault. The measurements of serum follicle stimulating hormone (FSH), luteinizing hormone (LH), oestradiol, thyroid stimulating hormone (TSH), progesterone, and prolactin concentrations confirmed normal ovulatory cycles. Semen analysis of her husband was also normal. Transvaginal three-dimensional (3D) ultrasound showed a unicornuate right uterus with endometrium and a rudimentary left horn without endometrium connecting to the right uterus. Haematometra was not seen in the unicornuate right uterus. An atretic cervix was detected but an atretic left blind hemivagina was not found (Figure 1). Laparoscopic examination revealed an enlarged ovoid uterus with a bulging mass at the left fundal corner. Both ovaries were normal and bilateral normal Fallopian tubes were present. Some endometriosis spots and mild pelvic adhesion were found. An intravenous pyelography (IVP) revealed normal urinary tracts bilaterally. Renal echo showed bilateral kidneys were normal in size and morphology. Her karyotype was of a normal 46, XX, female. Congenital cervical atresia and unicornuate uterus with functional endometrium connecting with a rudimentary left horn were provisional diagnoses. Ovulation induction with a total dose of 1350 IU FSH (Metrodin®; Serono, Aubonne, Switzerland) and 1200 IU of human menopausal gonadotrophin (Humegon®; Organon, Oss, The Netherlands) was administered in June 1998. Transvaginal oocyte retrieval under ultrasound guidance was performed 36 h after muscular injection of 10 000 IU of human chorionic gonadotrophin (Pregnyl®; Organon). Five of eleven oocytes were fertilized via IVF procedures. After 48 h, five embryos at the 8-cell stage were selected for TET and transmyometrial embryo transfer (Towako procedure) performed at the same time. Eight weeks later, vaginal ultrasound revealed an intrauterine gestational sac with fetal heartbeat. Pre-eclampsia had developed since 29 weeks gestation. Low dose (100 mg) aspirin and hydralazine (10 mg) t.i.d. were administered for hypertensive control. Fetal well-being was closely monitored with repeated ultrasound examinations in the outpatient department each week. Unfortunately, gestational diabetes was found by the oral glucose tolerance test at 30 weeks gestation. Dietary restrictions were imposed after nutritional counselling.

Because of progressive pre-eclampsia with the symptoms of headache and blurred vision, a Caesarean section was combined with uterovaginal canalization was performed at 36 weeks gestation. She delivered a healthy boy, weighing 2812 g, in a vertex presentation by a lower-segmental Caesarean section. The placenta was implanted normally. Four units of packed RBC were transfused. The patient resumed normal cyclic menses. She was regularly followed up at our outpatient unit for 5 months after the operation, and her condition has remained satisfactory thus far.

**Discussion**

The chance of spontaneous pregnancy occurring after successful canalization of the completely or partially atretic cervix is low because of cervical factors and severe endometriosis. There are only three cases reported in the literature (Zarou et al., 1973; Fraser, 1989; Hampton et al., 1990). However, recent advances in assisted reproductive technologies may afford a better opportunity to achieve pregnancy in patients with complete or partial cervical atresia (Table I). It was stated...
Table I. Summary of successful pregnancies by assisted reproductive techniques in patients with congenital cervical atresia

<table>
<thead>
<tr>
<th>Authors</th>
<th>Types of ART</th>
<th>Timing of uterovaginal canalization (age)</th>
<th>Materials of uterovaginal canalization</th>
<th>Gestational age at birth (weeks)</th>
<th>Events of antepartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thijssen et al., 1990</td>
<td>ZIFT&lt;sup&gt;b&lt;/sup&gt;</td>
<td>before pregnancy (15)</td>
<td>polyethylene T drain (Gortex)</td>
<td>38</td>
<td>abdominal cerclage</td>
</tr>
<tr>
<td>Anttila et al., 1999</td>
<td>Towako procedure&lt;sup&gt;c&lt;/sup&gt;</td>
<td>before pregnancy (24)</td>
<td>rubber catheter</td>
<td>32</td>
<td>pre-eclampsia</td>
</tr>
<tr>
<td>Present study</td>
<td>Towako procedure + TET&lt;sup&gt;d&lt;/sup&gt;</td>
<td>during Caesarean section (33)</td>
<td>amniotic membrane + Gortex + Foley tube</td>
<td>36</td>
<td>gestational diabetes</td>
</tr>
</tbody>
</table>

<sup>a</sup>ART = assisted reproductive techniques.
<sup>b</sup>ZIFT = zygote intra-Fallopian transfer.
<sup>c</sup>Towako procedure = transmyometrial embryo transfer.
<sup>d</sup>TET = transtubal embryo transfer.

(Thijssen et al., 1990) that a patient became pregnant after IVF cycles with zygote intra-Fallopian transfer (ZIFT). It was also reported (Anttila et al., 1999) that a pregnancy was achieved after IVF cycles with the Towako procedure in a patient with isolated complete cervical atresia. Nevertheless, both cases received cervical reconstruction operations before pregnancy. Here we present a case with complete cervical atresia that achieved pregnancy after IVF cycles with the TET and Towako procedures simultaneously before uterovaginal canalization. Moreover, we created the new uterovaginal canal at the same time during Caesarean section.

A total of 58 cases of congenital cervical atresia has been reported in the literature. About 48% of cases had isolated cervical atresia with a normal vagina and functional uterus (Fujimoto et al., 1997). These patients have pregnancy potential. However, there has been a lack of uniformity in the literature with regard to its management. Some authors claimed uterovaginal canalization might maintain menstrual outflow and restore fertility (Fujimoto et al., 1997; Tancer et al., 1998). However, most results of uterovaginal canalization with insertion of an indwelling stent, such as a rubber drain or stainless steel stem pessary, have generally been disappointing. Most of these cases received hysterectomy sooner or later because of the problem of canal stricture or stenosis (Geary and Weed, 1973; Rock et al., 1984). Lack of normal endocervical glandular function and epithelium may be one of the most important contributing factors resulting in stenosis and infertility. It has been proven that the human amnion is a readily available allograft with low antigenicity, high antimicrobial potential and the ability to foster epithelialization (Tozum, 1976; Tancer et al., 1979). Satisfactory results of vaginoplasty were achieved in cases of complete and partial vaginal agenesis, and there was improvement in all patients with vaginal strictures (Ashworth et al., 1986). According to the previously successful experiences of epithelialization with amniotic membrane in vaginoplasty, we chose amniotic membrane as the epithelialized material for epithelialization of the neocervix. The patient has been followed up for 5 months. Our results showed that normal menstrual outflow could be achieved and cyclic abdominal pain could be relieved soon after operation. Amniotic membrane appears to be a good endogenous source for epithelialization of the neocervix in uterovaginal canalization procedures.

We were also surprised that large endometriomas and severe pelvic adhesions could not be found in laparoscopic examination. Jacob and Griffin (1989) reviewed 41 cases of cervical atresia reported in the literature. Large endometriomas, severe pelvic adhesion and haematometra did not always appear. These depend on many factors such as the function of the endometrium, duration of retrograde menstruation, pelvic local immune reaction, and whether or not medication and surgical intervention has been used. In our case, mild endometriosis, mild pelvic adhesion, and no severe haematometra are the conditions which may have contributed to successful pregnancy after transmyometrial and transtubal embryo transfer.

From our case, we tried an alternative way to manage the patients with congenital cervical atresia in the presence of a normal vagina and functional uterus. With the assistance of IVF with the TET and Towako procedures, together with our unique procedure of uterovaginal canalization with amniotic membrane autograft performed during Caesarean section, these patients may have a better opportunity of pregnancy as well as symptom relief. Caesarean section and uterovaginal canalization could be performed at the same time. The number of patients suffering from repeat operations could be reduced. However, if maintaining menstrual outflow fails or cyclic abdominal pain does not subside after uterovaginal canalization, hysterectomy is the final way to resolve the symptoms related to obstruction.

In addition, the potential risk of ascending infection or sepsis after cervical and vaginal reconstruction could not be overlooked (Niver et al., 1980). Although the causes of ascending infection are not defined, the lack of protection from the natural endocervical mucosa in the neocervix may be the most important one. We believe that the risk of ascending infection could be reduced by using the amniotic membrane graft for covering the neo-endocervical wall. However, whether or not the neocervix remained patent and avoided ascending infection is uncertain. Further evaluation and long-term follow-up are necessary.

In summary, our case suggests that: (i) successful pregnancy in patients with congenital cervical atresia but functional uterus could be achieved by ART no matter whether cervical reconstruction could be achieved or not; (ii) hysterectomy is not the first option for managing these patients unless medical treatment and uterovaginal canalization have been unsuccessful; and (iii) amniotic membrane appeared to be a good
alternative endogenous material for epithelialization of the neocervix in uterovaginal canalization procedures.

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References


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