Severe Asherman's syndrome complicated with placenta increta conceived by intracytoplasmic sperm injection following hysteroscopic surgery

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Summary

Although severe Asherman's syndrome is a disease that may cause infertility, pregnancy and childbirth are possible by performing hysteroscopic surgery. However, the obstetrical outcome is not always satisfactory. We report a case where severe Asherman's syndrome occurred following a cesarean section. Hysteroscopic surgery was performed due to secondary infertility, and pregnancy was achieved through a subsequent intracytoplasmic sperm injection. At 23 weeks of gestation, the patient was hospitalized due to the threat of premature labor, and a cesarean section was performed at 29 weeks of gestation after pregnancy-induced hypertension occurred. It was determined to be abnormal adherent placentation such as placenta increta through intraoperative findings, and a cesarean hysterectomy was performed. The pathological diagnosis of the uterus was placenta increta. Due to the risk of complications from placenta increta in pregnancies following hysteroscopic surgery in patients with severe Asherman's syndrome, it is important to realize the high risk involved in such cases during the pregnancy course, and careful perinatal management should be required.

Key words: Severe Asherman's syndrome; Hysteroscopic surgery; Intracytoplasmic sperm injection; Cesarean hysterectomy; Placenta increta.

Introduction

Asherman's syndrome is a disease that presents various symptoms due to the partial or complete obliteration of the uterine cavity caused by endometrial damage. Major clinical symptoms are menstrual abnormalities, infertility, and recurrent pregnancy loss [1]. Although there are reports of cases where clinical symptoms improved through hysteroscopic surgery, thus resulting in pregnancy and childbirth, the reproductive outcome has not been always satisfactory following surgery for severe Asherman's syndrome [2]. This report describes a case where severe Asherman's syndrome occurred after a cesarean section, and although pregnancy was achieved through intracytoplasmic sperm injection (ICSI) following hysteroscopic surgery, a cesarean hysterectomy was required due to placenta increta.

Case Report

A 37-year-old female and her 37-year-old husband presented due to secondary infertility of three years duration. The patient had previously conceived spontaneously and delivered a normal mature infant by cesarean section at 39 weeks of gestation due to intrauterine infection at an other hospital. Her menstrual cycles were regular. However, she had pronounced hypomenorrhea. Her hormonal testing was normal. The semen analysis was also normal. Ultrasonography showed normal uterus size with thin endometrium. In hysterosalpingography, the uterine cavity was narrowed and both tubes were occluded (Figure 1). Hysteroscopy revealed dense intrauterine adhesions and marked reduction in the size of the uterine cavity. Both tubal ostial areas were occluded. The patient was diagnosed as having Asherman's syndrome and classified grade 4 according to the European Society of Hysteroscopy classification of intrauterine adhesions [3].

She underwent transcervical resection (TCR) to restore the normal size and the shape of the uterine cavity. TCR was performed under spinal anesthesia with the continuous flow resectoscope; a diameter of 8 mm fitted with a 3 mm of cutting loop electrode (Olympus Corp., Tokyo, Japan). D-sorbitol solution (3%) was used for uterine dilution. Treatment was performed by making four direct myometrial incisions using a 3-mm loop electrode for the longitudinal incisions into the myometrium extending from the uterine fundus to the isthmus (Figure 2). An intrauterine device was inserted immediately after surgery. She then received three cycles of Kaufmann therapy (Premarin and Provera; Pfizer Japan Inc., Tokyo, Japan). An intrauterine device was removed three months later. Menstruation improved after the operation. Ultrasonography showed 6.4 mm thickness of endometrium during the preovulatory period.

The patient elected to undergo *in vitro* fertilization. She received 900 μg of buserelin acetate (Suprecur; Mochida Pharmaceutical Co., Ltd., Tokyo, Japan) daily, starting at the midluteal phase of the pretreatment cycle and ending at the time of human chorionic gonadotropin (hCG) injection. The patient then received 150 IU of recombinant human follicle-stimulating hormone (rhFSH) (Follistim; Organon, Osaka, Japan) daily from day 3 of the treatment cycle until the day before the administration of 10,000 IU of hCG (HCG Mochida; Mochida Pharmaceutical Co., Ltd., Tokyo, Japan). HCG was administered when at least two follicles reached a diameter of ≥ 18 mm. Transvaginal follicular aspiration was performed approximately 34 hr after hCG injection. Seven oocytes were retrieved. Conventional insemination was performed. Four oocytes were fer-

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Fig. 1

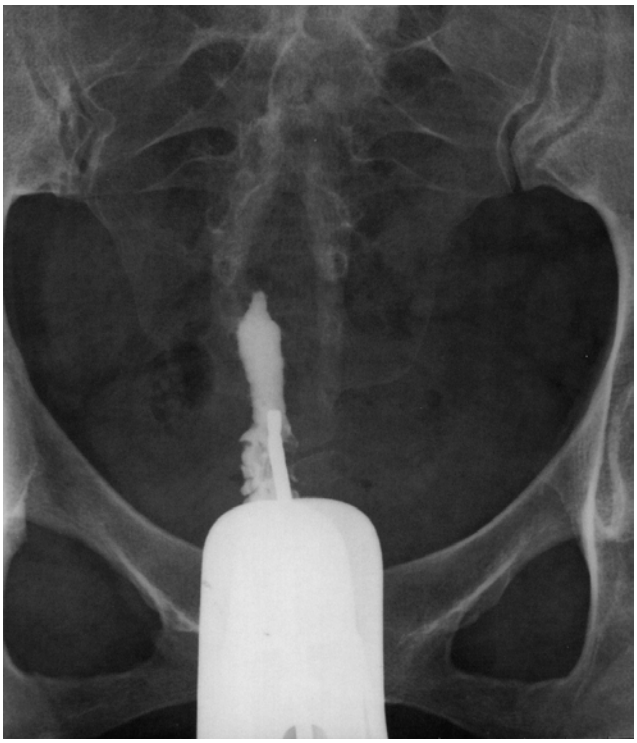

Fig. 2

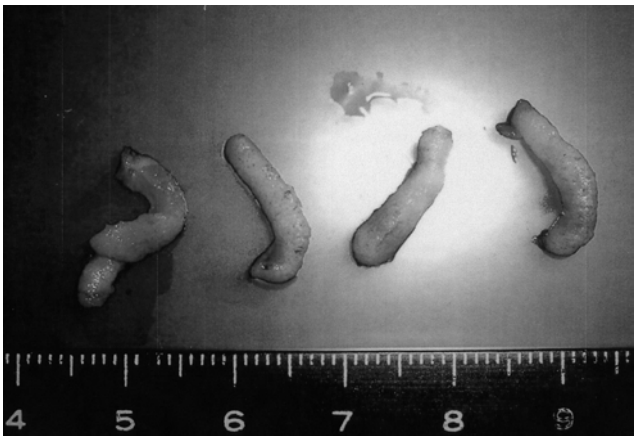

Fig. 3

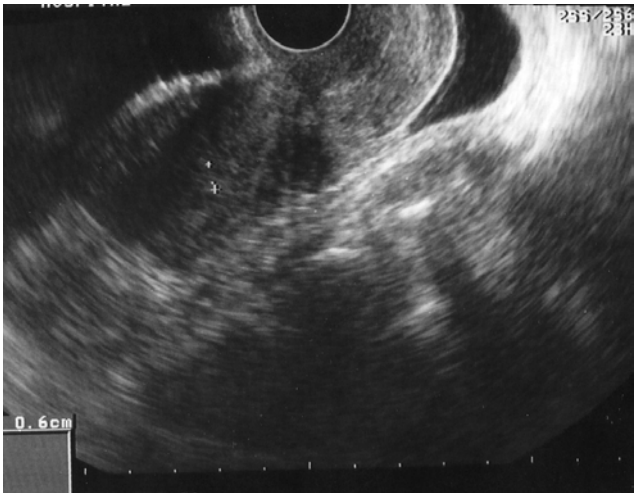

Fig. 4

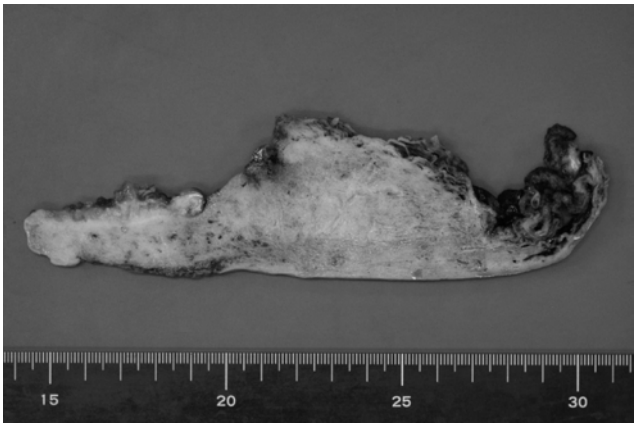

Figure 1. — Hysterosalpingography showing narrowed uterine cavity and both occluded tubes.
Figure 2. — A gross photograph of the myometrial tissue specimens resected by hysteroscopic surgery.
Figure 3. — Ultrasonography showing an endometrial thickness of 6 mm at the time of transfer.
Figure 4. — A gross photograph of the excised uterus, demonstrating the thin layer of the myometrium at the fundal portion *(right side)*.

tilized. Embryo transfer was performed on day 5 of culture. Two blastocysts were then transferred. The endometrial thickness was 6 mm at the time of transfer. The patient thereafter conceived. However, massive bleeding occurred at five weeks of gestation. Her serum hemoglobin level decreased to 5.6g/dl. Emergency operation (dilation and curettage) was carried out for hemostasis.

In the second attempt, the patient received the same controlled oravian hyperstimulation. Three oocytes were retrieved. Conventional insemination was performed. However, none of the oocytes became fertilized.

In the third attempt, the patient received 900 μg of buserelin acetate daily, starting at day 2 of the menstrual cycle phase and ending at the time of hCG injection. The patient received 225 IU of rhFSH daily from day 3 of the cycle until the day before the administration of 10,000 IU of hCG. Eight oocytes were retrieved. ICSI was performed. Six oocytes were fertilized. Embryo transfer was performed on day 5 of culture. Two blastocysts were then transferred. The endometrial thickness was 6 mm at the time of transfer (Figure 3). The patient successfully conceived. A single pregnancy was thereafter identified in the uterus at six weeks of gestation. The patient was hospitalized for premature labor at 23 weeks of gestation. Tocolysis with a β-sympathomimetic agent and bed rest were thus initiated. Hypertension (systolic pressure ≥ 140 mmHg and diastolic pressure ≥ 90 mmHg) and proteinuria (proteinuria > 300 mg in a 24-hour collection) were observed at 28 weeks of gestation. Therefore, she was diagnosed as having pregnancy-induced hypertension (PIH). The termination of pregnancy was decided due to hypertension and increased proteinuria. Cesarean section was performed at 29 weeks of gestation under spinal anesthesia. At laparotomy, the myometrium attached to the placenta was very thin. Placental cotyledons and engorged blood vessels were visible through the serosa in the same area. Based on these

findings, a diagnosis was made of abnormal placentation such as placenta increta. Cesarean hysterectomy was thus elected. A low transverse cesarean section resulted in the delivery of a 1,085 g infant [Apgar score 6 (1 min) and 9 (5 min)]. Next, total hysterectomy was performed (total blood loss: 2,320 ml; operation time: 1 h and 25 min). The pathological diagnosis of the uterus was placenta increta (Figure 4). The subsequent postoperative course was unremarkable.

Discussion

In the literature, reports of cases where hysteroscopic surgery was performed to handle severe Asherman's syndrome, subsequently leading to pregnancy and childbirth, are not scarce. Pregnancy rates following surgery have been reported as being 42.8% by Capella-Allouc *et al*. [4], 42.9% by Protopapas *et al*. [5], and 32.5% by Yu *et al*. [6]. However, subsequent pregnancy progress is not always satisfactory. Although Capella-Allouc *et al*. [4] observed a total of 15 pregnancies in 12 patients, second trimester fetal loss was observed in three cases, and in two of those cases Shirodkar cervical cerclage was reportedly executed following another pregnancy. In addition, as a complication during delivery, it has been reported that placenta accreta was observed in two out of nine cases of acquired newborns.

The effectiveness of the surgical treatment of Asherman's syndrome is determined by 1) whether the interior cavity of the uterus has returned to a normal anatomy; 2) whether menstruation has returned to normal; and, 3) whether or not pregnancy and a subsequent newborn was acquired in cases with a history of infertility or fetal loss. When considering the pregnancy and neonatal acquisition rate, the expansion of the uterine cavity and the recovery of fibrosed endometrial function are equally very important.

The spontaneous miscarriage rate following Asherman's syndrome surgery is reported to be approximately 20% [2]. On the other hand, Everett [7] has reported that the spontaneous miscarriage rate in the general population is 12%. Yu *et al*. [2] describe that although the number of cases must be increased and verified to determine whether the spontaneous miscarriage rate is increased after surgery due to Asherman's syndrome, it is thought that successful implantation is hampered with the presence of fibrosis of the endometrium. In our case, although pregnancy was achieved on the first *in vitro* fertilization, excessive bleeding occurred in the five weeks of gestation, and emergency surgery was therefore required to stop the bleeding. A blood transfusion was not done, but severe anemia occurred. This condition would rarely occur in a normal case, and dysfunction of the endometrium due to Asherman's syndrome is believed to be the cause of the miscarriage and significant blood loss.

In the literature, abnormally adherent placentation such as placenta accreta has been reported in pregnancies following Asherman's syndrome surgeries [2, 4, 8]. Although we considered this possibility and observed the condition of the placenta with ultrasonography, it did not lead to a diagnosis of abnormal placentation such as placenta accreta, and an examination of the placenta was planned using magnetic resonance imaging. Subsequently, PIH occurred, which led to a cesarean section. Prior to performing a cesarean section, the possibility of abnormal placentation could not be ruled out; therefore, surgery was performed after obtaining approval from the patient and explaining that if abnormal placentation was diagnosed at the time of surgery, a hysterectomy might be required. Placenta increta was suspected from findings during surgery, and a hysterectomy was performed after fetal delivery. A postoperative pathological finding concluded that it was placenta increta. In a macroscopic finding of the resected uterus, a primary focus was observed in the fundus of the uterus. The intrauterine cavity from the fundus of the uterus to the isthmus was enlarged by hysteroscopic surgery, and the fundus, which was the primary focus of the placenta increta, was not removed. It is not clear whether an abnormality of the endometrium due to Asherman's syndrome itself was the cause of placenta increta, or if it was related to the operation of the hysteroscopic surgery. However, TCR itself may cause abnormal placentation.

We have reported a case where hysteroscopic surgery was performed due to the presence of severe Asherman's syndrome, and the subsequent treatment led to successful conception. Following conception, a cesarean section was performed due to PIH, and a hysterectomy was required due to placenta increta. Although severe Asherman's syndrome is a disease where pregnancy is possible by surgery, it is believed that strict management is needed and it should be kept in mind that spontaneous miscarriage or second trimester fetal loss are possible, and additionally, complications of abnormally adherent placentation such as placenta accreta or placenta increta can develop at delivery.

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