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CASE REPORT

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Myomectomy scar ectopic pregnancy following a cryopreserved embryo transfer

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Abstract

Case: A 40 year old woman with a history of a myomectomy visited the Department of Obstetrics and Gynecology, Niigata University Medical and Dental Hospital, Niigata, Japan, following 2 years of infertility. Magnetic resonance imaging detected an abnormal endometrial-like pseudo-cavity. A hysterosalpingography also revealed an abnormal accumulation of contrast medium at the myometrial scar site. A transvaginal ultrasound showed a thin myometrium at the lower uterine body. The patient conceived via in vitro fertilization under a luteal phase down-regulation protocol (long protocol) for controlled ovarian stimulation, followed by a cryopreserved embryo transfer during her natural ovulation cycle. After the embryo transfer, the gestational sac was located at the subserosal site of the myomectomy scar.

Outcome: An emergent laparoscopic operation was performed and the embryo was removed successfully via laparoscopy under transvaginal ultrasonography.

Conclusion: A subserosal uterine pregnancy is a rare form of intramural pregnancy, which is a rare subtype of an ectopic pregnancy, which could occur at the myomectomy site, especially after an embryo transfer. It is believed that this rare ectopic pregnancy resulted from embryo implantation under the serosa through a microsinus tract that was a site of suture failure of the myomectomy scar and was partially affected by the embryo transfer. Clinicians should consider the possibility of an ectopic pregnancy after uterine surgery, including a myomectomy.

KEYWORDS

ectopic pregnancy, embryo transfer, laparoscopic surgery, uterine fibroid, uterine myomectomy

1 | INTRODUCTION

Although assisted reproductive technology (ART) has resulted in successful childbirths, complications have been reported; one of the common complications is an ectopic pregnancy. Traditionally, ART was believed to increase the risk of ectopic pregnancy; however, the incidence of ectopic pregnancy recently has decreased.[1] The risk factors for ART-associated ectopic pregnancy include the presence of more than one embryo, endometrial thickness, and the volume of the transfer medium.[2,3]

A surgical-site pregnancy is a rare type of ectopic pregnancy, wherein the pregnancy typically occurs at the site of a Cesarean

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section scar. Conversely, pregnancy at a myomectomy scar site is infrequent.[4,5] Moreover, an intramural pregnancy, the rarest form of ectopic pregnancy, occurs when the gestational sac is implanted in the myometrium.[6] Most intramural pregnancies occur in patients with a history of uterine curettage, Cesarean section, or adenomyosis.[7] This rare pregnancy is accompanied by hypervascular disease, of which the main symptom is atypical genital bleeding; surgical treatment is necessary when a ruptured pregnancy causes a hematoma and bleeding.[6]

Reported here is a rare subtype of an intramural uterine pregnancy that resulted from a cryopreserved embryo transfer (ET) after a myomectomy. Here, the embryo was implanted under the uterine serosa (ie a "subserosal uterine pregnancy").[8] This report discusses the pathogenesis and management of this notable case.

2 | CASE REPORT

A 35 year old Japanese, nulligravida woman presented with abdominal tension at Niigata University Medical and Dental Hospital, Niigata, Japan. Multiple myomas (≤8 cm in diameter) were detected in the uterine body. To improve her symptoms, a laparoscopically assisted myomectomy was performed. No obvious intraperitoneal adhesion or abnormality of the bilateral adnexa of the uterus was detected during surgery. After the injection of diluted vasopressin into the myometrium around the tumors, an incision was made with an electric scalpel. Myomas (≤4 cm in diameter) at the lower segment were removed after vertical incision of the uterus. Although the endometrium was not macroscopically injured, the myomas were located near the endometrium. After removing 15 tumors, a transvaginal ultrasound did not detect any residual tumor. The surgical sites were repaired in two layers with poligleaprone (2-0 monocryl® suture; Johnson & Johnson Patient Care, Inc., New Brunswick, NJ, USA). After the first continuous unlocked suture of the deep myometrium, the needle was continuously inserted from the deep aspect of the myometrium to the serosa on both sides of the incision in the second suture. An absorbable adhesion barrier (INTERCEED®; Johnson & Johnson Patient Care, Inc.) was used to prevent any unintended adhesion. For 5 months after the surgery, the patient's clinical course was uneventful.

She revisited the hospital following 2 years of infertility (at age 40 years). Multiple myomas were redetected in the uterus. Diagnostic magnetic resonance imaging (MRI) revealed a normal cervix and multiple myomas that were displacing the uterine cavity. An abnormal T2-weighted, high-intensity lesion was visualized, which appeared to be similar to the endometrial cavity (Figures 1A and 1B). A hysterosalpingography (HSG) revealed an abnormal accumulation of contrast medium at the site of the lower segment of the uterus without any deficit or deformation of the endometrial cavity (Figure 2); no other fertility abnormality was detected. Therefore, a laparoscopically assisted myomectomy was reperformed because the myomas were suspected as one of the causes of infertility and potentially future perinatal complications. Although the intestine extensively adhered to the fundus of the uterus, there was no

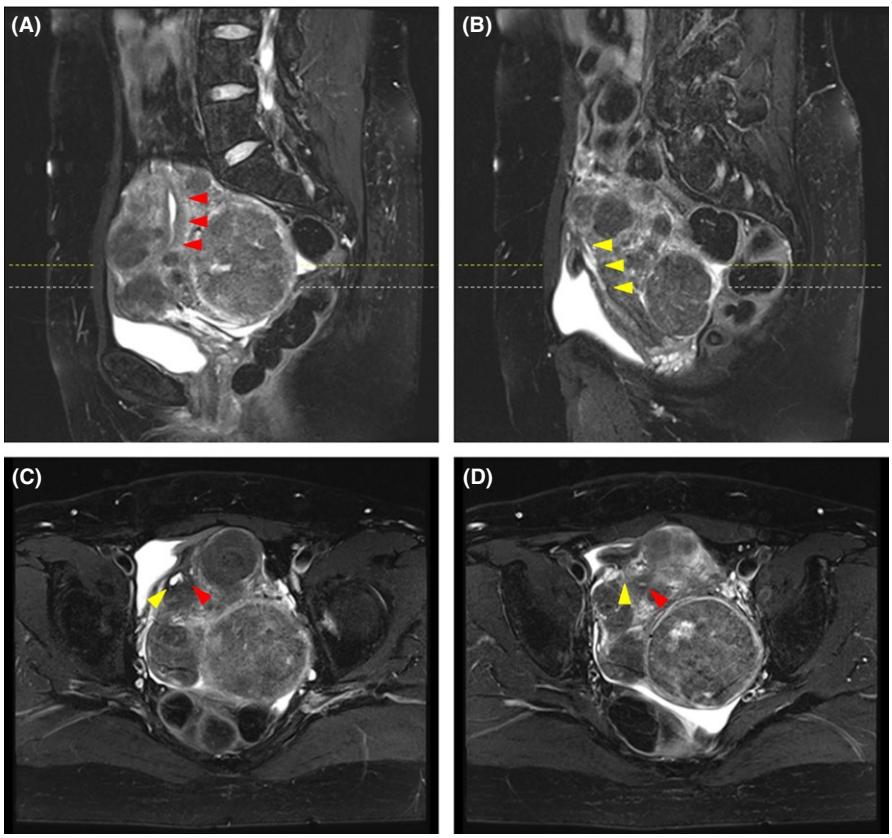

FIGURE 1 Magnetic resonance imaging (MRI) before the repeat myomectomy. The MRIs showed a normal endometrium (red arrowheads: A, C, and D) and a pseudo-endometrial cavity (yellow arrowheads: B, C, and D), both leading to the cervix. C and D are the transverse images at the height level of the yellow and white dotted lines of the sagittal images (A and B), respectively

adhesion at other previous uterine surgery sites. As with the first myomectomy, an incision was made after injecting diluted vasopressin. To remove the myomas around the pseudo-endometrial cavity, the uterus was incised vertically and the surgical site was repaired with double-layer continuous suture using 2-0 monocryl® as in the first myomectomy. Nineteen myomas (sized 1-7 cm) were removed and the actual endometrium was not injured during surgery. No obvious residual tumor was detected with the transvaginal ultrasound during the surgery and INTERCEED® (Johnson & Johnson Patient Care, Inc.) was used again.

Six months later, a HSG revealed the same abnormal accumulation of contrast medium and bilateral tubal occlusion. A transvaginal ultrasound showed a thin myometrium in the lower uterine body (Figure 3). One year after the repeat myomectomy, the patient conceived via in vitro fertilization (IVF) under a luteal phase down-regulation protocol (long protocol) for controlled ovarian stimulation, followed by a cryopreserved ET (Gardner grading system: grade 3AA) during her natural ovulation cycle. The ET procedure was performed under transabdominal ultrasonography guidance with a hard-tipped ET catheter (Wallace® malleable stylet; Origio, Målov, Denmark). The procedure was difficult due to flexion of the uterus and the catheter was inserted and removed multiple times. The embryo eventually was delivered by using a nearby uterine fundus. Although urinary human chorionic gonadotropin (hCG) was detected on post-ET days 15, 22, and 29, the gestational sac was not observed in utero. On day 38 (8 weeks of gestation), the urinary hCG was elevated to 2276 mIU/mL and a transvaginal ultrasound detected the gestational sac (16 mm in diameter with an embryo that was 10 mm in length) outside the uterus; these results were consistent with observations from five-to-six weeks of gestation. The

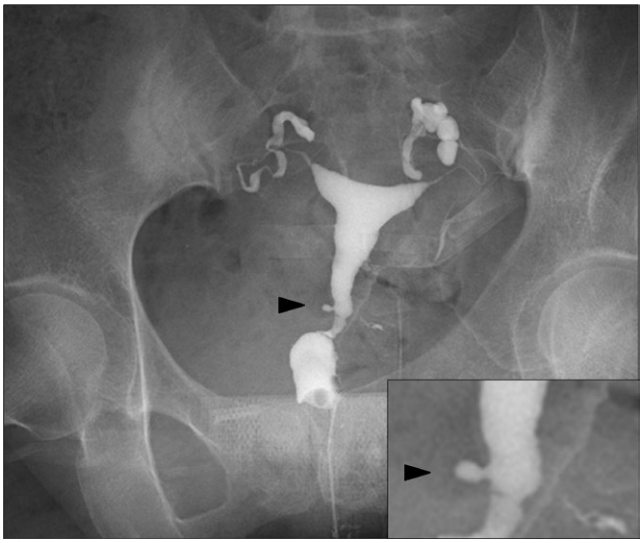

FIGURE 2 Hysterosalpingography showed an abnormal accumulation of contrast medium outside of the uterus (arrow head)

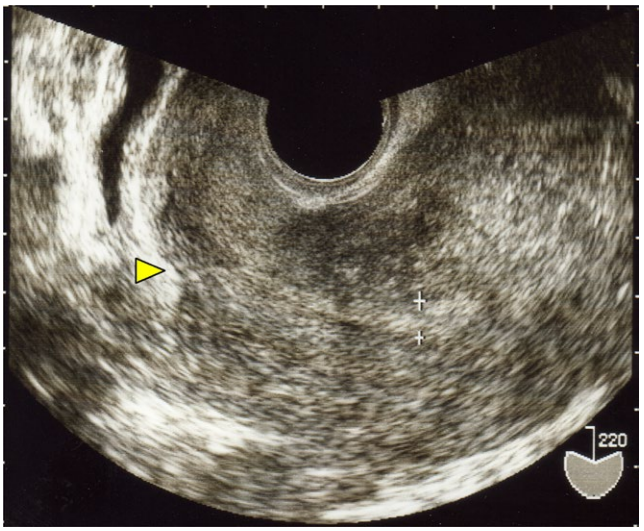

FIGURE 3 Ultrasound imaging after the second myomectomy. The imaging showed a thin myometrium at the lower segment of the uterine body (arrowhead)

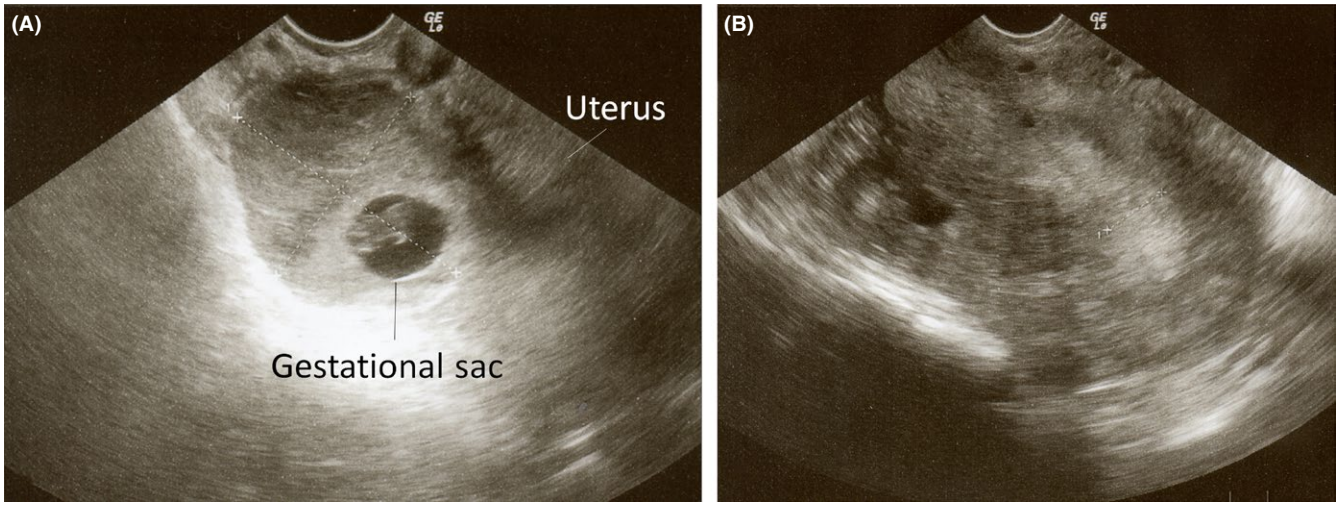

FIGURE 4 Ultrasonography revealed the gestational sac and product of conception in front of the uterus (A), while the uterus did not contain any product (B)

gestational sac was located between the bladder and the uterus and was covered with a low echoic hematoma-like mass (Figure 4); there was no embryo in utero. As a result of severe abdominal pain and the growing hematoma-like mass, emergency laparoscopic surgery was performed.

A severe inflammatory intraperitoneal adhesion obscured the bilateral adnexa (excluding the right tubal fimbriae), indicating that the INTERCEED® (Johnson & Johnson Patient Care, Inc.) that was used during the repeat myomectomy had a limited effect in preventing adhesions (Figure 5). After removing the adhesion and clarifying the tubes, both tubes swelled as a result of mild hydrosalpinges. Moreover, there was no ovarian abnormality or abnormal intraperitoneal bleeding; signs of tubal or ovarian pregnancy were not detected. Furthermore, a transvaginal ultrasound during surgery confirmed the gestational sac between the uterus and the bladder, which was consistent with a site of dark-purple peritoneum (Figure 5A). Soon after incising the peritoneum and splashing water under the peritoneum, the gestational sac protruded with the hematoma (Figure 5B). The product of conception with the hematoma was evacuated and ultrasonography did not detect any remnant. As there was no abnormal bleeding, INTERCEED® (Johnson & Johnson Patient Care, Inc.) was placed again over the incision of the peritoneum without suturing the peritoneum or myometrium. After surgery, there was no severe complication or small hematomas at the vesicouterine pouch.

Pathologic examination detected normal villi and deciduas without abnormal trophoblastic cells or myometrium. After surgery, the patient's hCG level gradually decreased. Three months later, the patient received IVF-ET treatment again but experienced a biochemical pregnancy only.

3 | DISCUSSION

It is pertinent to clarify the pathogenesis of the ectopic pregnancy in this case. It is believed that this eccentric ectopic pregnancy was not related to implantation of the embryo in the peritoneum of the vesicouterine pouch through the fallopian tube, but from the abnormal traversing of the embryo through the sinus tract of the scarred myometrium, resulting in implantation under the peritoneum at the vesicouterine pouch. The first reason for this hypothesis was based on the abnormal imaging findings before the ET. The MRI before the repeat myomectomy showed a pseudo-endometrial cavity, which might have arisen from the original uterine cervix (Figure 1). Moreover, after the repeat myomectomy, the contrast medium from the HSG abnormally accumulated at the anterior wall of the uterus (Figure 2) and ultrasonography detected a thinned lower segment of the uterine myometrium (Figure 3). These findings suggest that the microscopic sinus tract between the endometrial cavity and the subserosal or intramural cavity existed before the ET. The thin myometrium around the implant site and the ET procedure might have caused the subserosal pregnancy as the risk factors for an intramural pregnancy include adenomyosis, uterine trauma (which forms micro-sinus tracts), and difficult IVF, although the etiology and pathogenesis of this disease are unclear.[6]

The second reason was based on the intraperitoneal findings. Although there was severe adhesion, the implantation site of the gestational sac was covered by the peritoneum. Furthermore, the removed product did not include any myometrium. In addition, the HSG detected bilateral tubal occlusion after the repeat myomectomy, although right tubal patency slightly recovered. These conditions also support the implantation of the transferred embryo under the serosa through the micro-sinus tract.

It is also important to clarify if this ET procedure that used a hard-tipped ET catheter penetrated the myometrium or dilated the micro-sinus tract. Although it could not be confirmed, the pseudo-endometrial cavity might have misled the surgeons because the pseudo-cavity was straighter from the cervix than from the actual endometrial cavity (Figure 2). When the described abnormal imaging findings are detected, it is important to consider misplacement of the catheter. Moreover, after uterine surgery, physicians should evaluate the whole uterus, and if necessary, perform additional imaging, including MRI and a hysteroscopy, which might be useful.

The pseudo-cavity might be related to suture failure at the uterine muscle layer in the first myomectomy. Unfortunately, because the pseudo-cavity was detected retrospectively after the surgery for the ectopic pregnancy, the abnormal lesion was not repaired at the second myomectomy and the surgery for ectopic pregnancy. As the uterine surgical scar might cause endometrial thinning or myometrial defects, multilayer closure is useful.[9] In some cases, pregnancy occurred even after two-layer sutures to repair the myomectomy scar[4,5]; continuous sutures of the deep myometrium after a myomectomy are more likely to cause a uterine avascular area than single interrupted sutures.[10] Moreover, a continuous suture in a herringbone fashion to repair the

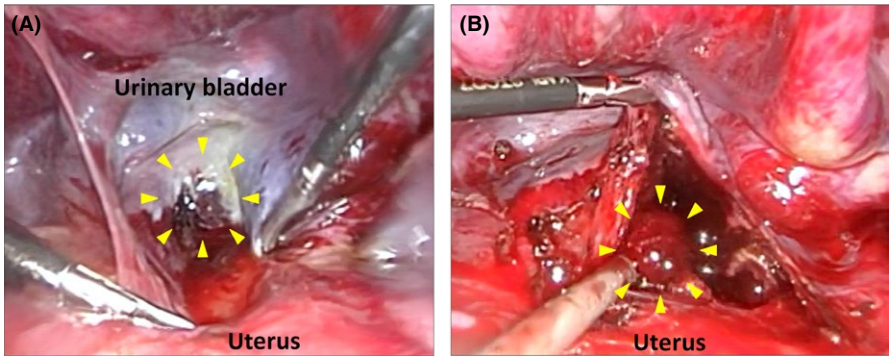

FIGURE 5 Intraperitoneal findings during surgery. There was a dark-purple peritoneum (arrowheads) at the vesicouterine pouch, with severe inflammatory intraperitoneal adhesion (A). After the incision of the peritoneum, the gestational sac (arrowheads) protruded along with the hematoma (B)

superficial myometrium with serosa reduces myomectomy complications.[11] Considering these reports, a double-layer suture with a first layer of single interrupted sutures and a second layer of a continuous suture might be useful in order to avoid suture failure, though future prospective studies are needed. Nevertheless, in postmyomectomy patients, clinicians should check carefully for uterine abnormalities.

Generally, the first choice of treatment for an ectopic pregnancy when faced with marked bleeding is the removal of the product of conception; performing surgery, with a salpingectomy or salpingostomy, for a tubal pregnancy. In contrast, the treatment for an intramural pregnancy is unclear. An adaptive treatment option should be selected, depending on myometrial involvement, patient status, and the desire for future fertility.[7] Moreover, the difficulty of the preoperative diagnosis of an intramural pregnancy hampers its treatment. It is more difficult to diagnose a subserosal pregnancy than an intramural pregnancy before surgery. A MRI and ultrasonography might accurately detect the implanted site.[12] Thus, previous laparoscopic surgical treatment first should be noted, when then the implantation site can be correctly identified in cases of subserosal pregnancy. Surgical treatment under ultrasonography might be an especially useful tool for rare-site ectopic pregnancy. If an intramural pregnancy, including a subserosal pregnancy, is suspected before surgery, a myometrial repair should be considered after removing the products of contraception in order to prevent a repeat intramural pregnancy.

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DISCLOSURES

Conflict of interest: The authors declare no conflict of interest. *Human rights statement and informed consent:* The authors obtained signed consent from the patient to publish the information. *Animal studies:* This article does not contain any studies with animal participants that have been performed by any of the authors.

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