A Case of Miscarriage Caused by a Small Uterus following Childhood Chemotherapy

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Keywords
After chemotherapy · In vitro fertilization · Miscarriage · Premature ovarian failure · Uterine deformity

Abstract
A majority of miscarriages have been thought to be caused by fertile ovum abnormalities; however, our findings suggest that a small uterus can also potentially cause miscarriage. There are no reports on the association between a small uterus and miscarriage. A woman in her late 20s, whose medical history revealed childhood acute lymphocytic leukemia, which progressed to remission after chemotherapy, radiotherapy, and bone marrow transplantation. Ultrasound revealed no ovarian follicles in either of the ovaries and small uterus (length, 32 mm). In cycle 15, after ovum collection, frozen embryos with Veeck's classification of G3b9 were obtained. Embryo transplantation was performed during the hormone replacement cycle, resulting in pregnancy. On day 5 of gestational week 18, the patient experienced mild lower abdominal pain, and she underwent a spontaneous delivery.

Background
A majority of miscarriages have been thought to be caused by fertile ovum abnormalities; however, our findings suggest that a small uterus can also potentially cause miscarriage. There are no reports on the association between a small uterus and miscarriage.
Case Presentation

A woman in her late 20s presented to our hospital with the chief complaint of infertility. Her medical history revealed childhood acute lymphocytic leukemia, which progressed to remission after chemotherapy, radiotherapy, and bone marrow transplantation. She underwent Kaufmann treatment for secondary amenorrhea. After getting married, natural menstruation occurred, and thus the treatment was temporarily withdrawn; however, 6 months after discontinuing treatment, she experienced amenorrhea, and Kaufmann treatment was recommenced. She was diagnosed with subclinical hypothyroidism based on a thyroid-stimulating hormone level of 5.67 µIU/mL and free thyroxine level of 0.91 ng/dL and was prescribed oral thyradin.

Remarkable findings at the time of initial examination at our hospital included serum E2 (Estradiol) <5.0 pg/mL, Luteinizing Hormone = 26.3 mIU/mL, Follicle-Stimulating Hormone = 57.6 mIU/mL, and Anti-Mullerian Hormone <0.1 ng/mL. Ultrasound revealed no ovarian follicles in either of the ovaries and small uterus (length, 32 mm) (Fig. 1AB–BC), suggesting a premature early menopausal stage.

Computed tomography examination for abnormal hepatic function (AST30U/L, ALT65U/L) revealed no abnormalities. Other biochemical blood tests were normal; cervical cancer cytodiagnosis results were negative for intraepithelial lesion or malignancy.

Premarin was used to promote ovarian follicle growth for ovum collection; dominant ovarian follicle growth was observed in cycles 7 and 12; however, despite ovum collection, no transplantable embryos were obtained. In cycle 15, after ovum collection, frozen embryos with Veeck's classification of G3b9 were obtained. Embryo transplantation was performed during the hormone replacement cycle, resulting in pregnancy. Fetal heart rate was observed in week 6. Estrogen and progesterone supplementation was given until 9 weeks of gestation. During week 15 of pregnancy, the patient was hospitalized for premature membrane rupture without significant uterine contractions or inflammatory reaction. On day 5 of 18 gestational week, the patient experienced mild lower abdominal pain, and she underwent a spontaneous delivery in the toilet. The infant was a boy weighing 246 g, with an Apgar score of 0 points/0 points.

Discussion and Conclusions

Miscarriage caused by uterine deformity is common in the second trimester. Additionally, the rate of newborn delivery is lower in spontaneous pregnancies in patients with bicornuate and septate uteri than in women with a normal uterus [1]. However, there are no reports on the association between a small uterus and miscarriage. Normally, in the presence of uterine myomas, the uterus size increases and possibly decreases the pregnancy rate; this complicates assessing uterus size and miscarriage association. Moreover, irreversible changes to the ovaries caused by chemotherapy are difficult to evaluate owing to differing individual characteristics [2], and are therefore controversial. However, our case highlights the importance of pregnancy monitoring in women with a small uterus following embryo transplantation.

- A majority of miscarriages have been thought to be caused by fertile ovum abnormalities; however, our findings suggest that a small uterus can also potentially cause miscarriage. We report a case of miscarriage in a patient with a small uterus (length, 32 mm).
- Chemotherapy may affect ovarian function, but the outcome of subsequent pregnancies may be difficult to prognosticate owing to differing individual characteristics.
Particular care should be paid to pregnancies attained using a precious ovum, following chemotherapy.

Availability of Data and Material

All data generated or analysed during this study are included in this published article.

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Statement of Ethics

Patient approval and consent was obtained.

Disclosure Statement

The author declares that there are no competing interests.

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Author Contributions

R.F. performed the histological examination and was a major contributor in writing the manuscript.

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Fig. 1. Small uterus of approximately 32 mm length (AB+BC).