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Case Report

Two cesarean deliveries after hemi-hysterectomy due to gestational trophoblastic neoplasia

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ABSTRACT

Objective: Although uterine didelphys per se is not associated with an impaired ability to conceive, the association between uterine anomalies and gestational trophoblastic neoplasia (GTN) remains unclear. The management of chemotherapy-resistant GTN in women with uterine didelphys raises a new issue regarding whether to perform a hemi-hysterectomy.

Case report: A 23-year-old, gravida 1, para 0 Japanese woman was referred with a failed intermittent cervical dilatation for hematometra. Four years previously, she developed a GTN Stage III, score 5. As two cycles of chemotherapy with methotrexate (MTX) and one cycle of EMA-CO (etoposide, MTX, actinomycin D, cyclophosphamide and vincristine) did not result in remission, we performed an abdominal hemi-hysterectomy. After a canalization procedure and cervicoplasty were performed, the patient conceived naturally and prematurely delivered by cesarean section twice.

Conclusion: A hemi-hysterectomy should be considered for fertility preservation when GTN develops on either side of a didelphic uterus and adjuvant chemotherapy does not result in remission.

Introduction

Uterine didelphys occurs as failure of fusion of the bilateral müllerian ducts, consequently producing duplication of the reproductive structures. It is seen in approx. 8% of all types of uterine anomalies [1]. In 15%–20% of women with uterine didelphys, unilateral anomalies are also present, such as an obstructed hemivagina and ipsilateral renal agenesis (OHVIRA syndrome) [2], Wunderlich syndrome or Herlyn-Werner syndrome. A septated vagina also occurs in 75% of women with uterine didelphys [3] and may cause difficulty with sexual intercourse or vaginal delivery.

This type of anomaly (i.e., uterine didelphys, sometimes called 'double uterus') per se is not associated with an impaired ability to conceive. When the proper management — including resection of the vaginal septum — is offered, women with uterine didelphys often have good reproductive outcomes [4]. However, little has been reported on the relationship between uterine anomalies and gestational trophoblastic disease (GTD), which could be the precursor of gestational trophoblastic neoplasia (GTN). The management of chemotherapy-resistant GTN in women with uterine didelphys raises the new issue of whether a hemi-hysterectomy should be performed.

Originally, hemi-hysterectomies were performed for women with a unicornuate uterus with a rudimentary horn (i.e., a non-communicating hemi-uterus) to alleviate dysmenorrhea, to prevent an intracornual pregnancy, and to possibly prevent endometriosis [5]. Although a hemi-hysterectomy has been performed for a small number of women with uterine didelphys and a complete bicornuate uterus who had two uterine corpi, two endometrial cavities, and two uterine cervices, the reproductive outcome of this procedure remains unclear.

We present the case of a young woman with uterine didelphys who presented a molar pregnancy with invasive and metastatic GTN, and we report her therapeutic course including the hemi-hysterectomy and reproductive outcome.

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Case presentation

A 23-year-old, gravida 1, para 0 Japanese woman was referred to Oita University Hospital with a failed intermittent cervical dilatation for cervical occlusion and hematometra which had resulted in the gradual development of hypomenorrhea and dysmenorrhea over a 1-year period. She had a noteworthy medical history.

Four years previously, she conceived naturally, and uterine didelphys with a longitudinal vaginal septum first diagnosed at Oita Red Cross Hospital. She underwent uterine evacuations for a presumed molar pregnancy in the left hemiuterus, which was diagnosed as a partial mole based on the microscopic findings of the focal hydropic change of chorionic villi. However, at her follow-up visit, she displayed nausea, and her urinary human chorionic gonadotropin (hCG) level was identified as increased to 3,276,800 mIU/mL. A hypervascular tumor in her left hemiuterus measuring 50 mm in dia. (Fig. 1A) and multiple nodules in bilateral lungs (Fig. 1B) were shown by contract-enhanced computed tomography (CECT). Dr. E. Hori (Oita Red Cross Hospital) diagnosed gestational trophoblastic neoplasia (GTN) Stage III, score 5. As two cycles of chemotherapy with methotrexate (MTX) with folinic acid did not result in remission, an EMA-CO regimen of etoposide, MTX, actinomycin D, cyclophosphamide and vincristine was initiated. After the 1st cycle of EMA-CO, her urinary hCG value rose and multiple pulmonary nodules increased in size, contrary to our expectations. She underwent abdominal hemi-hysterectomy and a resection of vaginal septum. Hydropic chorionic villi, some of which were invading in the myometrium with trophoblastic proliferation suggesting an invasive mole, were shown by a microscopic examination (Fig. 1C). A diploid diandric genome suggesting a complete hydatidiform mole was confirmed by a DNA genotyping test. After five adjuvant cycles of EMA-CO, complete remission was achieved. During the 2-year period of post-treatment severance, the patient had a regular menstrual cycle and was free from relapse.

On her initial visit to our unit (Oita University Hospital), a speculum examination did not show any menstrual blood in her vagina, but there was menstrual blood in the uterine cavity (hematometra). The uterine cervix with the residual side was unclear. A transvaginal sonography showed an extremely right-deviated uterus measuring 50 mm in dia. Magnetic resonance imaging revealed a retained right uterus with a hypoplastic cervix and right adnexa (Fig. 2A), and CECT demonstrated normal bilateral kidneys (Fig. 2B). We concluded that her primary disease was uterine didelphys with a hypoplastic right hemi-uterus at the cervix, bicollis, with vaginal septum (1988 American Fertility Society classification type III). We performed a canalization procedure with cervical dilators and a cervicoplasty under general anesthesia. Despite ultrasound guidance, we caused an intraoperative bladder injury. After 10 days of postoperative cervical canal canalization with a 14-Fr soft catheter, the patient was discharged uneventfully.

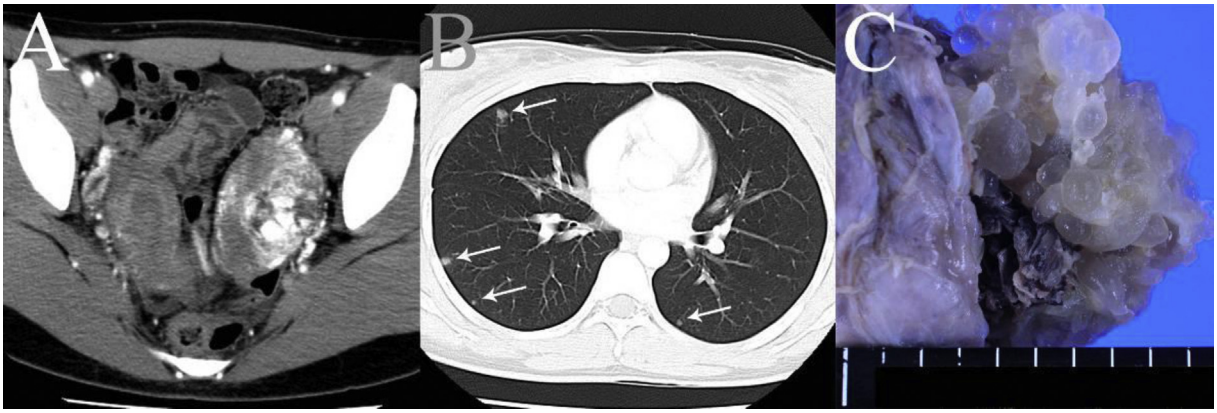

Fig. 1. A: Uterine didelphys and a hypervascular tumor occupying the intrauterine cavity of the left hemiuterus. **B:** Multiple and bilateral pulmonary metastases of gestational trophoblastic neoplasia (GTN) by contract-enhanced computed tomography. **C:** The resected specimen showed an aggregate of branching edematous villi.

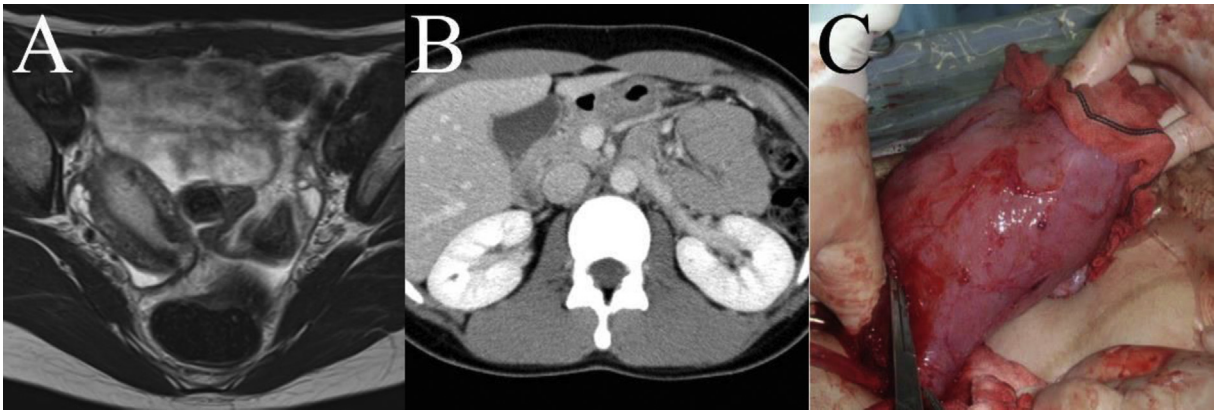

Fig. 2. A: The retained right uterus with a hypoplastic cervix. **B:** Bilateral kidneys were present without abnormal findings. **C:** Neither adnexa nor a suspensory ligament of the ovary was noted on the left side of the uterus at the time point of cesarean section.

Table 1
Pregnancy outcome of hemihysterectomy: Studies from 1947 to present.

Study	Year	Patient, n	Pregnancies, n	Abortions, n	Preterm deliveries, n	Term deliveries, n	Vaginal deliveries, n	Cesarean deliveries, n	Live birth, n
Smith et al. [13]	1947	1	1	0	0	1	0	1	1
Thelwall-Jones [14]	1976	2	3	0	1	2[a]	0	3	3
Phillips [12]	1976	1	1	1[b]	0	0	0	0	0
Candiani et al. [11]	1997	2	2	1	1	0	0	1	1
Berhan et al. [10]	2006	1	1	0	0	1	1	0	1
Present case	2016	1	2	0	2	0	0	2	2
Total		8	10	2	4	4	1	7	8

[a] One singleton pregnancy and one twin pregnancy.
[b] Heterotopic pregnancy (in the right hemiuterus and the remaining left cervix).

We administered three cycles of cyclic estrogen progesterone therapy in an attempt to prompt the elimination of menstrual blood and to prevent the formation of cervical synechiae. During her first natural menstrual cycle, she conceived an intrauterine pregnancy. During the course of this pregnancy, the estimated weight of the fetus was below the 10th percentile and showed normal growth velocity.

At 29 weeks of gestation, we hospitalized the patient with a diagnosis of threatened premature labor, and we administered a tocolytic drug, ritodrine-hydrochloride. At 35 weeks of gestation, spontaneous active labor started and we performed emergency cesarean (C)-section with the indication of increased risk for complications/injury from cervical dilation. At the laparotomy, we could not identify the left adnexa, a suspensory ligament of the ovary or a uterine artery or vein (Fig. 2C). A 2310-g male was delivered, with the Apgar scores 8/9 (1 min/5 min). Two years later, the patient delivered her second child during an elective C-section at 35 weeks of gestation. A 2392-g male was also delivered by C-section with the Apgar scores 6/9 (1 min/5 min).

Discussion

After cytotoxic chemotherapy and a hemi-hysterectomy, our patient conceived naturally and delivered prematurely. Her case has two major clinical implications. First, hemihysterectomy was a feasible treatment option for the local control of this patient's chemotherapy-resistant GTN. Second, her fertility was preserved after two lines of cytotoxic chemotherapy and a hemi-hysterectomy.

To our knowledge, the present case is the first of a conservative resection of hemi-hysterectomy for a metastatic and chemotherapy-resistant GTN. Hysterectomy may be employed: (1) to remove resistant disease in the uterus, or (2) to control excessive uterine bleeding for women who do not desire to maintain fertility [6]. Newlands et al. reported using hysterectomy in 9 of 20 patients who developed resistance to EMA-CO after other chemotherapy, and all patients received a combination of EP (etoposide and cisplatin)-EMA salvage chemotherapy with surgery [7]. Local uterine resection may be considered in highly selected patients with no evidence of metastatic disease who wish to preserve their fertility. Kanazawa et al. reported that lesions <3 cm in dia. associated with low hCG and no evidence of pulmonary metastatic involvement or pulmonary metastasis controlled with chemotherapy are likely to be completely excised [8]. Hemi-hysterectomy for women with uterine didelphys is a useful option that compensates for the disadvantages of total hysterectomy and local uterine resection. Since 1947, 10 cases of pregnancy after hemi-hysterectomy [9–14] were reported in the English literature (Table 1). The indication of hemi-hysterectomy was hematometra/pyometra in all cases except our patient.

Although the limited number of cases from the literature is not sufficient for a comparison, the live birth rate (8/10, 80%) was acceptable according to the reported live birth rates of uterine didelphys or bicornuate uterus (55.9% and 55.3%, respectively) [1]. Little has been reported on post-hemi-hysterectomy infertility. Haddad et al. described the long-term follow-up of five patients who underwent a hemi-hysterectomy and ipsilateral hemi-colpectomy, but the patients did not achieve pregnancy [15]. In our summary of the pregnancy outcomes of hemi-hysterectomy (Table 1), it is worth noting that hemi-hysterectomies have resulted in a high rate of C-section deliveries. The association between reproductive outcome and hemi-hysterectomy must be examined further with a greater accumulation of cases.

In conclusion, we treated a reproductive-aged woman with uterine didelphys who presented an invasive and metastatic GTN. She underwent a left hemi-hysterectomy, conceived naturally, and prematurely delivered by C-sections twice after cytotoxic chemotherapy. A hemi-hysterectomy should be considered for fertility preservation when a GTN develops on either side of a didelphic uterus and adjuvant chemotherapy does not result in remission.

Conflict of interest

Written informed consent for this report was obtained from the patient and her husband before the initial therapy. All authors declare no conflict of interest.

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