Case report

A case of severe uterine arteriovenous malformation treated with danazol followed by a transarterial embolization of unilateral uterine and ovarian arteries

Hiroyuki Yazawa a,*, Syu Soeda b, Tsuyoshi Hiraiwa a, Masayo Takaiwa a, Keiya Fujimori b

a Department of Obstetrics and Gynecology, Fukushima Red Cross Hospital, Fukushima, Japan
b Department of Obstetrics and Gynecology, Fukushima Medical University, School of Medicine, Fukushima, Japan

A R T I C L E   I N F O

Article history:
Received 1 October 2015
Received in revised form
5 October 2015
Accepted 14 October 2015
Available online 29 October 2015

Keywords:
3D-CT angiography
color Doppler ultrasonography
danazol
transarterial embolization
uterine arteriovenous malformation

A B S T R A C T

Uterine arteriovenous malformation (AVM) is a potentially life-threatening condition characterized by abrupt and profuse uterine bleeding from abnormal connections between arteries and veins in the myometrium. It is commonly associated with prior pregnancy or uterine trauma. We present a case of severe uterine AVM treated with danazol and transarterial embolization (TAE). A 38-year-old patient with a history of two abortions and a myomectomy was referred to our hospital for intermittent massive uterine bleeding. She was diagnosed with uterine AVM by transvaginal color Doppler ultrasonography and helical computed tomography (CT). Diagnostic three-dimensional CT (3D-CT) angiography clearly demonstrated hypervascular tangles of uterine vessels, feeding arteries, remarkably dilated draining veins, as well as early filling of the internal iliac vein and the inferior vena cava, indicating massive arteriovenous shunting in the uterus. Danazol was administrated for 10 months to reduce the shunting of the uterine AVM before TAE with N-butyl-cyanoacrylate of the left ovarian artery and left uterine artery was successfully performed. After the procedure, we confirmed that shunting through the uterine AVM was markedly reduced. The patient has not experienced any severe uterine bleeding since the treatment.

Copyright © 2015, The Asia-Pacific Association for Gynecologic Endoscopy and Minimally Invasive Therapy. Published by Elsevier Taiwan LLC. All rights reserved.

Introduction

Although uterine arteriovenous malformations (AVMs) are thought to be rare, the true incidence of this condition has not been documented in the literature. We recently performed a prospective study examining the incidence of uterine hypervascular lesions named ‘uterine vascular malformations’ (U-VM) including uterine AVMin patients after abortion, after delivery, and as outpatients for 2 years. During the study period while we were screening for UVMs, we observed one case of severe uterine AVM among ~1000 patients. The current report presents a detailed clinical course and clear diagnostic imaging of the case.

Case report

The patient is a 38-year-old gravida 2, para 0, abortus 2 woman. Her first pregnancy, which occurred 7 years previously, ended in spontaneous abortion during the early stages of pregnancy and did not require dilation and curettage (D&C). She also had undergone myomectomy 4 years previously. Based on magnetic resonance imaging (MRI) findings at the time, she was diagnosed with a uterine leiomyoma of ~6 cm in diameter in the posterior uterine body. Myomectomy was commenced with a laparoscopically assisted approach. The total intraoperative blood loss was 1330 mL and transfusion with 2 units of packed red blood cells was required. Post operative histopathological examination revealed a diagnosis of cellular leiomyoma of uterus. After the operation, a 1.88 μg monthly dose of a gonadotropin releasing hormone analogue (GnRHa), leuprolein acetate, was administrated subcutaneously for 6 months. Two years later, the patient presented to our hospital with positive urinary pregnancy test. A gestational sac was confirmed to be in the uterine cavity but fetal heart movements

http://dx.doi.org/10.1016/j.gmit.2015.10.001

Copyright © 2015, The Asia-Pacific Association for Gynecologic Endoscopy and Minimally Invasive Therapy. Published by Elsevier Taiwan LLC. All rights reserved.
Figure 1. Color Doppler ultrasonography and enhanced CT. (A, B) Color Doppler ultrasonography demonstrated a hypervascular lesion of tortuous vessels with a colored mosaic pattern of irregular turbulent flow in the entire posterior myometrium; (C, D) enhanced CT demonstrated a highly enhanced effect in the posterior myometrium. CT = computed tomography.
were not detected at 7 weeks of gestation. She was diagnosed with a missed abortion, and D&C was performed but abnormal uterine bleeding was not documented during the procedure.

Eighteen months later, the patient experienced massive vaginal bleeding and she was referred to our hospital due to continuous vaginal bleeding. Abnormal active vessel flow with a colored mosaic pattern was detected with color Doppler ultrasonography, and we suspected a uterine AVM (Figures 1A and 1B). We then performed three-dimensional computed tomography (3D-CT) angiography, which demonstrated early-filling hypervascular tangles of uterine vessels fed by the uterine and ovarian arteries bilaterally, and diagnosed severe uterine AVM. Remarkable dilatation of the uterine and ovarian veins bilaterally as well as early filling of the internal iliac vein and the inferior vena cava was observed, indicating massive arteriovenous shunting in the myometrium (Figure 2).

Given the severity of the uterine AVM and the risks involved with transarterial embolization (TAE) at this time, danazol was administrated (200–400 mg daily) orally. The uterine AVM was monitored with monthly color Doppler ultrasonography. Although abnormal vessel flow did not resolve after 10 months of danazol therapy, we confirmed that the abnormal flow had reduced slightly, and TAE was undertaken as a secondary treatment. After confirming with angiography that the main feeding arteries were the bilateral ovarian and uterine arteries, embolization with N-butyl-cyanoacrylate was performed in the left ovarian and uterine arteries (Figure 3). Embolization of the right side was not performed to preserve the patient’s ovarian function because she desired future childbearing.

We confirmed the TAE results using color Doppler ultrasonography and 3D-CT angiography. The abnormal vessels of the AVM had almost disappeared on the left side of the posterior myometrium whereas the vessels on the right side were persistent with slight improvement (Figure 4). The patient resumed menstruation 1 month after the procedure, because danazol was stopped prior to TAE. Although slight hypermenorrhea was observed, it ended within 1 week without massive blood loss or a decrease in hemoglobin levels. Preservation of her

---

**Figure 2.** 3D-CT angiography. Diagnostic 3D-CT angiography clearly demonstrated hypervascular tangles of uterine vessels, feeding arteries, and remarkably dilated draining veins. The hypervascular tangles of tortuous vessels were fed by the uterine and ovarian arteries bilaterally, consistent with a true uterine AVM. Remarkable dilatation of the uterine and ovarian veins bilaterally, as well as early filling of the internal iliac vein and the inferior vena cava, were observed, indicating massive arteriovenous shunting in the myometrium [(A) anterior/posterior view; (C) posterior/anterior view]. AVM ¼ arteriovenous malformation; 3D-CT ¼ three-dimensional computed tomography.
ovarian function was confirmed by the occurrence of regular menstrual cycles, 2-phase basal body temperature measurements, and follicular stimulating hormone level (3.80 mIU/mL, Architect FSH, Abbott Japan).

Discussion

An AVM can be defined as a tangle of abnormal connections between an artery and a vein without an intervening capillary network. In general, AVMs are most commonly seen in the brain and the lungs. Although most AVMs found in the brain and the lungs are congenital, AVMs in the uterus are more commonly acquired. Congenital uterine AVMs arise as a result of a defect in embryonic vascular differentiation or developmental arrest of the primitive capillary plexus between the 4th and 10th weeks of embryonic life, and typically involve other organs. Acquired uterine AVMs frequently develop after uterine trauma, which can induce the formation of abnormal vascular communications between arteries and veins during healing. Although uterine trauma associated with pregnancy such as D&C, prostaglandin E1 (PGE1)-induced abortion, cesarean section, and vaginal delivery have all been listed as primary causes of acquired uterine AVMs, a small number of cases have also been reported from the insertion of intrauterine contraceptive devices, uterine tumors (endometrial carcinoma or cervical carcinoma), gestational trophoblastic disease, and uterine infections.

Uterine AVM can lead to profuse, life-threatening uterine bleeding, typically diagnosed by imaging techniques including ultrasonography, helical CT, or angiography in patients suffering from severe vaginal bleeding. Although this condition is thought to be rare, the true incidence of uterine AVM remains unclear. We recently performed a prospective evaluation of the incidence of uterine vascular abnormalities (defining the lesion as uterine “vascular malformation” according to Timmerman et al) in patients after abortion or delivery and in outpatients. We identified six cases of U-VM among 959 patients observed. One of the six cases was a patient with severe “true uterine AVM” and is presented in this manuscript. The study is ongoing and so far we have evaluated over 1000 patients, and have detected only one true case of AVM. We estimate from the study that the incidence of true uterine AVM is < 0.1%.

Although the patient was first referred to our hospital over 4 years ago and myomectomy and D&C were performed in our hospital, her uterine AVM was only diagnosed after we started screening for U-VMs in 2011. We retrospectively checked her clinical records and past grey-scale ultrasonography findings, and found that the hypoechoic lesion and dilated veins in the posterior myometrium were already evident after myomectomy. From these
retrospective ultrasonography findings, we estimated that her AVM was formed after myomectomy and not after the earlier D&C. As her uterine myoma was a hypertensive uterine leiomyoma and massive blood loss occurred during the operation, it was possible that abnormal arteriovenous connections leading to a severe AVM were formed during the wound healing process postmyomectomy.

The management of patients with uterine AVMs depends on the degree of uterine bleeding, hemodynamic stability, and desire for future fertility. Although hysterectomy is the definitive treatment for patients who do not desire future fertility, a more conservative approach is typically required because most AVMs occur in women of reproductive age. Since the first report of TAE as a treatment for AVM was made by Forssman et al in 1982, this technique has been increasingly used as an effective treatment for uterine AVM, as it is preferable for the preservation of uterine function and reproductive capability. Due to a high clinical success rate and low complication rate for TAE in the literature, it has been proposed that TAE should be the first choice for the treatment of uterine AVM in all women, whereas hysterectomy should be reserved for cases with recurrence of heavy uterine bleeding or the failure of alternative treatments. Although several successful pregnancies and deliveries after TAE for uterine AVM have been reported, an increased risk of pregnancy-associated complications such as spontaneous abortion, fetal growth restriction, stillbirth, uterine rupture, and uterine atony after birth, which are associated with poor vascularization, remains a concern.

In our patient, because the AVM flow was very active, large, and involved the entire posterior myometrium at the time of diagnosis without uncontrolled profuse bleeding, we selected danazol as a primary conservative treatment to control her intermittent vaginal bleeding, correct her anemia, and reduce AVM flow, thereby reducing the risks associated with TAE such as embolization through the AVM shunt to the lung. As danazol only partially reduces the abnormal flow, we performed TAE as a secondary conservative treatment, and embolization of the left ovarian and uterine arteries was successfully performed. Embolization of the right uterine artery was not performed although this artery contributed as a feeding artery to the uterine AVM, because we took into account the risk of losing ovarian function.

Although the patient’s uterine AVM has been successfully treated by danazol and TAE with N-butyl-cyanoacrylate, strict follow-up to monitor for the reactivation of the uterine AVM and recurrence of profuse uterine bleeding is necessary. If it reappears, immediate and appropriate management will be needed as the patient desires to become pregnant in the near future.

References