Our experience in the management of patients with uterine arteriovenous malformations

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Abstract

Uterine arteriovenous malformation (UAVM) is an uncommon condition consisting of shunts formed between the uterine artery and the myometrial venous plexus, usually found in the myometrium, but also in the endometrium, whose pathological mechanism of appearance is unclear. Although rare, UAVM present clinical importance due to its impact on patients' fertility or even life, because of its massive bleeding potential. There are various diagnostic and treatment techniques, angiography and uterine artery embolization being used in both ways.

Keywords: *uterine arteriovenous malformation, management, angiography*

Rezumat

Malformațiile arteriovenoase uterine (MAVU) sunt o patologie cu o incidență scăzută, caracterizându-se prin existența unui șunt între o ramură a arterei uterine și plexurile venoase intramiometriale. Această malformație este localizată de obicei în miometru, însă poate fi localizată și în endometru. Mecanismele de apariție ale acestei patologii sunt încă neclare. Cu toate că MAVU sunt patologii rare, ele sunt importante din punct de vedere clinic, din cauza riscului important de hemoragie masivă, care poate pune în pericol viața pacientei. Există multiple modalități de diagnostic și tratament, angiografia cu embolizare putând fi utilizată în ambele sensuri.

Cuvinte-cheie: *malformații arteriovenoase uterine, management, angiografie*

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Experiența noastră în managementul pacientelor cu malformații arteriovenoase uterine

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Introduction

Definition

Uterine arteriovenous malformation (UAVM) is a rare, uncommon, possibly life-threatening condition due to abundant vaginal bleeding, defined as a vascular hamartoma found in the uterine myometrial layer and sometimes in the endometrial layer[1-5]. UAVM are high-flow systems and consist of arteriovenous shunts, which appear between intramural branches of the uterine artery and the myometrial venous plexus and which lack the capillary bed between these two components[1-3,6-9].

Etiology

UAVM are usually found in women of reproductive age, between 20 and 40 years old, with the mean age of 30 years old, although there have been studies which suggest that UAVM may occur in women by the age of 60[4,9-11]. Rarely, acquired UAVM may affect nulliparous women whose personal medical history does not include trauma secondary to gynecological procedures[9].

UAVM is classified as congenital and acquired, the latter being more common[4,5,7,10]. Congenital UAVM consist of a nidus formed by a multitude of poorly differentiated small vessels which connect arteries with the venous system[7,8]. They are thought to be abnormal vascular connections that appear due to a defect during the embryologic differentiation of the primitive capillary system in the fetal angiogenesis stage, which present histologic similarities to AVM found in other sites of the body[1,9,10].

Acquired UAVM appears after trauma and is usually a single large artery which communicates with a single large vein, hence it is an arteriovenous fistula (AVF), although some acquired UAVM consist of multiple AVF[3,7-9]. Acquired UAVM may appear in certain situations, such as[1-5,8-11]:

- dilatation and curettage
- uterine surgery
- myomectomy
- ectopic implantation in a prior caesarean scar
- miscarriage
- voluntary pregnancy termination
- uterus examination
- *placenta accreta*
- vaginal delivery
- in association with gestational trophoblastic disease (GTD)

- endometrial adenocarcinoma
- cervix neoplasm
- inflammatory processes
- endometriosis
- pelvic and direct uterine trauma
- fibroids
- uterine infection
- intrauterine devices
- exposure to diethylstilbestrol.

It is thought that UAVM which appear after ectopic implantation in a prior caesarean scar might be the result of the erosive nature of syncytiotrophoblastic tissue and chorionic villi. Here, abnormal connections among vascular structures are induced by the defective decidual layer, to establish an adequate blood supply for the placenta, vessels that later will fail to obliterate[6,8,11]. Abnormal angiogenesis might also be promoted by the restriction due to the fibrous tissues and defective endometrium of cesarean scars[6].

In the case of *placenta accreta*, the retained villi in the uterine wall may recruit collateral vessels[8]. Although the exact mechanism of UAVM formation is unknown, it is thought that acquired UAVM appear due to a local immune response and angiogenesis that are induced by endometrial agitation, or subinvolution of placental bed or abnormal vessel communication in the site of chorionic villi implantation[4]. Also, in patients with retained products of conception (RPOC), after the necrosis of chorionic villi, there might appear arteriovenous communications[3].

Due to the physical alteration of the embryo's implantation site and increased vascularization, a personal history of recurrent spontaneous abortion might also be a risk factor for acquired UAVM[9].

Some studies suggest that hormonal mechanisms might play an important role in the development of UAVM, considering the worsening symptoms of acquired UAVM in pregnant patients[5,9]. Elevated human chorionic gonadotropin might promote cellular proliferation in latent UAVM[9]. Due to elevated levels of estrogens, women undergoing fertility treatments may also be at risk, since estrogens are known to modulate angiogenesis[9,12].

In patients who required uterine surgery, packing and clamping for hemostatic control may be the cause of fistula formation, because of the shunting of blood from the capillary plexus to the less resistant venous system[9].

Diagnosis

Although some patients with UAVM may be asymptomatic, most of them present with[1,4,6,9-11]:

- menorrhagia
- metrorrhagia
- irregular uterine bleeding
- massive life-threatening uterine bleeding
- profuse bleeding during curettage
- lower abdominal pain
- dyspareunia
- urinary symptoms (polyuria and incontinence)
- vague pelvic discomfort
- congestive heart failure due to shunting of blood to the venous system (rare)
- recurrent pregnancy loss (rare).

UAVM should also be taken in consideration in patients who present with unexplained uterine bleeding after abortion procedures[3].

The medical examination might reveal:

- transcervical bleeding
- palpable pulsating mass on pelvic examination
- vascular thrill in the vaginal fornices
- anemia
- hypotension
- hemorrhagic shock[1,6,11].

UAVM can be diagnosed with various tools, such as ultrasonography, including Doppler mode, hysteroscopy, contrast enhanced computed tomography, magnetic resonance angiography and angiography[6,11].

Although the appearance is not specific, the suspicion of UAVM should be raised in patients with small cystic lesions located in the myometrial layer or below the endometrium, found on gray scale transvaginal ultrasound[4,9]. On transvaginal Doppler ultrasonography, UAVM appear as hypoechogenic structures located in the myometrium that exhibit an abnormal hypervascular area with high-velocity, low-impedance flow that is multidirectional, irregular and turbulent, with a mosaic pattern[1,2,4,7,9,10]. The color score is usually 3 or 4[1].

Hysteroscopy may be used as a confirmatory imaging modality[2].

On MRI, the uterus is enlarged by an undefined mass containing tortuous and dilated vessels that involve de myometrium and the parametrium, this imaging approach being helpful in determination of the size and the extent of the UAVM[1,3]. It is a multiplanar imaging technique and is capable of good tissue contrast, thus it helps delineating the surrounding pelvic organ involvement[9].

Computed tomography angiography shows a soft-tissue density mass and can offer information about the involved vessels but is an invasive imaging technique[1,9]. It can also evaluate the involvement of surrounding visceral structures[9].

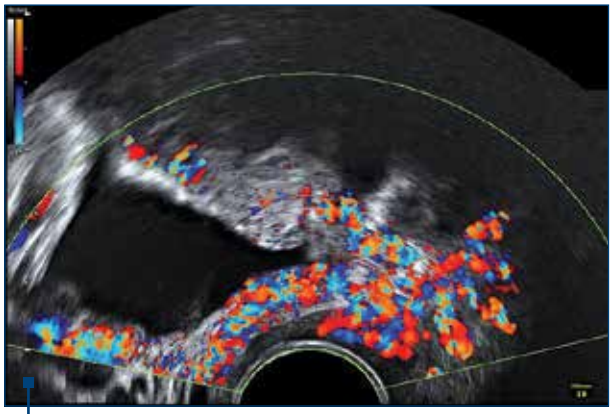

Figure 1. *Doppler ultrasonography in a 29-year-old patient illustrating the mosaic pattern caused by the anarchic flow of the blood inside the UAVM*

Angiography confirms the diagnosis by revealing tortuous expansion and engorgement of the blood vessels and early venous drainage into the myometrial and endometrial veins, suggesting the presence of AVS, but it is mostly used in patients requiring therapeutic embolization or surgical treatment[4,6,9,10]. Hence, angiography in association with arterial embolization is usually used for the treatment of UAVM[11].

Serial measurements of beta human chorionic gonadotropin might be appropriate, given that Doppler ultrasonography hardly differentiate between UAVM and GTD[1,9,10]. In GTD, but also in patients with RPOC, Doppler ultrasonography shows a hypervascular appearance with turbulent flow[1]. In both patients with RPOC and with UAVM, ultrasonography might illustrate echogenic material within the endometrial layer[7].

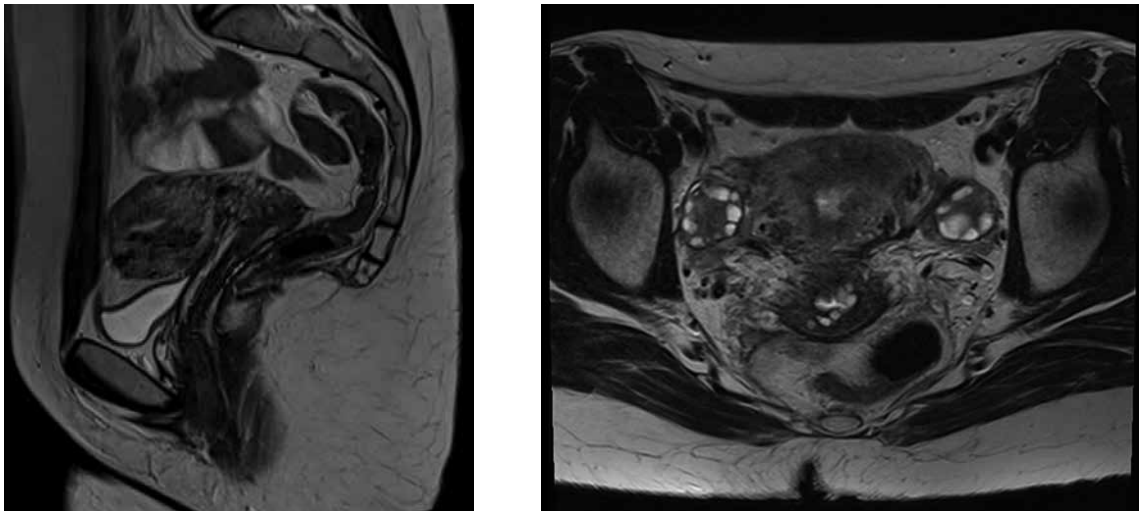

Figure 2. *On magnetic resonance, UAMV are suggested by the visualization of dilated and tortuous vessels in the myometrium*

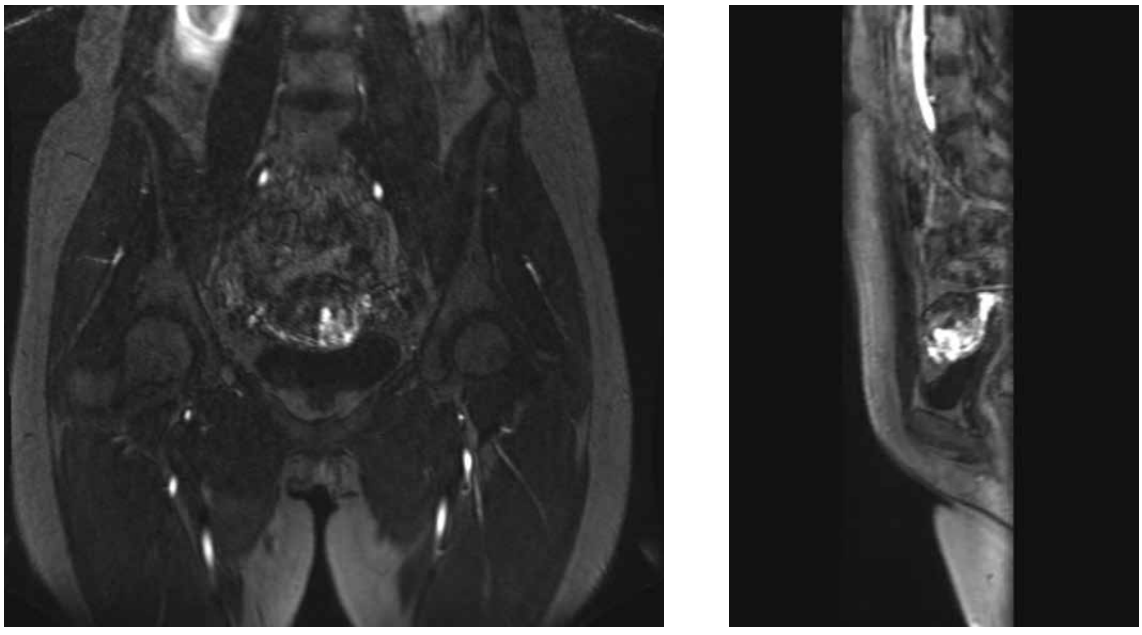

Figure 3. *Magnetic resonance angiography can be used to highlight UAVM*

However, on MRI, acquired UAVM primarily involves the myometrial layer and RPOC primarily involve the endometrium[9].

The differential diagnosis must also include adenomyosis and subinvolution of the placental bed, because both can present with hypervascularity and turbulent flow on ultrasound[9]. Also, vascular neoplasm and placental polyp may present with increased uterine vascularity and arteriovenous shunting[3].

The histopathologic exam reveals dilated blood vessels with irregular shape, found in the myometrial layer of the uterus[10]. There is a very thick venous structure, and the arteries lack the muscular tunica media and present an interrupted or absent elastic membrane[2].

Treatment

Due to its rare incidence, UAVM does not have a clear treatment strategy. Hence, the medical and surgical options are based on published case reports and clinicians' experience[2].

The treatment depends on the clinical presentation of the patient. Although rare, UAVM might be a cause of postpartum vaginal bleeding and represents 1-2% of genital and intraperitoneal hemorrhages[7]. Because of life-threatening uterine hemorrhaging, blood transfusions are required in approximatively 30% of patients[7,10]. Curettage is contraindicated, as it does not stop the bleeding and might even worsen this condition[6,10].

Angiography with uterine artery embolization is a minimally invasive procedure performed under local anesthesia or intravenous sedation[6]. It can use

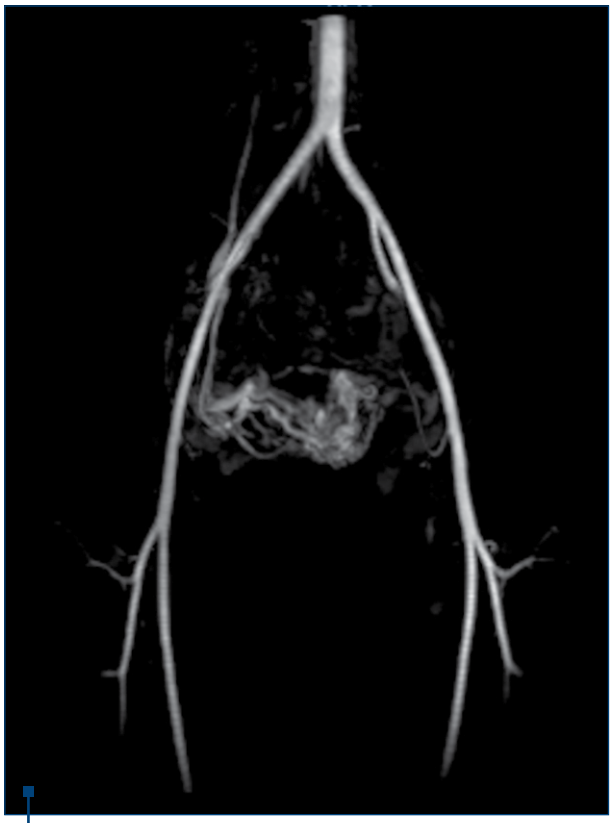

Figure 4. *Magnetic resonance angiography reconstruction of the UAVM with its arterial supply originating from the right uterine artery*

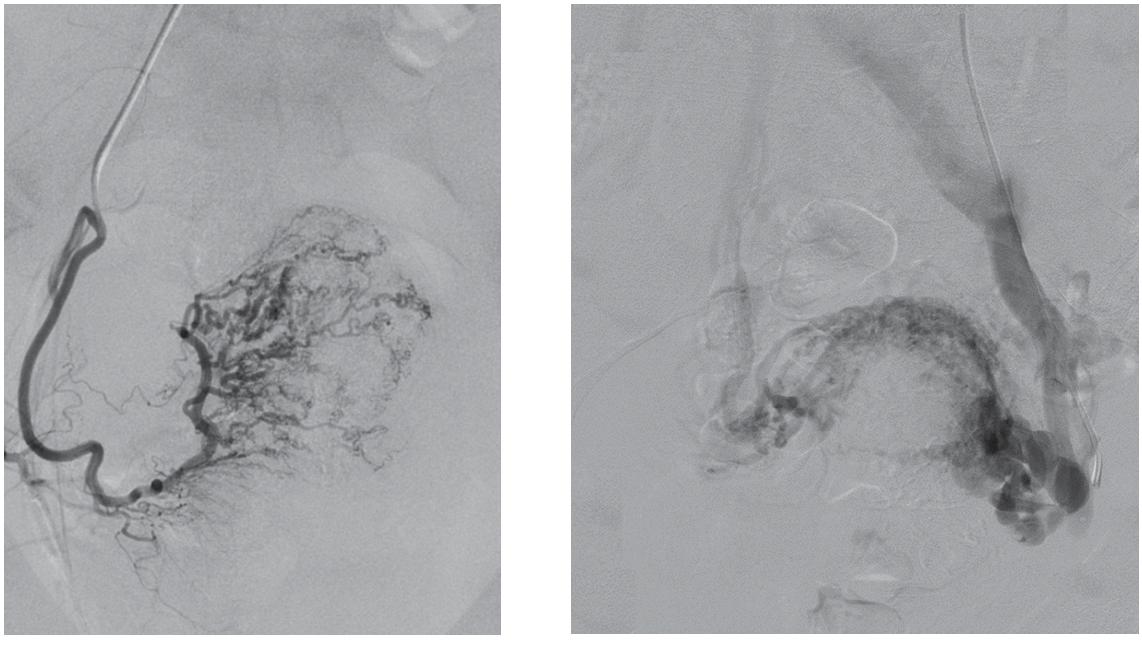

Figure 5. *Intraprocedural aspect (DSA – digital subtraction angiography) in a 29-year-old patient diagnosed with UAVM. Note the large dilated, tortuous left uterine vein (late phase)*

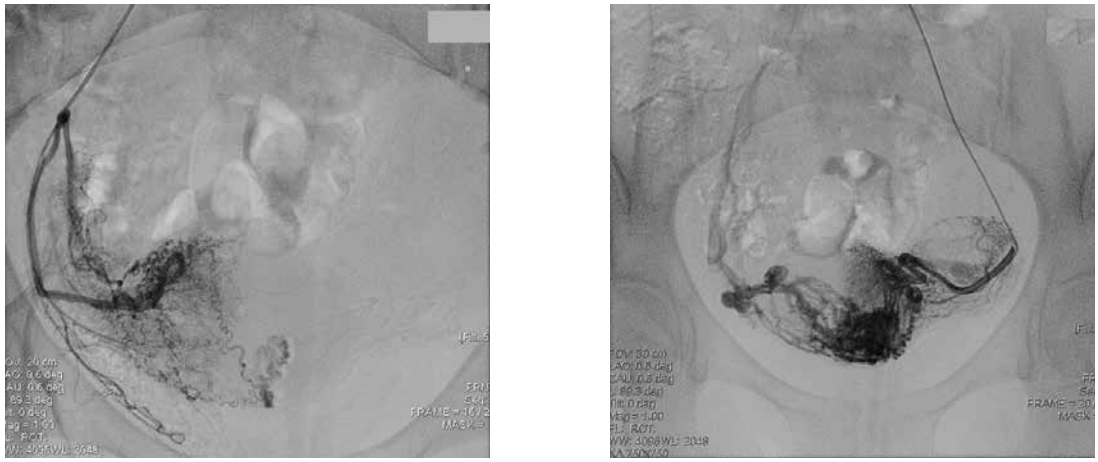

Figure 6. *Angiography revealed the fact that some of the UAVM are supplied from both uterine arteries*

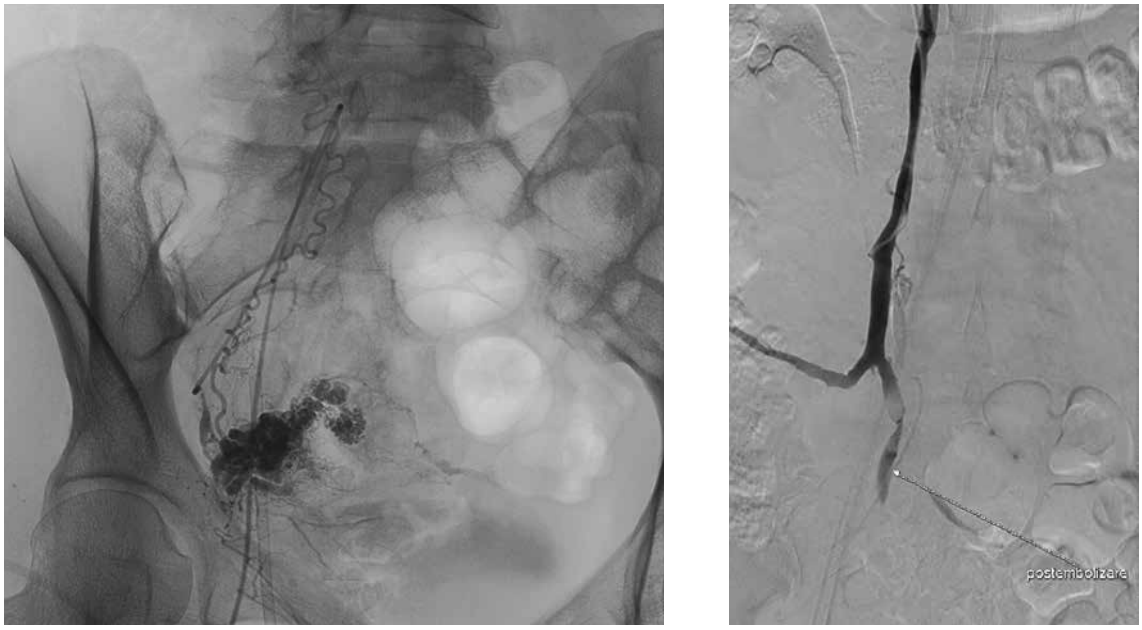

Figure 7. *Before and after embolization of a UAMV originating in the right ovarian artery (DSA – digital subtraction angiography)*

absorbable gelatine sponges, coils, glue, gelfoam, polyvinyl alcohol and microspheres[9,10]. The angiographic appearance determines, depending on the arterial supply of the UAVM, which artery should be occluded[9]. The advantages of the procedure include uterine preservation, shorter hospitalization period and lower morbidity[6]. The risks of uterine artery embolization include uterine ischemia, infarction and necrosis, uterine artery rupture, pelvic pain, transient or permanent amenorrhea and general complications, such as nausea and leukocytosis[2,6,9]. There are also the risks of the angiographic technique itself, such as puncture site hematoma, iatrogenic vessel dissection, contrast-induced nephrotoxicity and radiation exposure[2,9]. Some of the patients may experience recurrent bleeding after the procedure, depending on the embolization medium and because the UAVM may present multiple arterial feeders[6].

Other methods, such as second embolization, uterine embolization via laparotomy, UAVM excision,

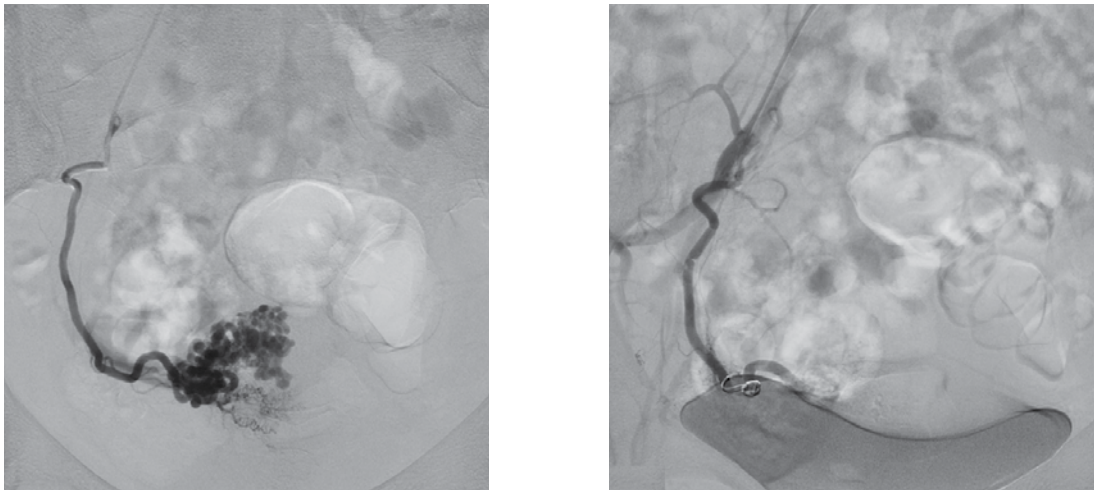

Figure 8. *Before and after embolization with a peripheral coil of a UAMV originating in the right uterine artery (DSA – digital subtraction angiography) in a 32-year-old patient*

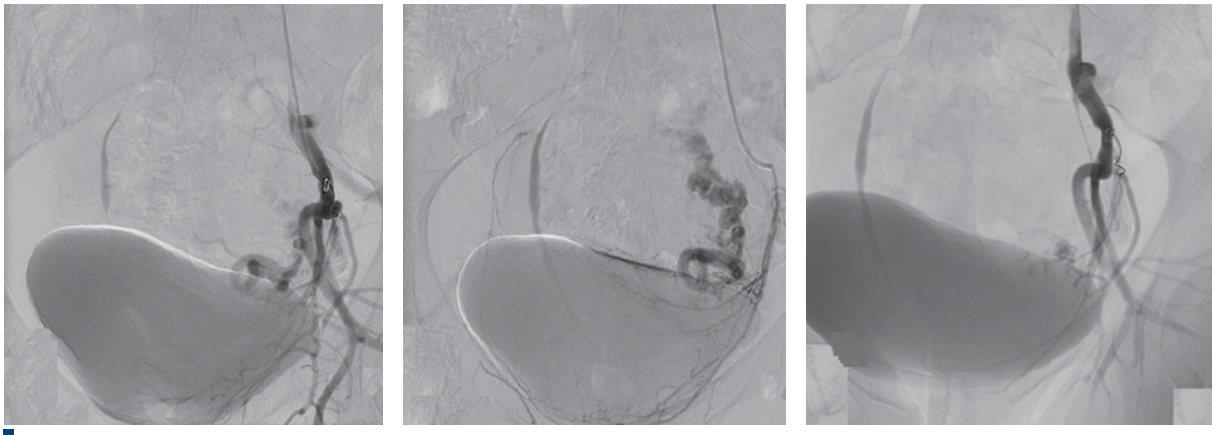

Figure 9. *Angiography with embolization series showing the occlusion with a peripheral coil of the supplying left uterine artery of the UAVM*

laparoscopic uterine or internal iliac artery ligation, unilateral or bilateral laparoscopic bipolar coagulation of the uterine arteries, laparoscopic UAVM excision, hysteroscopy and hysterectomy, are used less often[2,5,9,10]. Hysterectomy can be used in post-menopausal patients and in life-threatening cases[1,3,9].

The medical therapy can also be used in the treatment of UAVM for controlling bleeding, although there is a high rate of failure. The pharmacologic agents include methylergometrine, methylergonovine maleate, gonadotropin-releasing hormones agonists and danazol[1,2].

Ghizzoni et al. used the "watch and wait" management and observed the complete resolution of the uterine lesion, although the spontaneous UAVM resolution is not well studied[1].

Materials and method

Our study included 14 patients with acquired UAVM who were diagnosed between 2010 and 2021 in the Obstetrics and Gynecology Department of the Bucharest University Emergency Hospital, Romania. The inclusion criterion was the presence of UAVM on various imaging techniques, the most important of them being the ultrasonography. All patients underwent ultrasonographic examination (transvaginal and/or transabdominal). One patient was evaluated using magnetic resonance angiography. Computed tomography with contrast agent was used in one patient. One patient underwent hysteroscopy. Angiography was also used as a diagnosis tool, but mostly for treating UAVM, using gelfoam, coils and stents for artery embolization.

Figure 10. *Multiple coils and closure devices (Amplazer – white arrow) used in a 36-year-old patient to block a complex pelvic arteriovenous malformation*

Results

The mean age of the patients included in our study was 35 years old. Of our 14 patients, eight of them had a personal history of abortion (including voluntary pregnancy termination and miscarriage), five had a history of caesarean section, none of them had GTD and two of the patients did not have any risk factors, being nullipara nulligravida. Of the eight patients who had an abortion, four of them had difficult curettages.

In terms of symptoms, the patients presented with one or more symptoms. Hence, 13 of them had vaginal bleeding and secondary hypochromic microcytic anemia, four presented with vague pelvic pain, being scored 40-50 on a visual analogue scale, and one was asymptomatic.

All patients underwent ultrasonography, which illustrated myometrial anechoic areas of heterogenous aspect on grayscale and a mosaic pattern on Doppler examination (Figure 1).

Hysteroscopy was used in only one patient and did not show a specific aspect, since the UAVM was situated in the myometrium.

On magnetic resonance angiography, there were observed tortuous, dilated vessels in the thickness of the myometrial uterine layer (Figures 2, 3 and 4).

Computed tomography with contrast agent illustrated the UAVM along with its vascular arterial blood suppliers, right ovarian artery in this case. Beta HCG was measured in all our patients, but none of them had elevated levels suggesting the presence of pregnancy.

Angiography with embolization was used in 13 out of 14 patients, because one patient refused the procedure (Figures 5, 6, 7, 8, 9 and 10). In 12 patients, the procedure was a success, but one patient needed second embolization. None of our patients received medical therapy.

After angiography with embolization, ultrasonography was used to evaluate the success of the technique (Figure 11).

Discussion

Calzolari et al. report that, in a systematic review, 84% of patients presented with bleeding and in 30% of them blood transfusion was necessary[2]. In our study, 92.8% of the patients (n=13) presented with bleeding. Only one patient required blood transfusion.

Zhu et al. support the fact that the first treatment using angiography with uterine artery embolization had a success rate of 71%[10]. In our study, the success rate was 92.3% (12 out of 13 patients who underwent this procedure).

The method is used due to its ability to preserve fertility and to prevent the need for hysterectomy, although the literature results are conflicting[4,5,7,10]. In a study conducted by Zhu et al., the pregnancy rate after successful embolization of UAVM were low, probably because of a decreased blood flow of the placenta[10]. However, some of the patients associate obstetric conditions that can make it hard to determine the impact of uterine artery embolization on fertility[10]. Regarding the impact of angiography with embolization on the vasculature of the ovary, there is no consensus in the literature. On the one hand, Zhu et al. support that, although the arterial ovarian flow is transiently occluded, the clinically apparent injury of the ovarian function is low[10]. On the other hand, Ghizzoni et al. mention that uterine arterial embolization can be associated with the risk of ovarian insufficiency and, moreover, with the risk of placental abnormalities during the future pregnancies[1]. Pregnancy rate after uterine arterial embolization for UAVM varies between 17.4% in observational studies and 27% in case reports[2]. Also, if the pregnancy is obtained, there is a risk of spontaneous abortion, *placenta praevia*, *placenta accreta*, postpartum hemorrhage and a higher rate of caesarean section compared to the general population[2,9]. In cases of multiple embolization procedures, there was a poor pregnancy outcome or even secondary infertility[4]. Since the Bucharest University Emergency Hospital is a tertiary referral hospital which admits patients from all over the country, we were not able to monitor all our patients because of the lack of communication.

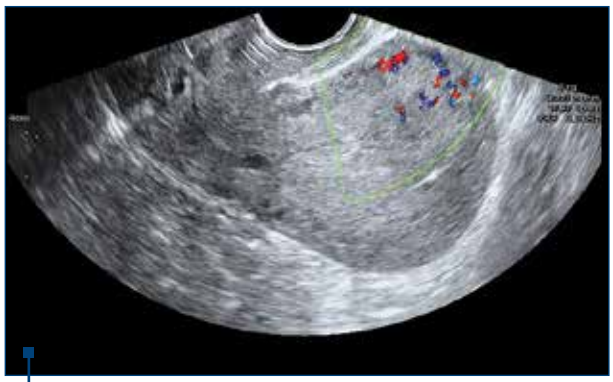

Figure 11. *Ultrasound examination of the 29-year-old patient presented in Figure 1 after the embolization*

Since one of our patients needed secondary embolization despite the appropriate procedure techniques, this might suggest that in some patients there are unknown mechanisms of persistence of the UAVM that are yet to be discovered.

Conclusions

UAVM management represents a challenge for the clinician, considering the absence of clear guidelines. Since its rare appearance in the obstetric and gynecologic field, larger multicentric studies might be appropriate in order to develop a management protocol of patients with UAVM. In those with persistent UAM despite the therapy, hormonal studies should be taken into consideration, since estrogens play an important role in angiogenesis. ■

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Conflicts of interests: The authors declare no conflict of interests.

References

1. Ghizzoni V, Gabbrielli S, Mannini L, Sorbi F, Turrini I, Fantappiè G, Noci I. Spontaneous resolution of an acquired uterine arteriovenous malformation in an elderly primigravida. Am J Case Repor. 2018;19:1140-5.
2. Calzolari S, Cozzolino M, Castellacci E, Dubini V, Farruggia A, Sisti G. Hysteroscopic management of uterine arteriovenous malformation. JSLS. 2017;21(2):532-41.
3. Goyal S, Goyal A, Mahajan S, Sharma S, Dev G. Acquired uterine arteriovenous malformation developing in retained products of conception: a diagnostic dilemma. J Obstet Gynaec Res. 2014;40(1):271-4.
4. Ho CY, Seow KM, Huang LW, Tsai YL. Fertility outcomes following pelvic embolization in women with acquired uterine arteriovenous malformation. Taiw J Obstet Gynec. 2017;56(6):831-5.
5. Vandenbroucke L, Morcel K, Bruneau B, Moquet PY, Bauville E, Levêque J, Lavoue V. Malformations artérioveineuses endo-utérines acquises. Gynéc Obstét Fertil. 2011;39(7-8):469-72.
6. Kim D, Moon NR, Lee SR, Won YD, Lee HJ, Park TC, Kim YH. Acquired uterine arteriovenous malformation in a cesarean scar pregnancy. Taiwan J Obstet Gynecol. 2013;52(4):590-2.
7. Scribner D, Fraser R. Diagnosis of acquired uterine arteriovenous malformation by Doppler ultrasound. J Emerg Med. 2016;51(2):168-71.
8. Moulder JK, Garrett LA, Salazar GM, Goodman A. The role of radical surgery in the management of acquired uterine arteriovenous malformation. Case Rep Oncol. 2013;6(2):303-10.
9. Yoon DJ, Jones M, Al Taani J, Buhimschi C, Dowell JD. A systematic review of acquired uterine arteriovenous malformations: pathophysiology, diagnosis, and transcatheter treatment. Am J Perinat Rep. 2016;6(01):e6-e14.
10. Zhu YP, Sun ZJ, Lang JH, Pan J. Clinical characteristic and management of acquired uterine arteriovenous malformation. Chin Med J. 2018;131(20):2489-91.
11. Roach MK, Thomassee MS. Acquired uterine arteriovenous malformation and retained placenta increta. Obst Gynec. 2015;126(3):642-4.
12. Losordo DW, Isner JM. Estrogen and angiogenesis: a review. Arteriosclerosis, thrombosis, and vascular biology. 2001;21(1):6-12.