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Uterine arteriovenous malformation

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Abstract

Background: Uterine arteriovenous malformations (AVM) are extremely rare entities, with less than 100 cases reported in the literature. Synonyms for AVM are arteriovenous fistula, branched aneurysm, hemangioma, pulsating angioma, and cavernous angioma. Incidence of uterine AVM according to the studies of O´Brien et al., who identified uterine AVM in 21 women based on 464 pelvic ultrasound examinations for uterine bleeding, reported an incidence of 4.5%. However, Yazawa et al. examined 959 patients prospectively and observed an incidence of 0.6% of uterine vascular malformation on ultrasound examination The etiology of uterine AVM can be congenital or acquired. The purpose of the study was to raise awareness on the existence of these injuries and understanding their risk factors, to study different treatment methods, especially conservative or minimally invasive ones, as well as methods for diagnosing of these malformations. The following key words were used as a search engine: uterine arteriovenous malformation, uterine malformation, circoid aneurysm. Only full-text articles were analyzed.
Conclusions: Uterine AVM is a rare cause of uterine bleeding. However, it is a potentially life-threatening disorder in which patients present with vaginal bleeding that may be profuse and cause hemodynamic instability.
Key words: malformations, uterine artery, venous system.

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Introduction

Uterine arteriovenous malformations (AVM) are extremely rare entities, with less than 100 cases reported in the literature. Uterine arteriovenous malformation (AVM) is defined as abnormal and nonfunctional connections between the uterine arteries and veins. The etiology of uterine AVM can be congenital or acquired; the incidence rate of acquired AVM is currently increasing [1-3]. Congenital lesions are considered to occur between the fourth and tenth week of embryogenesis as isolated, spontaneous failures of vascular development. Acquired malformations are more common and usually precede a pregnancy, being diagnosed after an uncontrolled uterine bleeding despite drug therapy [1]. Synonyms for AVM are arteriovenous fistula, branched aneurysm, hemangioma, pulsating angioma, cavernous angioma. AVM consists of proliferation of arterial and venous channels with fistula formation and a mixture of capillary-like vessels. It is difficult to distinguish between arteries and veins because secondary intimal thickening occurs in the veins due to increased intraluminal pressure [4]. Uterine AVM plays an important role in gynecologic practice due to the risk of massive bleeding that could be life threatening in some patients. In 1926, G. Dubreuil and E. Loubat described for the first time this pathology as a "branching aneurysm" [5]. Incidence of uterine AVM according to the studies of O´Brien et al. [6] who identified uterine AVM in 21 women based on 464 pelvic ultrasound examinations for uterine bleeding, reported an incidence of 4.5%. Instead, Yazawa et al. followed up 959 patients prospectively and observed an incidence of uterine vascular malformation on ultrasound of 0.6% [7]. Some authors consider that the term AVM is hyper-used once the number of examinations performed by ultrasnography or dopplerography has increased, and the lesions detected with hypervascular and/or turbulent flow are designated as unfounded "uterine vascular malformations". The term uterine AVM should be limited only to those lesions that prove a hypervascular mass, with early filling on angiography or on pathological examination of the uterus after hysterectomy. Uterine AVM can be the cause of unexplained uterine bleeding, the severity of which depends largely on their occurrence and the diameter of the hemorrhagic vessel. Commonly, the only way to stop the bleeding is surgical intervention. The described anomaly represents a direct communication between arteries and veins, formed by the internal iliac artery or its branches. These abnormalities consist of dysplastic vessels with an abnormal wall structure and usually persist lifelong, often without symptoms. All vascular abnormalities are divided into two main types: slow blood flow (capillary, venous, lymphatic) and fast blood flow (arteriovenous anastomosis), but sometimes mixed formations are found [8]. Acquired uterine arteriovenous abnormalities are most common in patients

with trophoblastic disease [9] or previous interventions on the uterus, which may be due to a previous uterine trauma (prior pelvic operation and curettage), pathologic pregnancy-related conditions and infections [10]. Although there are evidences that uterine AVM can be detected in patients under 18 years of age [11], usually this pathology is diagnosed at the age of over 30 years. According to J. Kasznica and N. Nissar arteriovenous abnormalities can also be congenital, being observed in an isolated uterine arteriovenous abnormality in a stillborn fetus [12]. Most of the described congenital arteriovenous abnormalities were diagnosed by ultrasonography in the prenatal and postnatal periods [13]. It should be noted that uterine AVMs are extremely rare in women who have not been pregnant. Apparently, pregnancy plays a role in the onset of uterine AVM [14]. Often the disease is combined with spontaneous abortion. All women of reproductive age with abnormal vaginal bleeding and a negative pregnancy test (absence of functional trophoblast tissue) may be susceptible to uterine AVM [6]. It is important to suspect uterine AVM in the differential diagnosis of unexplained vaginal bleeding, intermittent births and in women of reproductive age, postpartum or following surgical procedures in the uterus.

Acquired malformations may be due to previous uterine trauma (prior pelvic operation and curettage), pathologic pregnancy-related conditions, infections, and the treatment of gestational trophoblastic disease. Congenital AVMs are considered to arise from arrested vascular embryologic development resulting in anomalous differentiation in the capillaries and abnormal communication, between the arteries and veins. Moreover, congenital AVMs can have multiple vascular connections and may invade the surrounding structures. It is important to diagnose uterine AVM correctly and to start appropriate treatment promptly, because uterine AVM often causes life-threatening massive and persistent vaginal bleeding [15, 16].

Although the imaging characteristics of congenital and acquired AVMs may be similar, a detailed history may help to distinguish between these two. Congenital lesions are commonly presented by severe menorrhagia, which do not respond to traditional drug therapy. Traumatic uterine AVMs are often present with features suggestive of arterial bleeding. They tend to cause episodic vaginal bleeding, which is often torrential, leading to significant anemia and even shock.

Clinical manifestation

It is important to consider uterine AVMs in the differential diagnosis of unexplained, intermittent and heavy vaginal bleeding in women of reproductive age, after delivery or surgical procedures on the uterus. Although the imaging features of congenital and acquired AVMs may be similar, a thorough history may help to distinguish between the two [6].

Congenital lesions classically present with severe menorrhagia, irresponsive to conventional therapy. Acquired or traumatic AVMs are invariably associated with one of the risk factors previously mentioned. The symptoms can appear very slowly or suddenly. Vaginal bleeding occurs when the endothelial lining of the vessels in the AVM is disrupted, such as during menstruation or curettage [17].

Traumatic uterine AVMs often present with features suggestive of arterial haemorrhage. They tend to cause episodic vaginal bleeding, which is often torrential, leading to significant anaemia and even shock. It is critical under these circumstances to consider the diagnosis of uterine AVM and avoid attempts of uterine instrumentation (dilatation and curettage), which may significantly worsen the bleeding. Large AVMs may present as clinically recognizable pulsatile masses, which may aid in making the correct diagnosis [18].

Sonographic features suggestive of uterine AVM can be found in women, who present with vaginal bleeding and a positive pregnancy test. Under these circumstances, pregnancy-related conditions, such as intrauterine pregnancy, ectopic pregnancy, retained products of conception, or gestational trophoblastic disease should be considered. A combination of history of the specific pattern of vaginal bleeding, a negative pregnancy test and characteristic features on colour and spectral Doppler should be used to diagnose uterine AVM.

Investigation

Traditionally, uterine AVMs are diagnosed accidentally after hysterectomy based on histopathological evidence of arteriovenous fibers. Yet, the gold standard for diagnosing uterine AVM is pelvic angiography [15]. Findings with DSA include bilateral hypertrophy of uterine arteries that feed a tortuous, hypertrophic arterial mass with large accessory feeding vessels, and early drainage into enlarged hypertrophic veins [19]. However, angiography is rarely performed for diagnosis alone, due to its invasive nature and it is usually reserved when a patient requires surgical intervention or embolisation [20]. Gray scale ultrasound (US) can detect the presence of multiple tubular or "spongy" anechoic or hypoechoic areas within the myometrium of a normal endometrium. However, other conditions may present a similar appearance, such as retained products of conception, hemangioma, gestational trophoblastic disease, multilocular ovarian cysts, or hydrosalpinx. Thus, the use of colour and spectral Doppler US is important for obtaining more accurate information. A normal myometrial signal will show a PSV of 9–44 cm/s and RI of 0.6–0.8. In addition, uterine AVM will exhibit intense vascular and multidirectional flow (regions of juxtaposed reds and blues caused by multiple tortuous vessels of varying orientations). Spectral Doppler US will show high velocity (mean PSV: 136 cm/s), low resistance (mean RI: 0.3) flow, low pulsatility of the arterial waveform, and pulsatile high-velocity venous waveform. Differentiation between the venous and arterial waveform is often difficult, and the pelvic veins distal to the AVM may show pulsatile flow instead of the normal monophasic flow [15, 21].

Gadolinium-enhanced MRI demonstrates a hypervascular arterial-dominant flow. Similar to MRI, computed tomography (CT) may be used to determine the size, ex-

tent, vascularity, and involvement of the adjacent organs [22, 23]. In angiographs, the affected arteries appear thicker and more convoluted than the normal ones. AVMs appear as a complex tangle of vessels supplied by enlarged feeding arteries and show early venous drainage during the arterial phase [24]. Angiography, an invasive technique, allows the confirmation of the diagnosis and helps identify the leading feeder vessels where embolization may be indicated as a conservative treatment option.

Several cases of AVMs have been found during hysteroscopy, but their value is limited [25]. Uterine AVMs should be differentiated from the retained products of conception, gestational trophoblastic disease, dysfunctional uterine bleeding, subinvolution, hemangiomas, varicosities, and malignancies of the uterus, such as sarcomas. When the clinical history, ultrasonographic findings, and serum β-hCG test results are considered, AVMs can be differentiated potentially from these pathologic conditions with an arteriovenous shunt. Meanwhile, overdiagnosis of uterine AVMs should be avoided [22].

Principles of therapeutic management

The therapeutic management of uterine AVM depends on the following factors: hemodynamic status, size and location of the lesion, degree of hemorrhage, age, desire for future fertility. When a woman has severe vaginal bleeding, the basic principles of resuscitation must be followed, and stability and hemodynamic recession must be achieved and maintained. The mainstay for management of uterine AVM has been hysterectomy or the embolization of uterine arteries. However, the uterine artery embolization (UAE) remains the first choice of treatment in women at reproductive age having expectation of future fertility [26]. Whether this procedure is safe for women desiring future fertility is controversial; however, women who become pregnant after UAE are at risk of malpresentation, caesarean delivery, preterm birth, and postpartum hemorrhage.

Hysterectomy remains the last but the most appropriate treatment, especially for women with uncontrolled bleeding, who do not respond to drug therapy and for people who do not want to maintain fertility. Therapeutic options for uterine MAVs range from medical hormone therapy to uterine artery embolization or permanent hysterectomy. Internal iliac artery ligation or uterine artery ligation and/or hysterectomy were the traditional treatment options for counterproductive due to the development of a rich collateral blood supply distal to the ligature, resulting in a recurrence of hemorrhage after surgery. Advances in pelvic angiography and selective arterial embolization techniques have shown that embolization is currently the preferred therapeutic option for uterine AVM, and internal ligation of uterine AVMs in the past, and ligation of the internal iliac artery may prove that the iliac artery may have an important role in cases of failed embolization.

A minimally invasive approach through angiographic embolization of the AVM is currently the preferred treatment for uterine AVM. There are both permanent and temporary methods of embolic agents that can be used as an embolic agent. Various embolic materials can be used, including polyvinyl alcohol, histoacryl (glue), stainless steel coils, detachable balloons, and hemostatic gelatine. However, uterine artery embolization may not always be successful and multiple sessions may be required for recurrent episodes [15]. Imaging assessment of uterine AVMs, especially their vascular anatomy, is very important during the planning stages before embolization, such as Doppler ultrasonography, CT, and MRI [26-29]. Pre-procedural imaging evaluation is necessary in order to assess the presence of possible extra-uterine feeders. An example is the ovarian-uterine anastomotic connection, which is often detected when performing UAE for uterine fibroids [30, 31]. Possible complications of angiographic embolization include infection, perianal skin sloughing, uterovaginal and rectovaginal fistulas, and neurological deficit in the lower limb [6]. Fertility after UAE remains speculative. Despite advances in therapeutic techniques and embolic agents, pregnancy following successful embolization of uterine AVMs remains rare [32]. Decreased vascularization of the placenta has been proposed as being the main cause of adverse pregnancy outcomes following embolization.

This literature review was made by accessing and analyzing the MEDLINE and Hinari databases. The key words used as search engine were uterine arteriovenous malformation and uterine malformation. Only full-text articles were analyzed.

Conclusions

Uterine AVM is a rare cause of uterine bleeding. The vast majority of AVM cases resolve spontaneously or medically. The rest of the cases normally respond to conservative management options. Uterine AVMs have the potential to cause life-threatening bleeding, despite the fact that, with the availability of uterine artery embolization, hysterectomy is rarely necessary to stop the bleeding. The normal menstrual cycle and fertility are restored in the vast majority of women suffering of this condition.

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Author's contribution
CT designed the study, drafted the first manuscript and completed the final design.

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Ethics approval and consent to participate
No approval was required for this review study.

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