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Arteriovenous malformations (AVM) of the corpus uteri

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Summary

Introduction: The arteriovenous malformations (AVM) are sporadic lesions and they consist in a large number of tortuous, dilated, and thick-walled vessels with different sizes. AVM can be divided into two distinct types, in relation to their site: the superficial type and the deep type. Uterine AVM are precisely labelable as deep AVM and they are well-known in the gynaecological and radiological practice, but rarely reported in the histopathological literature. *Materials And Methods:* To fill this gap, the authors have retrospectively examined 25 cases of incidental uterine AVM from post-menopausal Caucasian women with a mean age of 68 years (range 63 and 74 years), who underwent hysterectomy with bilateral salpingo-oophorectomy for uterine prolapse. Surprisingly, in the anamnestic records, all the patients suffered from dysmenorrhea during their life. Moreover, they have reviewed about 300 cases of uterine AVM, reported in the gynaecological and radiological English literature, correlating them with their observations. *Results:* From their results, it emerged that the use of the term 'acquired' to describe uterine AVM should be avoided, because all the present lesions show a malformative morphology, related to a developmental disorder. Since no criteria exist to differentiate between AVM and placental bed sub-involution, a descriptive nomenclature should be preferred in the radiologic terminology. *Conclusion:* AVM should be routinely remarked in the histopathological reports, because their presence could be correlated with an explainable history of dysmenorrhea. Even if embolization remains an acceptable form of treatment in order to avoid hysterectomy in those patients presenting with heavy life-threatening bleeding, a vasoconstrictive therapy could be considered when other possible causes of disabling dysmenorrhea are excluded and the presence of AVM at high flow has been ascertained by eco-colour Doppler.

Key words: Arteriovenous malformation (AVM); Uterus; corpus uteri; Histology; Dysmenorrhea; Vasoconstrictors.

Introduction

The arteriovenous malformations (AVM) are infrequent lesions and they consist of a large number of tortuous, dilated, and thick-walled vessels with different sizes, showing at least a focal presence of the internal elastic lamina [1]. The AVM can be divided into two distinct types, in relation to their site. Deep AVM are commonly located in head and neck region, limbs, gastrointestinal tract, central nervous system or deep soft tissues. The superficial type, in contrast, is usually located in the skin of face or neck among middle-aged or elderly adults, it is much smaller, and it is not associated with any appreciable circulatory disturbance [1]. In clinical practice, the diagnosis of uterine AVM can be achieved by radiological procedures. The lesions appear as hypoechoic winding spaces inside the myometrium with a low impedance and a high flow on colour Doppler examination [2, 3]. Angiography may be a further diagnostic procedure to ascertain their presence [4], while their embolization has been proposed as an effective and safety therapeutic solution [5]. Here, the authors studied a 25-case series of deep AVM of the corpus uteri, correlating their observations with a critical review of the terminology in the medical literature, while providing also a possible non-invasive therapeutic solution for symptomatic patients.

Materials and Methods

We enrolled in this study 25 cases of incidental uterine AVM from post-menopausal Caucasian women with a mean age of 68 (range 63 and 74) years, who underwent hysterectomy with bilateral salpingo-oophorectomy for uterine prolapse at the *Santa Maria del Carmine* Hospital in Rovereto (Italy), from 2005 to 2015. During anamnesis, all the patients suffered from dysmenorrhea during their life. We applied clear and reproducible inclusion criteria in the diagnostic phase. Firstly, we have considered only AVM lesions characterized by thick-walled vessels, haphazardly arranged in myometrium and perimetrium. Secondly, the lesions had to involve more than the 75% of the myometrium, until they reached the basal endometrium. The surgical specimens were fixed in neutral-buffered formalin for at least 24 hours and then paraffin embedded. The tissue section, obtained from the paraffin blocks, were routinely stained with Haematoxylin and Eosin (H&E).

Results

On macroscopic examination, the uterus measured 7× 4.5×3 cm on average, while the ovaries appeared slightly enlarged in relation to age in every case. The most significant finding was a red-brown appearance of the corpus, which showed a myriad of vascular channels by sagittal sectioning (no lesion involved the cervix uteri). In four patients, small sub-serosal leiomyomas were found. On microscopic examination, the myometrium

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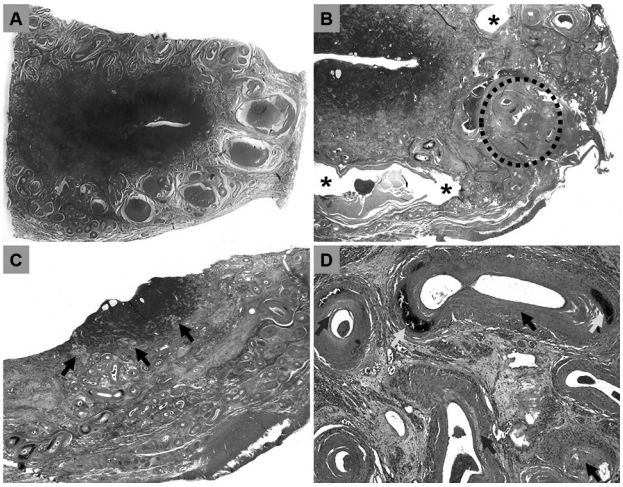

Figure 1. — In a panoramic view, MAV appears as a large amount of thick-walled engorged vessels of medium and large size anastomosed to each other, surrounding the endometrium and involving more than the 75% of the myometrium and the perimetrium (A, H&E, ×2.5). The vessels are arterial (circle) or venous (asterisks) in nature (B, H&E, ×5); they reach the basal endometrium (arrows), which is atrophic (C, H&E, ×5). At higher magnification, the vascular structures exhibit degenerative changes, such as tunica media calcification (yellow arrows), intimal proliferation with fibrosis (black arrows), and mucoid degeneration (blue arrows) of the wall (D, H&E, ×10).

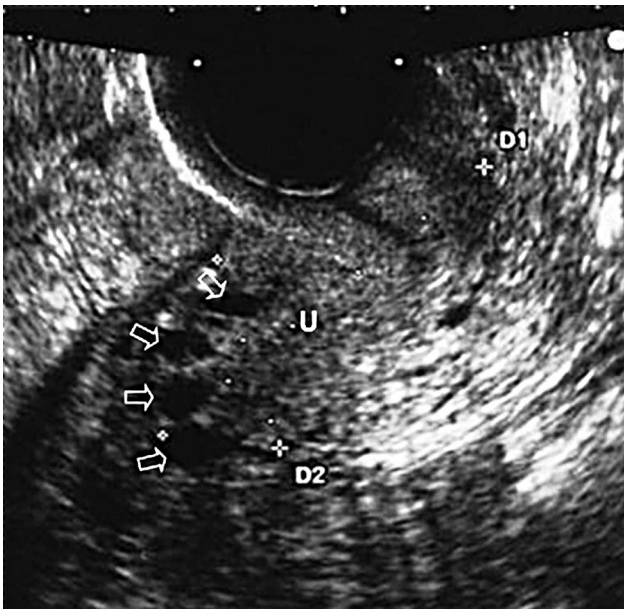

Figure 2. — An exemplificative ultrasound scan of the uterus (U), performed by a 6.5-MHz transvaginal probe, which shows multiple anechoic round and oval areas, 5 mm in maximum diameter (arrows), into the myometrium at level of the uterine corpus/fundus (D1 and D2).

and both ovarian hila were affected by a diffuse proliferation of medium and large sized arteries and veins, in close association, with a malformative nature (Figure 1, panels A and B). The endometrium was atrophic and surrounded by the underlying myometrial vessels (Figure 1, panel C). The arteries showed striking degenerative changes, including intimal proliferation, fibrosis, and medial calcific sclerosis, also called Mönckeberg's arteriosclerosis (Figure 1, panel D). The veins exhibited intimal thickening too.

Discussion

Uterine symptomatic AVM is associated with recurrent pregnancy loss, menorrhagia, menometrorrhagia or abnormal heavy bleeding after invasive procedure. Its possible presence should be always considered in patients presenting with abnormal heavy uterine bleeding and negative human chorionic gonadotropin values [6]. Moreover, the consequences of a curettage in case of undiagnosed AVM can be life-threatening [6]. In all patients of this series, hysterectomy was performed for uterine prolapse and the AVM of the uterine corpus was an incidental finding. In the assessment of uterine AVM, an evident discrepancy between few histological studies and numerous gynaecologic and radiological reports can be noted. Insun *et al.* associated AVM with massive operative bleeding in a 47-year-old patient and histologically documented irregular-shaped vessels grouped within the myometrium [7]. Chien *et al.* described another case of uterine AVM rupture suggesting that it can be the cause of copious and unexplained vaginal bleeding, sometimes difficult to treat [8]. Kasznica *et al.* reported in a 34-week stillborn female fetus the presence of vascular channels evenly distributed throughout the entire myometrium and the basal endometrium [9]. In a hysterectomy specimen, Busmanis *et al.* described the histological features of AVM, associated with florid myometritis in a 67-year-old Chinese woman [10]. Ciani *et al.* reported a haemorrhagic myometrial nodule of 20 mm in diameter, in a 56-year-old woman with grade III uterine prolapse. The lesion microscopically corresponded to a tangle of intermingled hyperplastic arteries and veins of intermediate size. The diagnosis was 'acquired AVM with massive endometrial stromal component' [11]. Brown *et al.* described a case of uterine AVM in a 29-year-old woman with gross and microscopic documentation. The patient had been treated with methotrexate for non-metastatic gestational trophoblastic disease [12]. To the present authors' knowledge, about 300 cases of AVM have been reported in gynaecological and radiological English literature, where they are curiously classified as congenital or acquired [13-15]. The first should be intended due to a disorder in the embryonic vascular development, while the second as the

result of a previous uterine tissue damage, such as trophoblastic disease, incomplete miscarriage, caesarean section, dilation and curettage, uterine infection, myomata, endometriosis, and exposure to diethylstilboestrol [13-15]. From the present series, the term acquired AVM should be avoided, because all the lesions show a malformative morphology. They are in fact composed of distinctive thick-walled vessels and not simple thin-walled capillaries, as observed in course of AVM in other districts [16]. Moreover, they are haphazardly arranged in the myometrium and perimetrium, involving more than the 75% of the myometrium, until they reach the basal endometrium. Timmerman *et al.* conducted a prospective study regarding 30 consecutive patients with uterine AVM diagnosed by ultrasonography and eco-colour Doppler imaging [17]. Spectral analysis of the vessels showed the presence of low impedance and high-velocity flow. Eight patients required embolization of uterine arteries and three of them had true AVM. In six cases, molar pregnancy was discovered and embolization of uterine arteries was not necessary. Trophoblast tissue was detected in six cases and unilateral embolization of uterine arteries was performed in two cases. The authors concluded that a conservative management is possible in more than two-thirds of patients. Moreover, in their study, no AVM without prior pregnancy was encountered in the examined patients [17]. This data supports the present authors' thesis, suggesting that many cases of AVM, labelled as acquired, could simply represent a sub-involution of the placental bed. At the present time, no criteria exist to differentiate between AVM and placental bed sub-involution, based on ultrasonography with colour Doppler imaging. For this reason, a descriptive terminology, such as 'arteriovenous shunt' or 'arteriovenous fistula', should be preferred in the radiological practice (Figure 2).

Conclusion

AVM should be always remarked in the histopathological reports because their presence can be correlated with an unexplainable history of dysmenorrhea, regardless of past pregnancies. Therefore, when other possible causes of dysmenorrhea are excluded and the presence of AVM at high flow has been ascertained by eco-colour Doppler, a vasoconstrictive therapy could be a viable approach in those patients affected by disabling pain. A low-dose use of methylergometrine, an analogue of the alkaloid ergonovine present in ergot, could be proposed to these patients; methylergometrine is in fact a well-known vasoconstrictor used as salt of maleic acid (methylergonovine maleate) in obstetrics and gynaecology to stop uterine bleeding [18]. However, patients presenting with heavy life-threatening bleeding must be immediately treated; embolization remains an acceptable form of treatment in order to avoid hysterectomy.

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