Pregnancy after uterine arterio-venous malformation – case series and literature review

Abstract

Purpose: To perform a retrospective audit of cases of uterine arteriovenous malformations (UAVM) at The Canberra Hospital and review of recent literature reporting pregnancies occurring after the diagnosis of UAVM aiming to devise a diagnostic and treatment protocol to optimise pregnancy post UAVM.

Methods: A retrospective audit of cases of UAVM at the Canberra Hospital from a prospectively managed patient database was performed. A search of the electronic database PubMed, for articles between 2000-2011 relating to pregnancy post UAVM. Individual case studies were analysed separately to case series.

Results: The study included 28 individual studies and five case series (61 women). Average age was 29.5 ± 6.7 (range 18–42). Most women (24, 85.7%, 100% in case series) presented with abnormal vaginal bleeding; 11 (41%) individuals presented post interruption of pregnancy. All women had had a previous pregnancy (mean gravidity 3.1 ± 3.1, range 1–15 for case studies) and only four women (14.2 %) had no history of uterine trauma. Only one woman (3.6 %) did not have any ultrasound and most women underwent colour Doppler ultrasonography (20, 71.4% in case studies; 61, 83.6% in case series). Of the women, 72 (53.6 % of case studies, 78.1% of case series) were treated with uterine artery embolisation, seven (25%) were treated expectantly. A total of 63 pregnancies occurred post treatment, seven (13.9%) ending in miscarriage. Average time to conceive post diagnosis was 19 months ± 16.3 (range 2–72). A total of 54 healthy infants were born to mothers post AVM diagnosis.

Conclusion: UAVM are likely to exist on a continuum with other pregnancy related pathologies, such as sub involution of the placental bed, making a single best diagnostic and treatment plan difficult. However, this study shows that successful uncomplicated pregnancy is achievable for women after the diagnosis of UAVM.

Keywords: uterine arteriovenous malformation, pregnancy, ultrasound.

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Introduction

Uterine arteriovenous malformations (UAVM) are abnormal connections between uterine arteries and veins.[1] UAVM can be congenital or acquired/traumatic. The clinical presentation of UAVM are variable – the classical clinical feature is intermittent, heavy vaginal bleeding, which can be life threatening. UAVM can also be fairly asymptomatic.[2] The incorporation of necrotic villi in the venous sinuses of scar tissue is thought to cause acquired UAVM.[3] An acquired UAVM almost always occurs after a uterine trauma, such as dilation and curettage or caesarean section but can also be associated with normal vaginal birth or malignancy.[4] UAVM may also be congenital, occurring rarely in the uterus, and usually invading surrounding structures.[5] Congenital lesions classically present with severe menorrhagia, unresponsive to conventional therapy.

UAVM can be diagnosed with grey scale and colour Doppler ultrasonography, MRI and CT angiography; radiographic angiography remains the gold standard.[6] There can be considerable overlap in the presentation and appearance of UAVM and other pathologies related to pregnancy and uterine trauma, such as sub involution of the placental bed (SPB),[3] retained products of conception (RPOC) and gestational trophoblastic disease (GTD).[7] UAVM can also occur concurrently with or post resolution of a spontaneous incomplete miscarriage as well as trophoblastic disease.[7] Accurate diagnosis is critical, as the treatment for RPOC and GTD (generally dilation and curettage) is contraindicated in UAVM, as there is the risk of causing massive haemorrhage and death.[8]

UAVM are characterised by a negative beta human chorionic gonadotrophin (BHCG) value, which is usually weakly elevated in RPOC and

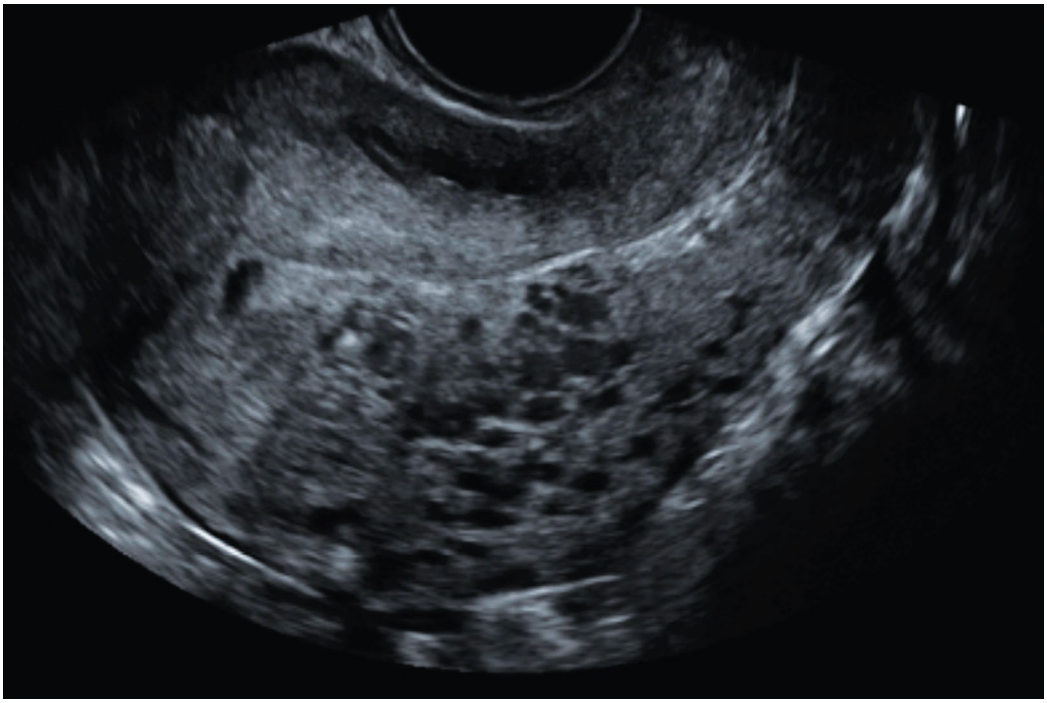

Figure 1: 2D grey scale images of an UAVM – note the multiple anechoic spaces.

grossly elevated with GTD.[9] RPOC, GTD, UAVM and SPB can present with vaginal blood loss or haemorrhage,[10–12] with RPOC and SPB exclusively occurring post pregnancy.[10,12] GTD and UAVM can be discovered during or post pregnancy.[11,13] UAVM appear as multiple anechoic spaces in the myometrium (Figure 1), with a typical spectral Doppler appearance of turbulent flow (Figure 2), low resistance, high velocity. A colour mosaic pattern is seen with colour Doppler imaging.[14] A key feature is that the colour Doppler images are vastly more informative than the grey scale imaging. SPB appear similar to UAVM.[3] RPOC are seen on ultrasound as a focal echogenic mass in the endometrium with low resistance flow[9], while GTD has anechoic spaces and an absence of a fetus.[11]

Standard of treatment for UAVM was previously hysterectomy, current fertility preserving techniques, mainly uterine artery embolisation (UAE), are becoming more widely accepted.[15] The uterine artery is embolised with micro particles, coils, glue or alcohol, while collateral supply maintains uterine perfusion, thus preserving fertility.[16,17]

There have been several case studies of pregnancy after embolisation for UAVM in the literature, but only a few reviews, and no classification scheme for best diagnostic methods and outcome incorporating clinical presentation and past medical history. This paper aims to review the literature and add a retrospective audit of a further case series to devise a diagnostic and treatment protocol for maximising fertility post UAVM.

Methods

Search strategy

The PubMed search engine was used, searching for English articles, between 1st January 2000 and 30th June 2011 with the search terms "uterine arteriovenous malformation". A MeSH search was also performed, using terms "uterine", "arteriovenous malformation" and "arteriovenous fistula". Cases where a pregnancy occurred after diagnosis and/or treatment of an UAVM as well as cases where UAVM was diagnosed and treated during a pregnancy were included in the current study. Articles pertaining to congenital UAVM were excluded. Case studies and series were used, although only case series in which sufficient individual patient data could be extracted were used in pooled calculations. Case series where there were insufficient individual data were collated separately. Cases where UAVM were diagnosed or treated during a pregnancy were included for completeness, but were not used in the frequency calculations

Retrospective case series

Thirteen women were diagnosed with uterine UAVM in the Fetal Medicine Unit (FMU) at The Canberra Hospital (TCH), Canberra, between 2000–2011. Only those patients who conceived post diagnosis were included in the current study. Ethics approval for the study was obtained from the ACT Health Human Research Ethics Committee (ETHLR.11.122).

Data

From both the literature and the cases seen at TCH, the following data was extracted (where it was supplied): author's names, date of publication, patients age, gravity and parity at time of diagnosis, brief summary of presenting complaint (menorrhagia, haemorrhage, abnormal vaginal bleeding), relevant past medical history (mainly obstetric history and uterine trauma), BHCG levels at time of treatment, diagnostic methods, size of AVM, length of time between AVM diagnosis and uterine trauma, treatment, number of UAE procedures, description of UAE procedures, embolic agent used, which uterine artery embolised (right, left or both), was the AVM diagnosed during a pregnancy, spontaneous pregnancy losses post treatment, how long was the time to conceive post treatment, at what gestation was the subsequent pregnancy delivered, what

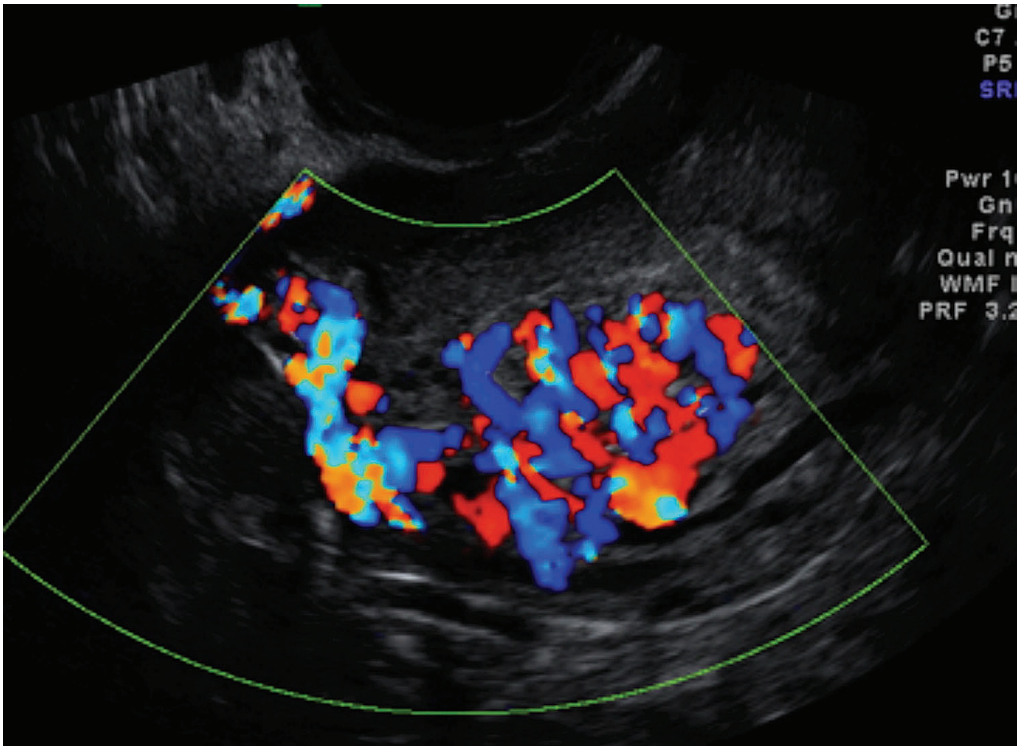

Figure 2: Colour Doppler image demonstrating turbulent flow creating a mosaic pattern.

type of delivery (vaginal, forceps or caesarean), complications of pregnancy/delivery (including problems conceiving or "minor" labour complications such as perineal tears), infant weight, sex and Apgar score and relevant follow up. The data was tabulated, and averages, medians and ranges were calculated for relevant data. Percentages were also calculated using Microsoft Excel (Microsoft Co, Seattle WA, USA).

Suggested diagnostic and treatment mechanism

A flow chart was devised, based on the patients seen through the Fetal Medicine Unit at the Canberra Hospital.

Results

Initial PubMed search yielded 112 articles. Of these, there were 86 cases or case series regarding acquired AVMs, with 25 reporting cases that resulted in pregnancy. Of the articles reporting pregnancy, 17 were case studies and eight were case series. Of the case series, three had enough data on individual patients to include in individual analyses, resulting in 24 patients from the literature, two of which were pregnant at the time of treatment. Six patients were seen through the FMU, resulting in 28 individual patients included in calculations (Table 1).

Patients

The mean age of women diagnosed with AVM was 29.5 +/- 6.7 SD, range 18–42 years. The mean gravity was 3.1 ± 3.1 SD (range 1–15) and parity was 0.81 ± 1.2 SD (range 0–3). The most common presenting complaint was per vaginal bleeding (24/27 – 85.7%). Eleven women (39.3%) presented with vaginal bleeding post interruption of pregnancy and six women (21.4%) presented with bleeding post spontaneous miscarriage. Two women (7.1%) presented post-delivery (one normal vaginal delivery and one caesarean section delivery). Three women (10.7%) presented with chronic menorrhagia or metorrhagia. UAVM were also diagnosed incidentally during infertility investigations or on a routine antenatal scan in two women (7.1%).

Fourteen women (50%) had a past medical history including interruption of pregnancy; eight women (28.6%) had a dilation and curettage (D&C) procedure. Four women (14.3%) had one or more caesarean delivery and three (10.7%) had been treated for molar pregnancy ± gestational trophoblastic disease (GTD). The average time since uterine trauma was 144.9 days (range 7–1095, SD ± 258.9). BHCG levels at time of diagnosis were not reported for 16 women (57.1%), with nine women (32.1%) having a negative BHCG and three women (10.7%) reported as having a positive BHCG level (Table 2).

Diagnosis

The most commonly reported modality used in diagnosis was colour Doppler ultrasound (CDUS), with 20 women (71.4%), followed by grey scale ultrasound (GCUS) which was performed in 14 women (50%). Power Doppler was performed in one woman (3.6%), 17 women (60.7%) underwent angiography and seven (25%) were diagnosed with magnetic resonance imaging or angiography (MRI/MRA). Other diagnostic modalities include CT (one woman, 3.6%). Four women (14.3%) were diagnosed with other modalities (e.g. hysterosalpingogram or laparoscopy). The average maximal width of the lesion (when reported) was 41.1mm ± 14.8 SD (range 26–67.5mm) (Table 3).

Treatment

Uterine artery embolisation (UAE) was performed in 15 women (53.6%). Seven women (25%) were managed expectantly, with no treatment. Five women (17.9%) were medically treated, most commonly with methylergonovine (three women, 10.7%). One woman (3.6%) had the lesion surgically excised and one woman

Table 1: Summary of key patient data.

Reference	Age	Gravidity Parity	Presentation	PMH	Time since trauma
Rebarber[13^]	34	Multi gravida	Vaginal Bleeding @ 20 wks.	2 LUSCS and scar separation	–
Castro–Aragon[24^]	29	G1P0	Routine antenatal scan	Myomectomy, fibroids	–
Kelly[25]	27	G3P0	Routine antenatal scan (pregnancy ended in SA)	GTD, MTX and suction curettage, D&C for SA	2 m
Nasu[26]	27	G1P0	Premature labour at 21 wks	Asymptomatic Ix for ovarian dysfunction	–
Reyftmann[27]#	28	G1P1	Secondary amenorrhea post delivery	NVD, 4 menses since	4 m
Gopal[28]	42	G6P0	Infertility investigations	Infertility, D&C 1 IP, 4 SA	NG
Delotte[29] Przybojewski[14] Tsai[30]	33 21 30	G2P0 G8P4	Metorrhagia, 6 months PV bleeding 1 week and menorrhagia 5–6yr hx or irregular excessive bleeding	Ovarian infertility, IP(medical), several BT 2 D&C for PV bleeding 3 SA, 1 MP	18 m 2 m NG
Nikolopoulos[31]	39	G1P0	PV post SA	SA (evacuation), BT	8 w
Chia[32]	37	G3P2	Profuse PV post SA	SA, D&C, menometorrhagia rx with tranexamic acid, 2 LUSCS, BT	3 m
Dar[4]*	26	G1P1	Profuse PV	Traumatic cervical dilation	NG
Garner[33]	31	G1P0	Heavy PV after cessation of OCP	D&C, GTD rx 6xMTX 1year prior	–
Amagada[34]	17	G1P0	PV bleeding post	–	1 w
Goldberg[35]	34	G15P3	PV post IP	8 IP	3 y
Nonaka[36]	30	G1P0	PV post IP	IP at 16 weeks	1 m
Onoyama[37] McCormick[38] Kim[39] Timmerman[3]	22 30 35 27*	G2P0 G7P3 G4P2 G1P0	PV post IP PV post IP PV post IP PV post IP	IP BT (2units) 2 D&C, C/S IV oxytocin and ergometrin, repeat D&C	4 w 3 m 4 m 6 w
	29	G3 P1+2	PV post IP	Late IP for foetal death	NG
	19	G2P1+1	Massive PV and pain	Placenta accreta, PPH, rx ergometrin, BT (2 units)	2 w
	36	G3P0+3	PV post IP	RPOC and fibroids	NG
	NG	G1P0+1	PV post IP	IP at 20 wks.	6 w
FMU Pt 1	31	G4P2	PV post SA	2 normal pregnancies, NVD, genital herpes, IP, D&C	1 y
FMU Pt 2	34	G3P0	PV post IP	2 x IP	3 m
FMU Pt 3	35	G2P1	PV post IP	LUSCS, D&C	2 w
FMU Pt 4	29	G4P0	PV post SA	3 SA, D&C	
FMU Pt 5	18	G1P1	Heavy PV post LUSCS	LUSCS (28 wks)	3 w
FMU Pt 6	36	G1P0	Heavy PV post SA	Menorrhagia, BT	2 m
Degani, *et al.* 2009 12 pts, 6 preg	24–34	G1+	Prolonged bleading, possible RPOC	7 post TA	NG
Ghai, *et al.* 2003 15 pt, 5pret (4pts)	23–43	G1+	Massive uterine bleeding	10 pt D&C 4pt – uterine instrumentation	1m – 7yr
Lim, *et al.* 2002 14 pts, 4 preg	18–43	G1+	Uterine haemorrhage	14 – GTD, BT	NG
Maleux, *et al.* 2006 17pts, 6 preg	25–38	G1+	Vaginal haemorrhage	7 – BT 13 – D&C	75d
Yang, *et al.* 2005 15 pts, 5 preg	25–42	G1+	Massive vaginal bleeding	15 ->2 D&C or LUSCS 4 – both	3d – 16m

Key: LUSCS – lower uterine segment caesarean section, PV – per vaginal bleed, CDUS – colour Doppler ultrasound, GSUS – grey scale ultrasound, TA – trans abdominal, TV – trans vaginal, MRI – magnetic resonance imaging, US – ultrasound, DUS – Doppler ultrasound, IP – interruption of pregnancy, GTD – gestational trophoblastic disease, RPOC – retained products of conception, MTX – methotrexate, MM – methylergonovine maleate, NVD – normal vaginal delivery, LFD, – lower forceps delivery,

Diagnosis	Treatment	TTC post Dx/Rx (m)	SA post Rx	Delivery	Complications
TA/TV GSUS, CDUS	UAE	–	No	LUSCS	Yes
GSUS, CDUS	Expectant	–	No	LUSCS	No
DUS, Ang	UAE	–	Yes	LFD	Yes
US, MRI, MRA, Ang (post-partum)	UAE	24	No	NVD	Yes
TA/TV GSUS Hysterosalpingogram CDUS, MRI, Ang	UAE	14	Yes	–	Yes
Hysterosalpingogram, MRI/ MRA, Ang	UAE	–	No	LUSCS	Yes
CDUS, Ang GSUS, Ang, MRI CDUS, Ang	UAE UAE UAE	12 48 24	No Yes (8wks) No	NVD NG NVD	Yes Yes No
DUS, Laparoscopy, hysteroscopy, Ang	Surgical removal of UAVM	14	No	LUSCS	Yes
US, PDUS,CT, Ang	UAE	9	No	LUSCS	No
GSUS, CDUS, Ang	UAE	72	No	NG	NG
US, MRA, Ang	D&C, UAE	15	Yes (2)	LFD	Yes
CDUS, Ang	Tranexamic acid and Iron, UAE	24	No	NVD	No
CDUS	MM	36	No	NVD	Yes
CDUS, MRI	MM &leuroprelin	5	No	NVD	No
TV GSUS, CDUS, Ang US, MRI, Ang CDUS, Ang CDUS	MM UAE UAE None	7 4 36 5 17	No No No N	LUSCS NVD LUSCS	No No NG No No
CDUS, GSUS	None	12	No	NG	No
Gynae exam, TV GSUS, CDUS, Ang	UAE	15	No	NG	No
GCUS, CDUS	hysteroscopy	9	No	LUSCS	Yes
GSUS, CDUS	None	2	No	NG	No
TA and TV GSUS and CDUS	Conservative	6	No	NVD	Yes
TA/TV, GSUS, CDUS	Conservative	12 48	No	LUSCS NVD	No
TA/TV GSUS CDUS	Conservative	24	No	LUSCS	Yes
TA/TV GSUS CDUS	Conservative	24	No		No
TA/TV GSUS CDUS	Primulet	4	No	LUSCS (prior)	Yes
TA/TV GSUS, CDUS, Ang	UAE	9	No	NVD	Yes
US, CDUS	3 – evacuation of RPOC 9 -monitor	NG	No	'uncomplicated	
TA/TV GSUS, CDUS, Duplex, Ang,	15 UAE	NG	0	1 LUSCS 4 NVD	
9 – CDUS 14 – Ang	14 UAE	NG	1	Two patients delivered 3 infants, one termination	
TA/TV GSUS, CDUS, Ang	17 UAE	15.6 m	0	6 pregnancies, 6 healthy, term babies	
4 – Palpation, CDUS, TV GSUS, 14 – Ang' 1– Histo	14 UAE 4 D&C 4 Hysterectomy	1–5 y	1	5 pts pregnant, 4 TA	

UAE – uterine artery embolisation, BT – blood transfusion, SA – spontaneous abortion (miscarriage), Ang – angiography, D&C –dilation and curettage, Ix – investigations, OCP – oral contraceptive pill, NG – not given, ^ - diagnosis of UAVM during a pregnancy, data not included in calculations *- patients went on to have multiple pregnancies post diagnosis of UAVM # - Patient did not go on to have a successful pregnancy, but did conceive post UAVM diagnosis

Table 2: Patient data, past medical history, diagnosis and treatment.

Parameter	Median / Range or Number / Percentage
Patients – 28	
Age (years)	30 / 18–42
Gravity	32 / 1–15
Parity	0 / 0–4
Presenting complaint	
Per vaginal bleeding	24 / 85.7%
Post TA	11 / 39.3%
Post SA	6 / 21.4%
Post delivery	2 / 7.1%
Menorrhagia / metorrhagia	3 / 10.7%
Other / unspecified	2 / 7.1%
Infertility investigations / incidental	2 / 7.1%
Secondary amenorrhea	1 / 3.6%
Routine antenatal scan	1 / 3.6%
Past medical history	
TA	14 / 50%
D&C	8 / 28.6%
LUSCS	4 / 14.3%
Infertility	3 / 10.7%
GTD / MP	3 / 10.7%
Other – CIN ii, fibroids No uterine trauma	4 / 14.3% 4 / 14.3%
Time since uterine trauma (days)	60 / 7 – 1095
BHCG	
Not given	16 / 57.1%
Negative	9 / 32.1%
Diagnostic methods	
Any type of ultrasound Ultrasound (unspecified)	27 / 96.4% 4 / 14.3%

Parameter	Median / Range or Number / Percentage
Transvaginal ultrasound	9 / 32.1%
Transabdominal ultrasound	7 / 25%
Grey scale ultrasound	14 / 50%
Doppler ultrasound (unspecified)	2 / 7.4%
Colour doppler ultrasound	20 / 71.4%
Power doppler ultrasound	1 / 3.6%
Mri / mr angiography	7 / 25%
CT	1 / 3.6%
Angiography	17 / 60.7%
Other	4 / 14.3%
Size of lesion – max width (mm)	40 / 26–67.5
Treatment	
UAE	15 / 53.6%
Expectant / none	7 / 25%
Medical	5 / 17.9%
Surgery	1 / 3.6%
Hysteroscopy	1 / 3.6%
UAE procedures – 15 pts, 18 procedures	
Number of procedures per patient	1 / 1–2
Embolic agent	
Pva / particles	7 / 48.9%
Glue /nbca	2 / 11.1%
Coils / micro coils	4 / 22.2%
Gelfoam / gelatine sponge	4 / 22.2%
Histoacryl and I	4 / 22.2%
Alcohol	1 / 5.6%
Not given	6 / 33.3%
Positive	3 / 10.7%

Table 3: Pregnancy and Infants post UAVM diagnosis.

Pregnancies – 36	
Time to conceive post dx/rx (months)	14 / 2–72
Delivery	
Normal vaginal delivery	10 / 257.8%
Lower forceps delivery	2 / 5.6%
Caesarean section delivery	9 / 25%
Complications miscarriage	5 / 13.9%
Antenatal	8 / 22.2%
Postnatal	5 / 13.9%
None	10 / 27.8%
Not given	2 / 5.6%

Infants – 32	
Gestation	39w / 28w2d–41w
Weight (g)	3081 / 1140–4015
Sex	
Male	11 / 34.4%
Female	11 / 34.4%
Not given	9 / 28.1%
Apgar	
1 minute	8 / 2–9
5 Minute	9 / 8–10

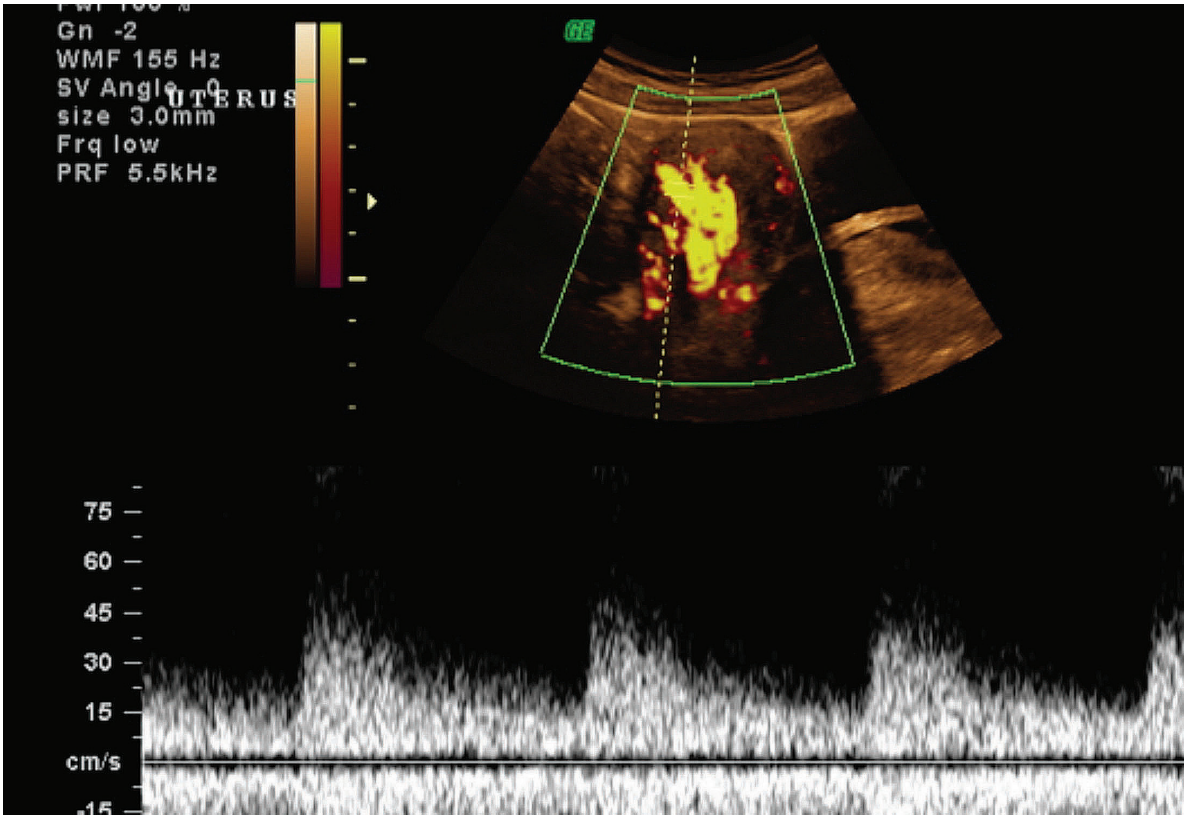

Figure 3: Spectral Doppler wave.

(3.6%) had hysteroscopic removal of retained products of conception (RPOC) which also resolved her AVM.

Of the women, 15 had a total of 18 UAE procedures, with the average number of procedures per patient being 1.2 ± 0.4 SD (range 1–2). The most commonly used embolic agent was PVA or other particles (seven procedures, 48.9%). Other embolic agents included: Glue/NBCA (two procedures, 11.1%), coils or micro coils (four procedures, 22.2%), gel foam or gelatines sponge (four procedures, 22.2%), histoacryl and lipiodol (four procedures, 22.2%) and alcohol (one procedure, 5.6%). Embolic material was not given for six (33.3%) of procedures (Table 3).

Pregnancies

The 28 patients included in the study had a total of 35 pregnancies. Five of these pregnancies (13.9%) ended in miscarriage after diagnosis and/or treatment of the UAVM. The average time to conceive post diagnosis/treatment was 19 months ± 16.3 SD (range 2–72 months). Nine (25%) pregnancies resulted in caesarean delivery, ten in normal vaginal delivery (27.7%) and two (5.6%) instrumental deliveries. Eight of the pregnancies (22.2%) had antenatal complications(including difficulties conceiving and premature labour) and five (13.9%) had postnatal (e.g. post-partum haemorrhage) complications. Ten pregnancies (27.8%) reported no complications either antenatally or postnatally. The average gestation for pregnancy post UAVM was 264.8 days (range 198–281, SD ± 23.4) (Table 4).

Infants

There were 32 live infants from the 36 pregnancies, with two women (5.6%) conceiving twins, one woman (2.8%) having two children post diagnosis and one woman (2.8%) having three children. The average birth weight was 2969 g (range 1140–4015, SD ± 1123.6). There were 11 males (34.4%) and 11 females (34.4%) born (nine studies (28.1%) did not report infant sex). Mean Apgar scores at one and five minutes were 6.6 and 9.0 respectively (see Table 4).

Case series

Five case series did not have enough data to individually analyse patients that became pregnant. These cases were grouped and analysed, resulting in 73 patients, 28 of which became pregnant, resulting in 22 infants. The patients ranged in age from 18–43, and all had a gravidity of at least one. The presenting complaint for all patients in the case series was vaginal haemorrhage. Thirty-five patients (47.9%) had a history of D&C, 8 (11%) or therapeutic abortion and 6 (8.2%) of LUSCS. Twenty-two patients (30%) had a history of GTD, a bias accounted for by one of the papers, which exclusively looked at patients with UAVM resulting from GTD. BHCG was not performed or given in 29 (39.7%) patients, and was negative in 30 (41.1%). BHCG was positive in 14 (19.2%) patients, again accounted for by the study focussing on GTD. Diagnosis was achieved by CDUS in 61 patients (83.6%) and by angiography in 45 patients (61.6%). Treatment was predominantly UAE (61 patients, 83.6%), with 14 patients (24.6%) requiring more than one embolisation procedure. The most common type of embolic material was PVA (30 patients, 35.3%), followed by glue (12 patients, 14.1%), gelfoam (10 patients, 11.8%) and coils (8 patients, 9.4%). Bilateral embolisation was done in 44 patients (51.8%) and the left uterine artery in 8 (9.4%) of patients. Most of the pregnancies (19, 67.9%), were 'normal, term deliveries', one (3.6%) was a LUSCS. Four patients (14.3%) had elective

Table 4: Case series analysis parameters.

	Median / Range or Number / Percentage
Studies	
Number of patients (total = 73)	15 / 12–17
Number of pregnancies (total = 28)	6 / 4–6
Number of infants (total = 22)	5 / 0–6
Age (median of average)	31.4 / 18–43
Presenting complaint	
Vaginal haemorrhage Past medical history	73 / 100%
Dilation and curettage Therapeutic abortion LUSCS GTD Other BHCG	35 / 47.9% 8 / 11.0% 6 / 8.2% 22 / 30.1% 16 / 21.9%
Not given / performed Negative Positive	29 / 39.7% 30 / 41.1% 14 / 19.2%
Diagnosis	
Ultrasound GSUS CDUS MRI Angio Other – hysteroscopy, histopathology, etc	29 / 39.7% 15 / 20.5 61 / 83.6% 6 / 8.2% 45 / 61.6% 13 / 17.8%
Treatment	
UAE Hysterectomy Not specified	57 / 78.1% 4 / 5.4% 12 / 16.4
Embolisation	85 procedures in 61 patients
>1 procedure	14 / 24.6%
Embolic agent PVA Particles Glue Coils Gelfoam Dura mata	 30 / 35.3% 7 / 8.2% 12 / 14.1% 8 / 9.4% 10 / 11.8% 1 / 1.2%
Side Not given Left Right	 16 / 18.8% 8 / 9.4% 1 / 1.2%
Pregnancies n = 28	
Normal term delivery LUSCS Termination Miscarriage	19 / 67.9 1 / 3.6% 4 / 14.3 2 / 7.1

terminations of their pregnancies post embolisation, and two patients had miscarriages (7.1%).

Suggested Diagnostic and Treatment Mechanism (Figure 3)

Discussion

Uterine arteriovenous malformations are a rare cause of abnormal vaginal bleeding, most commonly seen in women who have been pregnant and experienced some type of uterine trauma, such as D&C.[18] UAVM can be difficult to diagnose, not only because they are rare, but because they may present similarly to, or in conjunction with, other pregnancy related pathologies, such as sub-involution of the placental bed, retained products of conception and gestational trophoblastic disease[9]. It is important to make an accurate diagnosis of UAVM, as treatment for RPOC and GTD may include D&C, which is contraindicated in UAVM.[19] Three women (10.7%) in the current study had a history of gestational trophoblastic disease, eight women (28.6%) had a history of at least one D&C and 14 women (50%) reported previous interruptions of pregnancy. Two women (7.1%) had a history of RPOC. None of the women in the current study were nulligravid and most women (24 / 85.7%) presented with per vaginal bleeding.

The gold standard of diagnosis of UAVM is angiography, although colour Doppler ultrasound is now the most widely used first line of investigation. Angiography has the benefit of allowing treatment (in the form of embolisation) at the time of diagnosis.[20] Sixteen women in the current study underwent angiography as a diagnostic modality, and all but one woman (27 / 96.4%) underwent some form of ultrasonography.

It has been proposed by Timmerman, *et al.*[3] that SPB and UAVM constitute a spectrum of disease rather than distinct pathologies. This could explain why some women are able to be treated medically, or why sometimes no treatment is needed, whilst in others, lifesaving embolisation of the uterine arteries is required.[21] Timmerman[3] suggests the term uterine vascular malformations for those diagnosed by ultrasound, with arteriovenous malformation describing only those lesions seen on angiography to have the appropriate characteristics (early venous filling). Aside from angiography, the clinical picture and ultrasonographic features of uterine vascular malformations are very similar: hyper vascular areas within the myometrium, showing turbulent, low resistance flow, often associated with varying degrees of vaginal bleeding.[3] Therefore while arteriovenous malformations can be suspected with ultrasound, only angiography can differentiate true UAVM from potentially more benign vascular lesions.[19,22]

Uterine artery embolisation has been used for many causes of vaginal bleeding, including UAVM, fibroids and post-partum haemorrhage.[22] It is the preferred method because it has the potential to preserve fertility.[16] In cases that require embolisation, there are a range of embolic materials which may be used.[20] In this study, the most common embolic agent was particles (seven procedures, 48.9%). It does not appear that embolic agent choice has an impact on future fertility, as the 14 patients embolised in this study went on to have normal pregnancies, regardless of embolic material used. Although it is not possible to make conclusions from the current study, it seems likely that the clinical presentation and perhaps lesion size[23] is more important than the embolic agent used for determining future fertility.

This study is an important first step in looking at how to maximise fertility post diagnosis and treatment of UAVM. However, there are some weaknesses. First, it is hard to get

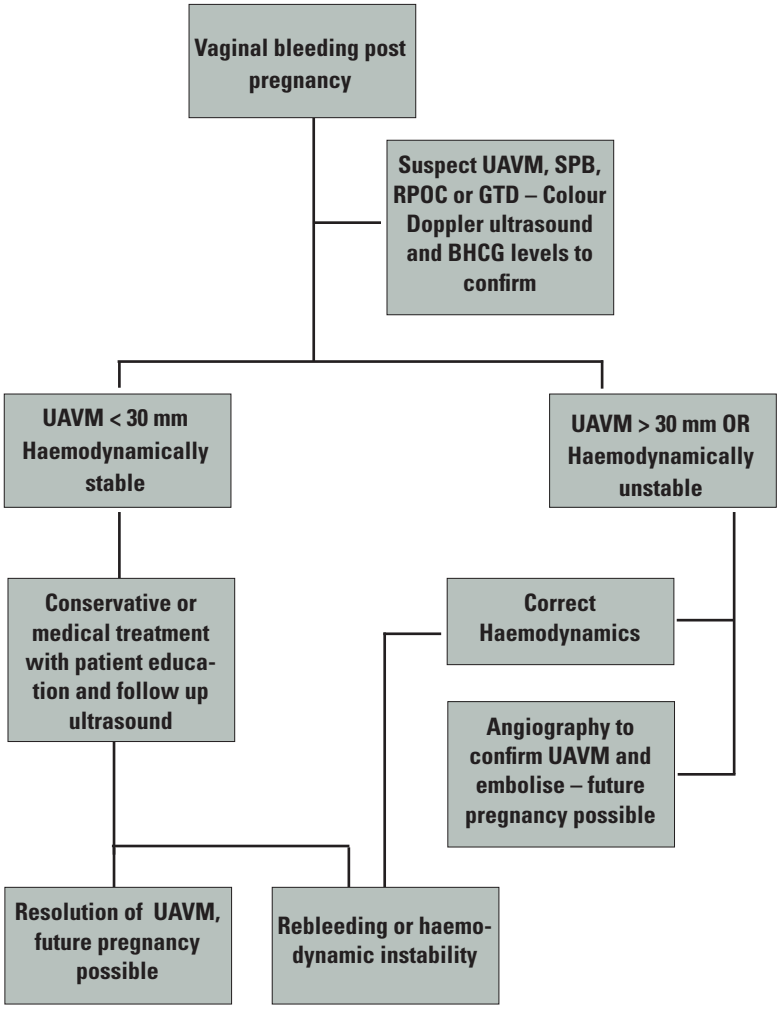

Figure 4: Suggested diagnostic and treatment flowchart based on patients seen at the Fetal Medicine Unit, The Canberra Hospital, Canberra.

all the details needed from the literature, as most cases are published as individual studies, each with a different focus (such as diagnostics or treatment), meaning other important details are omitted. Also, not all cases of UAVM will be documented in the literature, and only one database was searched in this study, which may possibly result in a publication bias. Second, this study is only looking at women who became pregnant post diagnosis and treatment; to make any definitive statements about diagnosis and treatment to maximise fertility, a comparison of these patients needs to be made with those who have had a diagnosis and treatment of UAVM and who have not become pregnant. This in itself would be difficult, as pregnancy is usually a conscious choice, not an invariable outcome. Other factors, such as patient age and other causes of infertility, will affect the rates of pregnancy post diagnosis and treatment of UAVM. Last, the diagnostic and treatment flowchart devised was based only on the six patients seen at the FMU, embolisation was required when the maximum diameter of the AVM was greater than 30 mm. Smaller lesion were either managed expectantly or supported with Tranexamic acid. It would not be appropriate to generalise this flowchart without further study.

Conclusion

In conclusion, UAVM are rare, potentially life threatening causes of vaginal bleeding that can be effectively treated with UAE, but some may also be safely managed conservatively. This study looked at 27 women, who became pregnant 34 times, giving birth to 31 infants post UAVM diagnosis. It is particularly reassuring that there were no catastrophic complications of pregnancy and labour post diagnosis, such as severe growth restriction or abnormal invasion of the placental bed (accreta) in this group of patients, and minor complications were limited. Ultrasound is a safe and reliable method for suggesting an UAVM, although angiography remains the gold standard for definitive diagnosis. UAVMs are likely to exist on a continuum with SPB, making it difficult to establish a single best diagnostic and treatment regime, although a possible mechanism has been suggested, based on the patients seen at this institution. Further studies to compare the women in the current study with those diagnosed with UAVM and who have not become pregnant, wider review of literature databases and perhaps collaboration between multiple centres would be useful in determining best course for diagnosis, treatment and fertility preservation in the setting of uterine UAVM.

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The development, structure and blood flow within the umbilical cord with particular reference to the venous system

Abstract

The umbilical cord is a helical and tubular blood conduit connecting the foetus to the placenta. The umbilical cord achieves its final form by the 12th week of gestation and normally contains two arteries and a single vein, all embedded in Wharton's jelly. The structure of the umbilical cord receives only a cursory glance during many obstetric ultrasound examinations: with imaging limited to documenting the number of vessels within the cord and the insertion sites at the foetus and placenta. Extensive research into blood flow characteristics of the umbilical cord arteries has been undertaken and is now widely applied in contemporary ultrasound practice. In contrast, investigation of umbilical vein blood flow is only instigated in instances of foetal compromise when the spectral waveform of the ductus venosus and pulsations in the vein are scrutinised. The current level of ultrasound imaging of the umbilical vein demonstrates a lack of appreciation and knowledge about a structure that is crucial to sustaining foetal life.

The goal of this review is to increase awareness of the importance of the umbilical cord. In addition, this review will provide an information platform for undertaking and critically analysing research into the umbilical cord by providing a summary of cord embryology, structure, foetal venous circulation and mechanisms of blood flow within the umbilical cord vein.

Keywords: umbilical cord, umbilical cord vein, venous blood flow.

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Introduction

The umbilical cord provides the pathway for unhindered blood transport from the placenta to the foetus and vice versa. Aristotle (384–322 BC) originally identified the umbilical cord as the connection between the mother and unborn child.[1]

This article is the consequence of a systemic review of established texts, peer reviewed articles and credible websites which was undertaken to develop a knowledge base about the development, structure and blood movement within the foetal venous system in preparation for undertaking research into quantifiable aspects of the umbilical cord vein.

The following pages review the development, structure, foetal venous circulation and mechanisms of blood flow within the umbilical cord vein with the aim of fostering an increased appreciation of a structure that is often neglected during routine obstetric ultrasound examinations and to provide an information platform for research into the foetal venous network.

Umbilical cord embryology

The rudimentary umbilical cord is formed during the 4th to 8th weeks of gestation (calculated from the first day of the last menstrual cycle) by the expanding amnion enveloping tissue from the body stalk, the omphalomesenteric duct and the umbilical coelom.[2] Blood flow is established within the umbilical cord by the end of the 5th week of gestation.[3]

Coursing through the body stalk are two umbilical arteries, two umbilical veins and the allantois. Initially, the left and right umbilical arteries are caudal continuations of the primitive dorsal aortae, but after several revisions finally arise from the internal iliac arteries.[4] After birth, the proximal portions of the intra-abdominal umbilical arteries become the internal iliac and superior vesical arteries, while the distal portions are obliterated and form the medial umbilical ligaments.[5] The umbilical veins arise from a convergence of venules that drain the extra-embryonic allantois.[4] Obliteration of the right umbilical vein by the end of the 6th week of gestation[6] results in a single persisting left umbilical vein. Obliteration of the intra-abdominal umbilical vein at birth produces a hepatic remnant termed the ligamentum teres.[5]