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Medical Management of a Complicated Uterine Arteriovenous Malformation with Successful Fertility Preservation

Curtis Wong, MD, William Boyd, MBBS, Sujatha Anand, MBBS
Obstetrics & Gynaecology, Mackay Base Hospital, Queensland Australia
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Background

Uterine arteriovenous malformations (uAVM) are rare vascular malformations characterized by a **direct abnormal connection between arteries and veins, bypassing a capillary system**.

- They **can be a serious cause of uterine bleeding** that can lead to rapid hemodynamic instability.
- Uterine arteriovenous malformations are thought to either develop congenitally or are acquired, secondary to uterine surgery or pregnancy.

Traditionally, treatment of uterine AVMs has been hysterectomy. In cases where fertility preservation is desired, uterine artery embolization has been the treatment of choice.

- **Medical management of uAVMs has had growing evidence** since it was first trialled in 1996, although data is limited to several case series trialling a handful of different treatment regimens across several dozen patients.

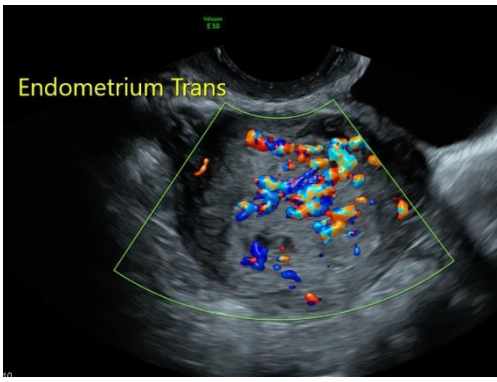

Figure 1: Pre-treatment USS Pelvis demonstrated enhanced myometrial vascularity

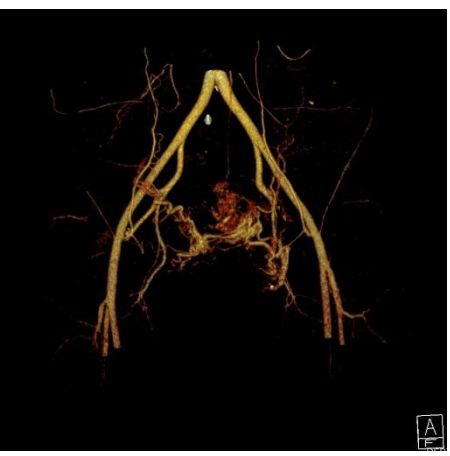
Figure 2: CT Angiogram confirming uterine arteriovenous malformation

Case

A 28-year old woman was referred to gynaecology due to ongoing amenorrhea two months after a **surgical termination of pregnancy (STOP)** at an estimated 8wk gestation

- Ultrasound scans performed 2 months and 3 months post-STOP suggested enhanced myometrial vascularization (*Figure 1).*
- HCG 22 IU/L (Normal range: <5 IU/L), 4 months post-STOP.
- Hysteroscopy incidentally found a large obvious pulsation of the anterior uterine wall with associated superficial capillary filling seen, consistent with arterial flow.
- Subsequent CT Angiogram Pelvis confirmed the presence of a moderate-sized uAVM *(Figure 2)* with bilateral ovarian artery contributions
    - **Interventional radiology stated that, while uterine artery embolization would be technically feasible, there was risk of iatrogenic premature ovarian failure.**

Medical Management

Progestins, Gonadotropin-releasing hormone (GnRH) agonists, and methotrexate are significantly more efficacious compared to chance

- **GnRH Agonist was selected for treatment**:
    1. The primary study documenting GnRH agonist treatment of uAVMs noted fertility as a secondary measure and reported that 100% of patients who attempted pregnancy following treatment spontaneously conceived
    2. Progestins are known to increase superficial blood vessel fragility. The treating team wanted to avoid further haemorrhage risk to the patient due to the already superficial location of the patient's uAVM.
- **Current hypotheses of GnRH Agonist Mechanism of Action in uAVM treatment**
    1. The hypoestrogenic state GnRH causes uterine atrophy and decrease in uterine volume -> **decrease in uterine volume alters blood flow**
    2. **Decrease in estrogen directly leads to constriction of the myometrial arterial system**

The patient was treated with Goserelin 3.6mg (28d duration), Letrozole 2.5mg PO OD x5d, Tranexamic Acid 1000mg PO TDS PRN

- Readmission on treatment day 5 due to an oestrogen withdrawal bleed
- Interval USS Pelvis 1mo and 2mo post-treatment start demonstrated AVM resolution; treatment was stopped after 1 cycle.
- Menses resumed 88 days after treatment stopped.

The patient accidentally fell pregnant 1 month after menses resumed.

Medical regimens used to treat uterine AVM.

Treatment	Success rate
Progestin (2 studies, 57 patients)	
Medroxyprogesterone acetate intramuscular every 3 months	82.5%
Oral norethisterone 10 mg p.o. twice daily	
Gonadotropin-releasing hormone agonist (7 studies, 28 patients)	
Leuprolide acetate or goserelin ± letrozole 2.5 mg daily orally × 5 days on initiation	89.2%
Chemotherapeutic (3 studies; 11 patients)	
Methotrexate intramuscular single dose or weekly	90.9%
Combined hormonal contraception (7 studies; 7 patients)	
Various doses of ethinyl estradiol + progestin (levonorgestrel or norgestrel) orally, some continuously, ± TXA	42.9%
Uterotonics (5 studies, 6 patients)	
Methylergonovine maleate intramuscular or intravenous followed by daily oral dose	100%
Methylergonovine maleate 0.2–0.5 mg orally daily	
Danazol (3 studies, 3 patients)	
Danazol 200–400 mg orally daily	66.6%
Combinations (8 studies, 9 patients)	
GnRH-a + methylergonovine	77.8%
Misoprostol + progestin	
GnRH-a followed by progestin-IUD	
Methylergonovine maleate + progestin + GnRH-a	
Methylergometrine + danazol 200 mg orally daily for 2 months	
GnRH-a + etamsylate + progestin + ulipristal acetate	

Note: OCP = oral contraceptive pill, GnRH-a = gonadotropin-releasing hormone agonist, TXA = tranexamic acid , IUD = intrauterine device, mg = milligram, p.o. = orally.

Rosen. Arteriovenous malformation treatment. Fertil Steril 2021.