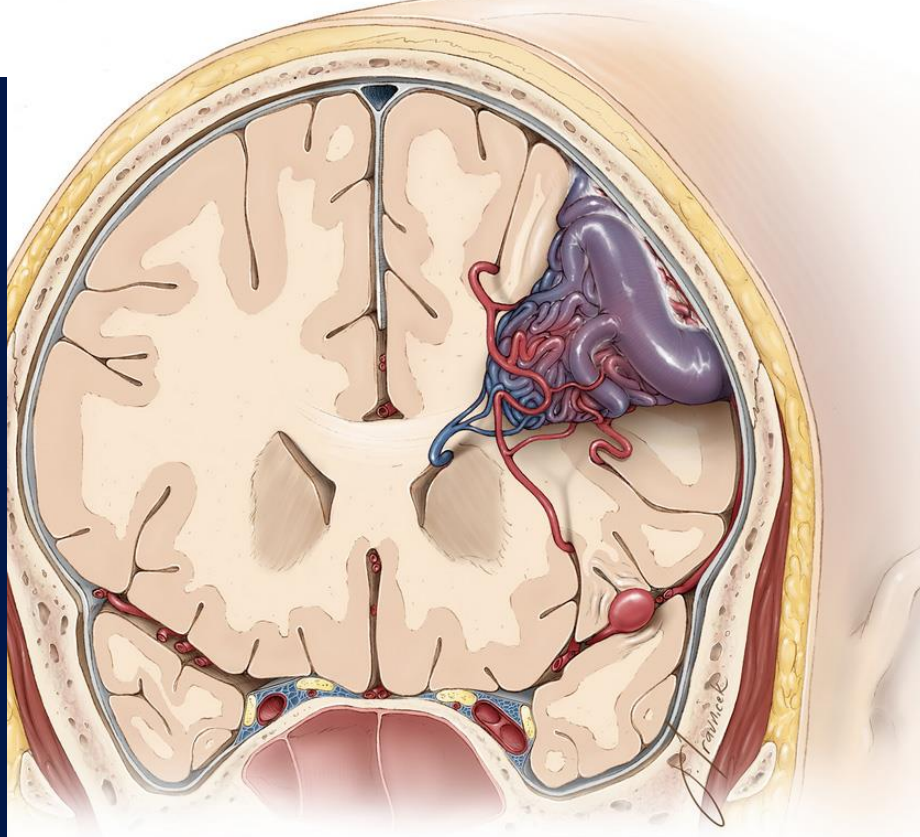


A case series of recent Arteriovenous Malformations (AVM) and Intracranial Haemorrhage (ICH)

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OBJECTIVE

This case series explores three cases of rare AVM and ICH over the last year at our local DGH and explores their extremely varying clinical presentation, sequelae and outcomes. Though AVM and ICH in pregnancy is rare, it represents a significant proportion of maternal death and foetal mortality, making these cases in quick succession of particular interest. We aim to discuss some of the signs and symptoms of AVM and ICH in pregnancy, it’s management and considerations for treatment in pregnancy.

CASE SERIES ONE – A MATERNAL DEATH

- ❖ 33-year-old
- ❖ P1 (14 years ago)
- ❖ BMI 20
- ❖ Active smoker
- ❖ High risk pregnancy
- ❖ Background: herpes, previous LLETZ, previous domestic violence, previous depression and anxiety.
- ❖ At 17+1- Cardiac arrest at home, transferred to the emergency department, then the critical care unit.
- ❖ CT confirmed subarachnoid hemorrhage with ruptured aneurysm.
- ❖ FH present at time of admission.
- ❖ Intra uterine death of baby confirmed the following day.
- ❖ Patients' death by neurological criteria confirmed, shortly after foetal death.

CASE SERIES TWO – THE SYMPTOMATIC PATIENT

- ❖ 33-year-old.
- ❖ P1
- ❖ BMI 21
- ❖ Low risk pregnancy prior
- ❖ Background of migraine with aura, previous depression and polycystic ovaries.
- ❖ Reported two week history of dizziness followed by acute onset right sided weakness and dysarthria.
- ❖ 31/40- presented to ED where a CT head demonstrated bleed secondary to AVM with midline shift, followed by transfer and craniotomy, with clot evacuation at tertiary centre.
- ❖ ITU admission followed
- ❖ 34+4/40- secondary AVM operation to repair underlying AVM.
- ❖ 34+6/40- CT angio confirms successful AVM surgery
- ❖ Protracted period of rehab required for right sided limb symptoms and slight aphasia
- ❖ Delivered by elective cesarian section at 39 weeks.
- ❖ Patient significantly improved with power >90%, some residual mild upper limb numbness and occasional slurred speech when tired or fatigued.

CASE SERIES THREE – THE INCIDENTAL FINDING

- ❖ 27-year-old.
- ❖ P1
- ❖ BMI 20
- ❖ High risk pregnancy
- ❖ Background of T1DM, EUPD
- ❖ Admitted at 23+2/40, under the medical team with onset of persistent headache.
- ❖ CT venogram revealed an AVM.
- ❖ Case discussed with neurosurgery and their MDT, confirmed a diffuse parietal AVM.
- ❖ Whilst she was suffering with a headache it was felt this was not caused by her AVM.
- ❖ Recommendation made for a planned cesarian section at term and an MRI/MRI-A and cerebral angiography, following delivery, as an outpatient.
- ❖ At 30/40- patient had detailed discussion with professor of neurosurgery, outlining three treatment options and recommendation not to intervene whilst pregnant with plan for post-natal imaging and follow-up.
- ❖ Reattended 31+2/40 with reducing insulin requirements over the last week. Normal scan. Subsequently discharged
- ❖ Reattended with reducing insulin requirements and reduced foetal movements at 33+1/40. CPR<5th centile. Discharged again, with outpatient follow-up including twice weekly dopplers and thrice weekly CTGs. Aiming for elective cesarian section at 36-37/40.
- ❖ However, CTG not meeting criteria, patient experiencing hypoglycaemic episode. Therefore Cat 3 cesarian arranged at 34+6/40 with previous steroid cover.

BACKGROUND

- Definition:** An arteriovenous malformation (AVM) is a rare, abnormal tangle of blood vessels in which arteries connect directly to veins, bypassing the capillary system. This disrupts normal blood flow and oxygen exchange.
- Aetiology:** Majority of intracranial AVM are congenital, forming during early fetal development as a result of abnormal persistence of primitive arteriovenous channels without the development of intervening capillaries resulting in direct artery-to-vein connections. More rarely, AVMs can be associated with hereditary genetic conditions, such as Osler-Weber-Rendu syndrome. There have been case reports of possible acquired AVMs following trauma or surgery, however evidence is limited and debated due to the rarity of these cases and often a lack of prior imaging.
- Prevalence:** 10–20 per 100,000 people. Average age of diagnosis is 30-40years old.
- Presentation:** Most common presentation is intracranial haemorrhage (ICH). Bleeding risk is 2-4% per year for unruptured AVMs. Mortality rate is dependent on many factors but is generally quoted at 10-15% for a ruptured AVM. Other presenting symptoms include seizure, headache, focal neurological deficit and progressive neurological deficit secondary to deprivation of local tissue of blood supply. 15% of AVMs are asymptomatic at diagnosis.
- Diagnosis:** Catheter cerebral angiography is considered gold standard for diagnosis, providing detailed images of the arterial feeders, nidus, and venous drainage with dynamic imaging of blood flow pattern to allow for optimal surgical planning. However, this is invasive with associated risk of bleeding and stroke. MRI is the most accurate non-invasive imaging, with MRA able to detect larger AVMs. CT is most useful in the acute setting however CTA may miss low-flow AVMs.
- Treatment:** Highly individualised with consideration of risk of haemorrhage, risk of surgery, symptoms and patient factors (age, comorbidities) along with patient choice. There are three main treatment modalities, sometimes used in combination:
 - Microsurgical Resection** – Best for small, superficial AVMs. This offers definitive cure with immediate removal of nidus. It is invasive and has significant risk where AVMs are situated in eloquent brain areas. Risk of procedure related mortality 1-5%, and includes permanent neurological deficit, infection, bleeding, seizure and CSF leak.
 - Endovascular embolization** - Rarely curative alone. Typically used as an adjunct, prior to surgery to reduce AVM size or to target specific feeder vessels. Minimally invasive with a catheter injecting embolic agents. Risks of ischaemic stroke from vessel occlusions 6-10%, risk of haemorrhage during the procedure, risk of incomplete occlusion.
 - Stereotactic radiosurgery** - Best for small (<3cm), deep AVMs. Also method of choice for AVMs in eloquent brain regions. It is non-invasive, using focused radiation to induce vessel obliteration over 2–3 years. Latency factor therefore risk of haemorrhage in the interim, risk of seizure, neurological deficit and radiation associated tissue injury.
- Observation** ie conservative treatment may be considered in low-risk cases. Aruba trial (2014) found fewer adverse neurological outcomes in the conservative group compared to treatment group, however follow up was limited to the short-term (mean <3 years) and selection bias was a key limiting factor.

Risks of AVM in pregnancy:

- There is disagreement within the literature as to whether pregnancy increases risk of AVM rupture in comparison to risk in the non-pregnant cohort. A literature review reveals the majority of studies assessing AVMs in pregnancy quote annual bleeding risk between 2% and 6% however a 2022 meta-analysis by Yusuf et al concluded a rupture risk of 16% per pregnancy for women with known AVM; although the authors do acknowledge difficulties related to small study numbers.
- Theories for increased rupture risk centre on known physiological changes of pregnancy, increased blood volume, cardiac output, and hormonal vasodilation, which may increase haemodynamic stress on AVMs.
- A 1997 retrospective study by Mast et al found no significant increase risk in first time bleed rate (3.5% in pregnancy vs 3.1%) however found a significant increase in risk of re-bleed following an initial bleed during the pregnancy, quoted at 26% compared to a general population re-bleed risk of 6%. Note limitations of this study with small numbers of women due to the rarity of AVM bleeds during pregnancy and the fact that many of these women will have had treatment immediately following the first bleed. Subsequent studies have found 1 year rebleed risk in non-pregnant populations to be higher, up to 18%.
- **Maternal risks:** as per non-pregnant population
- **Fetal risks:** Hypoxia, pre-term delivery including iatrogenic, IUD.
- **Pregnancy considerations:**
 - **Imaging:** MRI at 1.5T is preferred modality, with no evidence of MRI-induced teratogenesis where no contrast is used. However, CT should still be used in acute settings where MRI may delay diagnosis or the patient is unstable. Cerebral angiography is considered safe as with appropriate shielding fetal radiation exposure is well below thresholds for harm.
 - **Management:** all options can be considered. Embolisation and radiosurgery involve risk of radiation exposure to the fetus which must be taken into consideration and will be variable depending on radiation dose and gestation. In the case of significant ICH, surgery will likely be indicated and in this case optimal management must also consider delivery by emergency C-section, depending on maternal stability and gestation.
 - Close blood pressure monitoring during pregnancy to enable prompt diagnosis of developing PIH or PET and tight blood pressure control to reduce rupture risk.
 - **Mode of delivery:** There is no definitive evidence that vaginal delivery increased AVM rupture risk; elective C-section may however be recommended as it allows for more optimised haemodynamic control. If labouring, epidural should be considered to aid blood pressure control and limitations for duration of second stage may be advised.

REFERENCES

1. Al-Shahi, R., & Warlow, C. P. (2001). *A systematic review of the frequency and prognosis of arteriovenous malformations of the brain in adults*. Brain, 124(10), 1900-1926.
2. Spetzler, R. F., & Martin, N. A. (1986). **A proposed grading system for arteriovenous malformations**. *Journal of Neurosurgery*, 65(4), 476-483. <https://doi.org/10.3171/jns.1986.65.4.0476>
3. Lawton MT, et al. *A supplementary grading scale for selecting patients with brain AVMs for surgery*. Neurosurgery. 2010
4. Mast H et al. *Risk of recurrent intracranial hemorrhage after AVM rupture in pregnancy*. Stroke. 1997;28(5):853–856.
5. Horton JC, Chambers WA, Lyons SL, Adams RD, Kjellberg RN. *Pregnancy and the risk of hemorrhage from cerebral arteriovenous malformations*. Neurosurgery. 1990;27:867–872
6. Mohr JP et al. *ARUBA trial*. Lancet. 2014
7. Starke RM et al. *AVM management review*. Neurosurg Focus. 2014.
8. Chew Kah Teik, MD1* et al, Management Options and Outcome of Cerebral Arteriovenous Malformation in Pregnancy: Case Series, Arch Iran Med. June 2019;22(6):340-343
9. Mo’nica Santosa and Diana Aguiar de Sousaa,b,c, Cerebrovascular disease in pregnancy and postpartum, www.co-neurology.com, Feb 2022.
- 10.Che Yusuf, R et al, Arteriovenous Malformation Hemorrhage in Pregnancy: A Systematic Review and Meta-Analysis. Int. J. Environ. Res.Public Health 2022, 19, 13183.

DISCUSSION AND CONCLUSION

Discussion:

Our second case study described a patient who becomes significantly symptomatic with focal neurology following a first bleed from an AVM. Initial management was in the form of clot evacuation to manage symptoms and prevent further neurological deterioration secondary to tissue oedema and compression. Given the high risk of a second bleed during the same pregnancy as evidenced in the literature, the balance of overall risk would support the decision for second step surgical treatment to excise the AVM during the pregnancy. The decision was made to continue the pregnancy, rather than deliver prematurely, likely due to early gestation of 31/40 at initial presentation and the fact that the patient was haemodynamically stable.

Our third case describes an incidental finding of AVM. The patient presented with headaches which subsequently resolved with analgesia however she underwent imaging which detected an AVM. Given that she was stable and asymptomatic the literature does support a conservative approach during pregnancy, with the plan for options to be discussed with the patient following delivery. The obstetric team should consider appropriate contraceptive counselling following delivery to allow time for follow up and neurosurgical planning to occur prior to further conception, although note that there is no evidence to advise against pregnancy in women with asymptomatic unruptured AVMs.

Conclusion:

ICH secondary to AVM rupture is a rare but serious presentation, with significant associated morbidity and mortality. There is good evidence surrounding safety of different modalities of investigations for suspected AVM during pregnancy however there remains a lack of evidence as to the true risk of AVM rupture posed by pregnancy and therefore the risk/benefit of intervention. In general, the approach is to intervene following a rupture, due to the high risk of re-bleed, however to delay any possible intervention until following delivery in cases where there is no bleeding and no significant neurology. We should however take into consideration the impact of this incidental diagnosis on the mental health of the mother and ensure steps are put in place to support her emotional wellbeing. Advice regarding mode of delivery should be undertaken with an MDT approach, taking into consideration other obstetric risk factors and maternal preference.

Prospective cohort studies are needed to assess AVM rupture risk during pregnancy vs. non-pregnancy and allow risk to be further stratified, specific to the pregnant population. In addition, there are no standardized guidelines on delivery mode. Multicentre studies are required to analyse maternal AVM outcomes by delivery method, including the impact of regional anaesthesia during labour.