CURRENT MANAGEMENT OF INCIDENTAL AND ASYMPTOMATIC CEREBROVASCULAR LESIONS: APPROACH TO UNRUPTURED ANEURYSMS AND AVMS

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ASYMPTOMATIC AND UNRUPTURED INTRACRANIAL ANEURYSMS

Natural History

- ISUIA prospective data with unruptured intracranial aneurysm (UIA), 49 ruptures during mean observation of 4.1 years of 1692 prospective unoperated patients.[1]
- UCAS, Japanese study of 110 aneurysmal ruptures during mean observation period of 3.5 years and 11,660 patient-years of follow-up.[2]

Advances in Treatment

- ISAT 2002 and 2005
- Increased experience in treatment with improved safety

Epidemiology

- Prevalence of depends on population studied, range 0.0%-41.8%. Overall mean prevalence of 2.8%.
- Estimated prevalence of UIA in a population without comorbidity and with a mean age of 50 years 3.2%[3]

Risk Factors

- Risk of aneurysm development, risk for growth and change and risk for rupture.[4]
    - Behavioral risk factors for aSAH include:
        - Hypertension
        - Smoking
        - Alcohol abuse
        - Use of sympathomimetic drugs (eg, cocaine)
    - Nonbehavorial risk factors:
        - Unruptured cerebral aneurysm that are symptomatic[4], larger in size (>7 mm)[5] and located on the posterior communicating artery or vertebrobasilar system.[5]
        - Genetic inheritance may play a role in aneurysmal development and vulnerability to SAH[4]
    - History of previous aSAH[5]
    - Aneurysm morphology can influence risk of rupture:
        - Aneurysms with an irregular surface
        - High aspect ratio (height/neck >3) or bottleneck ratio (width max/neck)
        - Daughter sacs
        - Small associated parent artery and/or draining vessels also carry a higher risk of rupture.

Familial Intracranial Aneurysm

- Specific genetic abnormality associated with intracranial aneurysm formation is not clear.
    - Large meta-analysis of genetic studies identified 19 single nucleotide polymorphisms associated with sporadic intracranial aneurysm.

- Strongest association found on chromosomes 9, 8 and 4.[6, 7]
- Meta-analysis of the Familial Intracranial Aneurysm cohort showed polymorphisms on chromosomes 9 and 8.[7]

aSAH Prevention

- Current evidence suggests inflammation plays an important role in the pathogenesis and growth of intracranial aneurysms.
  - Some suggest statins and calcium channel blockers may retard aneurysm formation through the inhibition of prominent mediators of the inflammation.[4]
  - Evidence is lacking for formal recommendations.
- Current recommendations to reduce the risk of aSAH:[4]
  - Hypertension should be treated
  - Tobacco use and alcohol misuse should be avoided
  - Consumption of a diet rich in vegetables may lower the risk of aSAH (Class IIb; level of evidence B)
  - It may be reasonable to offer noninvasive screening to patients with familial (at least 1 first-degree relative) aSAH and/or a history of aSAH to evaluate for de novo aneurysms or late regrowth of a treated aneurysm, but the risks and benefits of this screening require further study.

Screening and Imaging Modality for Evaluation

Recommendations for Management of UIA[8, 9, 10]

- **Natural history**
  - Many factors should be considered including:
    - Aneurysmal factors
    - Patient factors
- **Treatment of UIAs**
  - Surgical ligation versus endovascular treatment
    - Specific risk factors to consider
    - Patient characteristics
    - Aneurysm characteristics
  - Imaging follow-up in aneurysms treated conservatively

APPROACH TO UNRUPTURED AVMS

AVM Biology and Pathophysiology

- AVMs are an abnormal connection between arteries and veins via a network of vessels called the nidus and are absent an intervening capillary bed.
- AVMs are considered congenital vascular lesions, however, the precise pathogenetic mechanism(s) leading to the lack of capillaries in the AVM nidus remains unclear.
- While it is assumed that AVMs appear during fetal development, they are actually rarely detected *in utero* or found in infants.
- Approximately half of AVMs are situated at the border-zone "watershed area" [11]

Natural History

- Arteriovenous malformations (AVMs) of the brain account for approximately 1.4% to 2% of hemorrhagic strokes.
- The estimated prevalence of AVM varies from less than 10 to 15 and 18 per 100,000.[12, 13]
- The familial incidence of brain AVMs appears to be rare, with only a few reported cases in the literature; although, there is an association with other abnormalities (Osler-Weber-Rendu disease and the Sturge-Weber syndrome).
- Brain AVMs are found incidentally on 0.05% of brain magnetic resonance imaging screens.[14]

- The natural history of asymptomatic brain AVMs was poorly understood and conflicting information can be found on symptomatic lesions in the literature.
- The ARUBA trial (A Randomized trial of Unruptured Brain Arteriovenous malformations) provided some understanding of the natural history of brain AVMs and whether treatment improves morbidity and mortality for unruptured brain AVMs.[15]

Clinical Presentation

- Brain AVMs can lead to intracranial hemorrhage, epilepsy, headaches, and long-term disability. When symptomatic, the most common presenting symptoms are hemorrhage and seizure.

Diagnosis and Imaging Modality for Evaluation

- Cerebral angiography is considered the gold-standard in the evaluation of AVM architecture,
    - Morphology, location of nidus, presence and location of associated aneurysms, and venous drainage pattern, and is commonly used for treatment planning.
- Computed tomography (CT), computed tomography angiography (CTA), dynamic CTA, magnetic resonance imaging (MRI), and magnetic resonance angiography (MRA), may be used to visualize AVMs, however, they are limited in their sensitivity.
- Functional MRI may provide guidance and information that can be helpful in treatment planning.

AVM Management

- Management of cerebral arteriovenous malformations includes observation with medical management, endovascular embolization, surgical resection, and stereotactic radiotherapy.
- AVMs that have not bled present a more challenging decision, in the setting of a poorly defined natural history and the seemingly low annual hemorrhage rates.

Observation

- Observation is considered for management of asymptomatic AVMs, however, it is rarely considered for those patients who have presented with hemorrhage.
- Conservative management may include management of associated symptoms, general medical care, and surveillance imaging of the AVM.
    - Presentation can include seizures, which may be related to hemorrhage, hemosiderin deposition from recurrent microhemorrhages, venous hypertension, and ischemia from high flow shunting.
    - General medical care includes management of hypertension and conventional regimens for headaches.
    - Time intervals for surveillance imaging are not well-defined and may include non-invasive MRI brain imaging annually or biennially.

Treatment

- Treatment may include single or multimodal therapy with the goal of eradication.
    - Endovascular
    - Surgical resection
        - Spetzler-Martin grading system
    - Radiosurgery
- AVM characteristics including size, location, surgical or endovascular accessibility, venous drainage, and presence of high risk features such as a feeding artery aneurysm.
- Technological advancements continue to shape treatment modalities and multimodal therapy is increasingly being used for brain AVM treatment as combination therapy can utilize the various benefits (Table 1).

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