Management of intracranial atherosclerotic stenosis (ICAS)/intracranial atherosclerosis

Tim Mikesell, D.O.

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Stroke facts

• Despite progress in decreasing stroke incidence and mortality, stroke remains:
  • first leading cause of disability
  • fifth leading cause of death (greater than 1 in 15 deaths are from stroke)

http://www.cdc.gov/nchs/data_access/Vitalstatsonline.htm
Types of Stroke

- Divided into ischemic or hemorrhagic
- Ischemic: 88%
- Hemorrhagic: 12%
  - Intracranial Hemorrhage: 67%
  - SAH: 33%
Ischemic stroke subtypes

- Complex heterogeneous disease with different subtypes...
  - Cryptogenic stroke: 30%
  - Penetrating Artery Disease/Lacunae: 25%
  - Cardioembolic: 20%
  - Atherosclerotic Cerebrovascular***: 20%
  - Other: 5%
Ischemic stroke subtypes

- ICAS accounts for about 10% of ischemic stroke cases but depends on ethnicity
  - 5–10% of strokes in white people
  - 15–29% of strokes in black people
  - 30–50% of strokes in Asian people

ICAS mimickers

- Arterial dissection (subadvential vs. subintimal)
- Fibromuscular dysplasia
- Primary or secondary vasculitis
- Moya moya
- Cerebral vasoconstriction syndrome
- Other vasculopathies
There are three main mechanisms of stroke related to ICAS

• hypoperfusion
• artery-to-artery embolism
• plaque extension over small penetrating artery ostia (also known as branch atheromatous disease)
Imaging for ICAS

• TCD and MRA
  – useful screening tools for the exclusion of ICAS
  – Unreliable to establish the diagnosis and the degree of stenosis

• CTA is more accurate than MRA for the diagnosis for ICAS

• Cerebral angiography remains the gold standard

Case Presentation

- 56 RH M with DM, HTN, CAD with CABG
- Did not have sudden onset but insidious of swaying to the left
- One episode of difficulty word finding
- Fine the next two days but the swaying returned
- Came to the ED and was admitted
- Was on aspirin 81 mg daily already
Case Presentation

• On neuro exam…
  – Very mild left upper motor neuron facial droop
  – Questionable arm/shoulder weakness
• Stroke work up performed
• Several areas of infarction in the right MCA territory
Several areas of infarction in his right MCA distribution
Several areas of infarction in his right MCA distribution
Case Presentation

• Etiology from severe right MCA stenosis
• Long segment in the M1 branch at 95%
Severe stenosis of the right middle cerebral artery
CTA brain was done to confirm the MRA
Case Presentation

• Unable to get a CTP
• Was placed on
  – Clopidogrel with the aspirin
  – Atorvastatin 80 mg
  – Blood pressure medication was held
• If was to fluctuate neurologically…
  – Transfer to MICU
  – IVF with HOB flat
  – Even induce hypertension
• Was stable but a decision needed to be made…
Case Presentation

• Conventional cerebral angiogram was done...
Case Presentation 2

- 72 RH M with DM, HTN, HL presented with RHP and dysarthria
- NIHSS was 10
- Got IV tPA and NIHSS improved to 3
- R facial droop (UMN), R arm ataxia, dysarthria
- CTA showed critical basilar artery stenosis and possible thrombus distal to the stenosis
- Since he was improved an emergent angiogram was not done
Case Presentation 2

- That night a conventional cerebral angiogram was performed
  - Confirmed the critical basilar artery stenosis (95%) and post-stenotic thrombus
  - Distal basilar artery was supplied by the PCOM’s
  - Distal R vertebral artery was occluded proximal to the R PICA (which filled from the L vertebral)
- a MRI/DWI brain was done immediately after the cerebral angiogram
  - Bilateral “patchy” pontine and a punctate right cerebellar strokes
Case Presentation 2

• Heparin drip was started after 24 hours of systemic thrombolysis

• 3 days later…
  – Repeat MRI/DWI brain was without new infarcts***
  – Repeat CTA’s showed resolution of the thrombus in the distal basilar artery and the critical basilar stenosis
Case Presentation 2

- The Heparin gtt was stopped and the patient was placed on Clopidogrel with the aspirin
- Atorvastatin 80 mg was continued
- Blood pressure medications were held for perfusion purposes
- A decision needed to be made…
Literature on ICAS
WARSS (Warfarin-Aspirin Recurrent Stroke Study) trial

- Though not directly evaluating ICAS; a lesson was learned in stroke management...
- 2206 patients enrolled
- compared aspirin (325 mg/day) with warfarin at an INR 1.4 to 2.8 with non-cardioembolic ischemic stroke
- Oral anticoagulation (OAC) was not better than aspirin for preventing ischemic stroke in patients with ICAS
- Study found similar rates of ischemic stroke, death, or major hemorrhage for both warfarin and aspirin treatment arms
- Issue of why the trial was done…

– Mohr, et al. NEJM 2001; 345: 1444
WASID (Warfarin-Aspirin Symptomatic Intracranial Disease) study

- First medical management trial of ICAS
- TIA or non-disabling stroke from an angiographic verified stenosis at 50 to 99% of a major intracranial vessel
- Compared aspirin 1300mg/day with Warfarin with an INR 2.0 to 3.0
- Study was stopped prematurely because of safety concerns for patients in the warfarin arm after enrolling 569 patients with an average follow-up of 1.8 years

» Chimowitz et al. NEJM 2005; 352: 1305
WASID (Warfarin-Aspirin Symptomatic Intracranial Disease) study

- rate of stroke recurrence in the territory of the stenotic intracranial artery
  - was high for both aspirin and warfarin treatment
  - primarily occurred within the first year from the qualifying event
- Aspirin treatment was associated with a significantly lower rate of...
  - death than warfarin
  - major hemorrhage (mostly systemic) than warfarin

Chimowitz et al. NEJM 2005; 352: 1305
WASID (Warfarin-Aspirin Symptomatic Intracranial Disease) study

• In reality, both warfarin and aspirin were ineffective, given the rate of stroke and death in both arms
  – Warfarin arm 21.8% (n = 289)
  – Aspirin arm 22.1% (n = 280)
• confirmed that OCA was no better than aspirin for preventing ischemic stroke in patients
• poorly controlled risk factors that contributed to recurrent vascular events…
  – systolic blood pressure > 140 mm Hg
  – Mean cholesterol level > 200 mg/dL

Chimowitz et al. NEJM 2005; 352: 1305
WASID (Warfarin-Aspirin Symptomatic Intracranial Disease) study

• Imaging characteristics associated with recurrent stroke risk
  – Degree of stenosis did effect risk of recurrent events
    • At least 70% stenosis had a higher risk of stroke compared to stenosis of 50 to 69%
    • Presence of robust collaterals in patients > 70% stenosis mitigated the risk of stroke recurrence

• Timing of enrollment
  – If within 17 days or fewer had significantly higher risk of recurrent stroke
  – If more than 17 days (up to 90 days) of the qualifying event had lower risk of recurrent stroke

SAMMPRIS (Stenting and Aggressive Medical Management for the Prevention of Recurrent Ischemic Stroke)

- The failure of WASID to answer the question led to this trial
- enrolled patients with 70 - 99 percent stenosis of a intracranial vessel who had a TIA or ischemic stroke within 30 days prior
- randomly assigned to treatment with…
  - intracranial angioplasty and stenting (Wingspan system) plus aggressive medical management
  - or to treatment with aggressive medical management alone
    - Max antiplatelet regimen
    - Systolic blood pressure < 140 mmHg
    - LDL < 70 mg/dL
    - comprehensive lifestyle modification program

» Derdeyn et al. Lancet 2014; 383: 333
SAMMPRIS (Stenting and Aggressive Medical Management for the Prevention of Recurrent Ischemic Stroke)

• enrollment was halted after recruitment of 451 of the planned 764 patients...
  – the combined rate of stroke or death within 30 days of enrollment (the primary outcome)...
    • significantly higher for patients treated with angioplasty and stenting (14%)
    • compared with those treated with medical therapy alone (5.8%)
  – the periprocedural rate of stroke was higher than expected for the stenting group, and lower than estimated for the medical management group

SAMMPRIS (Stenting and Aggressive Medical Management for the Prevention of Recurrent Ischemic Stroke)

• Even at study end…
  – with a median follow up of 32 months
  – max medical (12.2% rate of stroke) was superior to intracranial angioplasty (25%)

• The long term result were largely driven by the 30 day outcomes
  – since the rate of stroke and death after 30 days were similar

SAMMPRIS (Stenting and Aggressive Medical Management for the Prevention of Recurrent Ischemic Stroke)

- The higher stroke rate in the stenting arm was driven by
  - Inclusion of patients with
    - Perforator syndromes
    - Smaller vessel size
    - Diffuse stenosis (oversizing of devices)
  - Procedural considerations
    - Stringent blood pressure control
    - General anesthesia use
    - Operator experience
  - Improved max medical treatment*
    - Interesting that the rate of stroke or death in the aggressive med management arm was substantially lower than in the historical WASID controls (5.8% vs. > 20%)

  Derdeyn et al. Lancet 2014; 383: 333
Intracranial bypass surgery (EC-IC bypass)

- was published in 1985
- 1377 patients
- symptomatic extracranial carotid occlusion, distal carotid occlusive disease, or middle cerebral arteries (MCA) stenosis
- randomized to either medical therapy alone (aspirin 1300 mg/day in four divided doses) or to extracranial-intracranial anastomosis surgery (joining the superficial temporal artery and the middle cerebral artery) combined with medical therapy
- mean follow-up was 55.8 months
- Results revealed the EC-IC bypass was ineffective for preventing stroke

  The EC/IC Bypass Study Group. NEJM 1985; 313: 1191
Recommendations

• Max medical treatment
  – Antihypertensive agents***
  – Statins
  – Antiplatlet agents (aspirin and Plavix for 90 d) then monotherapy (even including aspirin-extended-release dipyridamole)…..MATCH and CHARISMA trials

• Lifestyle modifications
  • No smoking
  • Exercise
  • Weight reduction, etc.
Outcomes...
Outcome

- Residual:
  - No deficit but symptoms of being off balance
  - Modified Rankin of one
Modified Rankin Scale

- 0
  - No symptoms at all
- 1
  - No significant disability despite symptoms; able to carry out all usual duties and activities
- 2
  - Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
- 3
  - Moderate disability; requiring some help, but able to walk without assistance
- 4
  - Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
- 5
  - Severe disability; bedridden, incontinent and requiring constant nursing care and attention
- 6
  - Dead

Outcome 2

- Residual:
  - Right INO
  - Mild dysmetria of limbs (left > right)
  - Modified Rankin of four at discharge to acute rehab
Evidence based medicine

• My thoughts…
  – No guidelines for ICAS from the American Stroke Association
  – Dr. L. Caplan, M.D. argument
  – Example of migraine prevention
    • Topamax
    • TCAs and BP medications
  – that being said…..must not be used as an excuse to do what one wants! Must be justification for reasoning
The future for ICAS?

• Angioplasty alone
• Indirect surgery bypass procedures
• Use of newer anticoagulants
Questions?
Case Presentation 2