Unusual Causes of Ischemic Stroke

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Epidemiology

- Stroke is the fourth leading cause of death in America and a leading cause of adult disability.
- 130,000 people die per year in US
- There are 7 million stroke survivors in US over age 20.
- 2010, over $73 billion in direct and indirect costs from stroke
- More common in males
- Females have a greater disability and mortality
- Approximately 80% of strokes are preventable.
How Many Strokes Can be Prevented by Risk Factor Control in the United States

Based on estimated 731,000 strokes annually
CASE #1

• 65 yo woman who was diagnosed with left BG stroke 4 months prior presents with new-onset GTC seizure
  – PMH: Hypertension
  – SH: 40 pack year history of smoking
  – ROS: mildly progressive cognitive decline

• Exam shows somnolence and left sided hemiparesis
FOLLOW-UP MRI
Differential Diagnosis

- Vasculitis/ Vasculopathy
- Lymphoma
- Multifocal glioma
- Infection
- Demyelination
Causes of CNS
Vasculitis/Vasculopathy

• Infectious: Varicella, CMV, HIV, Syphilis, Lyme, TB, strep
• Systemic angitis: PAN, Churg Strauss, Cogan’s, Temporal, Takayasu’s, Wegener’s, Kawasaki’s, Burgers, Susacs
• Systemic disease: Sarcoid, Behcet’s, Sjorgen’s, SLE, RA, Celiac
• Neoplasm: Lymphoma, Malignant
• Histocytosis, Hairy Cell Leukemia
Primary CNS Vasculitis

- Multiple terms: Primary CNS angitis, granulomatous angitis
- Incidence: 1: 2,000,000
- Clinical presentation: Headache, male>female, all age ranges, cognitive and behavioral issues, rarely (SAH), seizure, cranial neuropathy
- Pathophysiology- infiltration of mononuclear cells in vessel wall of small and medium sized arteries (preservation of the media), T cell mediated
Primary CNS Vasculitis

• Diagnosis
  – Angiography
  – Brain biopsy

• Treatment
  – Immunosuppressants:
    • High dose steroids
    • Cytoxan vs Rituxan
Intravascular Lymphoma

• Large B cell lymphoma
• Lumina of small and medium sized vessels
• 6th-7th decade of life
• Prognosis generally poor
• Clinical: Constitutional systems
• Mulitfocal infarction, progressive encephalopathy, seizures, cranial or neuropathy
• Diagnosis: Skin biopsy or brain biopsy
Intravascular Lymphoma
Case # 2

HPI: 67 year old migrate worker who presents with progressive headache and subjective fever. While in the hospital, he develops sudden right hemiplegia

PMH: Lymphoma – recently completed treatment with Rituxan

SH: Previous smoker, no recent travel
CSF studies

- RBC 39, WBC 790 (88% lymphs), glucose 17, protein 175, GS negative

- Basilar meningitis, associated vasculopathy, cranial neuropathy

TB Meningitis
Case 3

• 47 yo woman, morbidly obese, mother of 7 children, presented to her primary with complaints of decreased visual acuity and vertigo
• PMH: Obesity
• SH: Married, non-smoker, housewife
• Exam: Flat affect, visual ataxia
Case 3
Case 3

• Initial stroke work-up was negative, including labs, MRA, TTE

• She improved and was discharged on aspirin

• Two weeks later, she presented with acute aphasia and right hemi neglect
Case 3

- TEE was done and showed a mobile mass of the left atrium
- MRI of the heart was done for surgical planning
Atrial Myxoma

• Most common primary cardiac tumor
• Usually occurs in the left or right atria
• Benign tumor, but can metastasize
• Carney Syndrome (Autosomal Dominant)
  – Atrial Myxoma
  – Cutaneous and ocular pigmentations
  – Pituitary and adrenal tumors
Case 4

• 32 yo woman who presents with the acute onset of left sided numbness, mild weakness and slurred speech.

• PMH: Migraines, infertility issues
• SH: No tobacco
• FH: Mother with DVT
Sneddon syndrome

- Antiphospholipid antibodies
- Stroke
  - Brain, spinal cord, or retinal events
- Livedo reticularis
Antiphospholipid Antibody Syndrome

Clinical
- One or more episodes of confirmed thrombosis
  - Arteries
  - Veins
  - Small vessels
- Pregnancy morbidity and fetal loss

Immunological
- Serum anticardiolipin antibody of high titer
  - IgG or IgM isotype in blood
  - On 2 or more occasions, at least 6 weeks apart
- Prolonged antiphospholipid-dependent coagulation
  - Lupus anticoagulant
Antiphospholipid Antibody Syndromes

- Primary antiphospholipid antibody syndrome
- Antiphospholipid antibody syndrome associated with other conditions
  - SLE, rheumatoid arthritis, other autoimmune disorders
Antiphospholipid Antibody Syndrome: Described CNS Complications

- Stroke
- Transient ischemic attack
- Amaurosis fugax
- Cerebral venous sinus thrombosis
- Ocular ischemia
- Acute ischemic encephalopathy
- Multi-infarct dementia
  - May involve micro-infarcts
- Seizures
- Cognitive impairment
- Optic atrophy
- Transverse myelopathy
  - Esp. with SLE
- Multiple-sclerosis-like disease
- Chorea
- Migraine
- Psychiatric disturbances
Antiphospholipid Antibody Syndrome: Treatment

- Antiplatelet therapy
  - Clearly ineffective in many patients
- Anticoagulation
  - INR 2-3
  - INR 3-4
- Immunosuppressive treatment
  - Prednisone
  - IVIgG / Plasma exchange
  - Cyclophosphamide (may not affect antibody titers)
  - Rituximab
- Only limited data from controlled trials
77 year old female with history of recurrent esophageal stricture who just completed an EGD with esophageal dilatation under sedation when she suddenly became aphasic with right hemiplegia.

PMH: Chronic anemia, esophageal dysmotility and stricture.

ROS: Frequent epistaxis.
Physical Exam
HHT - Hereditary Hemorrhagic Teleangectasia (Osler-Weber- Rendu)

- Prevalence: 1:10,000
  - AVM pulmonary 15-50%
  - Cerebral/AVM (10-15%) AVM
  - Presents with air embolism, stroke, seizure, brain abscess
  - Phenotype: Epistaxis (90% age by age 45), migraine, chronic anemia, chronic dyspnea
  - Neurologic manifestations present 3^{rd}-6^{th} decade
Case 6

• 53 year old woman with frequent migraines who presents with acute onset right sided weakness, confusion, vomiting and sleepiness
• PMH: migraine
• FH: Mother had stroke, maternal GM had stroke and dementia
• SH: no tobacco or drug use
Exam: slow mentation, frontal lobe release signs, moderate right HH, bilateral Babinski
• CADASIL: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
CADASIL

• Migraine with aura in 20s
• Ischemic stroke in 5\textsuperscript{th} and 6\textsuperscript{th} decade
• Mood disturbance
• Seizures
• Progressive Dementia

• ATTACKS: may be odd with confusion, coma, fever, atypical aura prolonged
CADASIL

• Genetics- Mutations of the Notch 3 gene. Notch 3 expressed only in vascular smooth muscle
• Pathophysiology: Dysfunction of vascular smooth muscle contractility and accumulation of extracellular Notch 3 protein component
• Diagnosis: Genetic Testing or skin biopsy
• Treatments-Vasoconstrictive drugs for migraine not recommended
Radiologic Correlation

- **Lacunes** in white matter and deep gray
  - Periventricular (96%), brainstem, external capsule, corpus callosum, frontal, spinal cord
- Increased T2 white matter hyperintensities in asymptomatic
- **Microbleeds** in 31% of symptomatic (Oberstein 2001)
- Cerebral Angiography contraindicated
- Disability associated with (Viswanathan 2007)
  - volume of lacunar lesions, cerebral microhemorrhages, bp
Small vessel arteriopathy
Skin Biopsy in CADASIL

- **Generalized arteriopathy**
  - Skin biopsy 96% sensitive 100% specific (Joutel 2001)

- Granular Osmiophilic Material deposits
Final Case

• 42 year old woman with long history of migraine headache who presents with transient left sided weakness
MOYAMOYA
MOYAMOYA SYNDROME

- Progressive obliteration of the distal ICA and proximal ACA
- 10% unilateral
- Neovascularization and collateralization
- Incidence in NW: 0.086/100,000
- Clinical- Young adult, women>men, children (headache)
- Ischemic > ICH> SAH
- (sp remote radiation, SS, NF1, FMD, Down’s, PKD)
- TREATMENT: Revascularization (STA-MCA Bypass)
Take Home

• Common causes for stroke are still Common
• Red Flags for uncommon causes
  – Recurrent
  – Progressive
  – Seizure
  – Constitutional
  – Cognitive decline
  – Headache

The answer lies in the History and Physical