STROKE AND MULTIPLE SCLEROSIS

2019 ACOI Internal Medicine Review Course

Baltimore Marriott Waterfront Hotel

Baltimore, Maryland

May8-May 12, 2019

Scott Spradlin D.O. FACP, FACOI

I have no **relevant financial or nonfinancial relationships** in the products or services described, reviewed, evaluated or compared in this presentation.

Stroke or Brain Attack

- 5th Leading cause of Death for men
- 4th leading cause of Death for women
- 3rd leading cause of death for Blacks
- Acute brain injury due to a vascular etiology
- Sudden onset
- Persist at least 24 hours
- Associated neurological deficit/deficits

TIA

-Neurological deficits lasting less than 24 hours

Stroke Imaging

















Stroke Imaging- diffusion/perfusion





- Occurrence and Financial Facts:
 - 795,000 Strokes Occur each year
 - 87 percent of those strokes are ischemic
 - Stroke kills 130,000 Americans/year
 - Stroke costs the US an estimated 34 billion/yr
 - Leading cause of serious long term disability

STROKE

- Race/Sex/Geography
 - Black risk of death is 1.49X Whites
 - Males greater risk than females
 - Hispanics higher risk for lacunar infarcts
 - Southeastern US has higher risk

-Age

- Stroke occurs in all ages
- Stroke risk increases with age
- Age >64 is where 75% of occurrence

STROKE BISK FACTORS

Non-modifiable Risk Factors

- Age
- Race
- Sex
- Ethnicity
- History of Migraine
- Sickle Cell Disease
- Fibromuscular Dysplasia
- Heredity

STROKE BISK FACTORS

- Laboratory Monitoring Risk
 - Glucose and Electrolytes
 - CBC with Platelets
 - Prothrombin Time/ Partial Thromboplastin Time
 - Cholesterol/LDL/HDL
 - ANA/RF/Homocysteine/ESR
 - Protein C/ Protein S/ Antithrombin III/ Leiden
 - Anticardiolipin Antibody
 - Lupus Inhibitor/ Antiphospholipid Antibodies

VASCULAR RISK FACTORS

 Modifiable conditions and lifestyle characteristics identified as a risk factors for stroke:

High blood pressure Atrial fibrillation Smoking

Heavy alcohol use Myocardial infarction Physical inactivity Obesity High Cholesterol Diabetes mellitus Carotid artery disease

SLEEP-RISORRERER BREATHING

- Background
 - Sleep-disordered breathing (SDB) is both a risk factor and a consequence of stroke
 - More than 50% of stroke patients have SDB, mostly in the form of obstructive sleep apnoea (OSA).
 - SDB is linked with poorer long-term outcome and increased long-term stroke mortality¹
 - Continuous positive airway pressure is the treatment of choice for OSA.

MANAGEMENT OF COMPLICATIONS

Falls

- Are common in every stage of stroke treatment
- Risk factors include cognitive impairment, depression, polypharmacy and sensory impairment¹
- A multidisciplinary package focusing on personal and environmental factors might be preventive²
- Exercise, calcium supplements and bisphosphonates improve bone strength and decrease fracture rates in stroke patients^{3,4}

1: Aizen E et al.: Arch Gerontol Geriatr (2007) 44:1-12 2: Oliver D et al.: BMJ (2007) 334:82 2: Papa MV et al.: Clip Popabil (2006) 20:07,111

3: Pang MY et al.: Clin Rehabil (2006) 20:97-111 4: Sato Y et al.: Cerebrovasc Dis (2005) 20:187-92

MANAGEMENT OF COMPLICATIONS

Dysphagia and feeding

- Dysphagia occurs in up to 50% of patients with unilateral hemiplegic stroke and is an independent riskfactor for poor outcome¹
- For patients with continuing dysphagia, options for enteral nutrition include NG or PEG feeding
- PEG does not provide better nutritional status or improved clinical outcome, compared to NG^{2,3}

1: Martino R et al.: Stroke (2005) 36:2756-63

2: Dennis MS et al.: Lancet (2005) 365:764-72

3: Callahan CM et al.: J Am Geriatr Soc (2000) 48:1048-54

BEHABILITATION *Early rehabilitation-*

More than 40 % of stroke patients need active rehabilitation

 Active rehabilitation should start early, providing the patient is clinically stable

 Passive rehabilitation should be given if the patient is unconscious or paralyzed

Rehabilitation should be continued as long as perceptable recovery is taking place

REHABILITATION

- Multidisciplinary stroke team for rehabilitation
 - Stroke physician
 - Nurses experienced in stroke management
 - Physiotherapist trained in stroke rehabilitation
 - Occupational therapist skilled in stroke
 - Speech therapist familiar with speech problems in stroke patients
 - Neuropsychologist accustomed to stroke rehabilitation
 - Social worker familiar with the problems of stroke patients

Calculating Risk **ABCD2**

To identify individuals at high early risk of stroke after transient ischemic attack.

A (Age); 1 point for age <a>60 years,

- **B** (Blood pressure > 140/90 mmHg); 1 point for hypertension at the acute evaluation,
- **C** (Clinical features); 2 points for unilateral weakness, 1 for speech disturbance without weakness,

D (symptom Duration); 1 point for 10–59 minutes, 2 points for \geq 60 minutes. **D** (Diabetes); 1 point

Total scores range from 0 (lowest risk) to 7 (highest risk).

Scale: Scores 0-3:low risk

Scores 4-5:moderate risk

Scores 6-7:high risk

Types of Stroke

Ischemic- *most common* >70%

- Thrombotic
 - -Atherosclerosis
- Embolic
- -Emboli from the Heart or Great Vessels Hemorrhagic-
 - Intracerebral

-*Hypertension or Amyloid Angiopathy* Subarachnoid

-Berry Aneurysms



Stroke and Multiple Sclerosis Thrombotic Strokes

Atherosclerosis involving:

-Internal Carotid -Middle Cerebral -Vertebrobasilar

Symptoms

-Slow stepwise progression of symptoms -Usually preceded by TIA's

Other Causes

-Lupus anticoagulant -Polycythemia -Syphilis -Thrombocytosis -Dissecting Aortic Aneurysm

Embolic Stroke

- Not usually preceded by TIA
- Emboli
 - ≻Heart
 - >Large Blood vessel

>Usually effects middle>posterior>anterior cerebral

• Symptoms

>Neurodeficits worst at onset

> Weakness is greater in distal extremities

Stroke Symptoms By Region

Middle cerebral-

Anterior cerebral-

Posterior cerebral-

Single Hemisphere-

Vertebrobasilar-

Lateral Medullary syndrome-

Lacunar-small vessel-

Middle Cerebral Artery Occlusion

- >Contralateral hemiplegia
- >Contralateral hemianesthesia
- >Homonymous hemianopsia
- >Impaired conjugate gaze in opposite direction
- >Impaired spatial- nondominant
- >Impaired language-dominant
- >If lesion high- >loss face/upper ext
 - ➢ If it is in the main trunk- deficit same throughout

Anterior Cerebral Artery Occlusion

- >Most affected in distal contralateral leg
- >Urinary incontinence
- Gait abnormalities
- If includes corpus callosum the patient will have tactile anomia (cannot name what they touch)

Posterior Cerebral Artery Occlusion

- > Contralateral homonymous hemianopsia
- > Usually upper quadrantanopsia
- > Mild contralateral hemiplegia/anesthesia
- Color anomia= corpus callosum damage
- > Memory loss
- > If occlusion bilateral memory will be severe/persistent

Single Hemisphere injury

- > Does not affect paraspinal muscles
- Does not affect pharynx
- Does not affect jaw
- > Does not affect the forehead
- > If any or all of the above are affected think:
 - Bilateral hemispheric infarct
 - Brainstem infarct

Vertebrobasilar Artery Occlusion

- >Associated with brain stem strokes
- >Bilateral extremity motor/sensory dysfunction
- >Quadraplegia in severe cases
- Crossed motor and sensory deficits
- >Horner syndrome
- Cerebellar signs/stupor/coma
- >Cranial nerve dysfunction

Lateral Medullary Syndrome

-Also called Wallenberg Syndrome

- > Nausea
- > Vomiting
- > Nystagmus
- > Ipsilateral Horner Syndrome
- Ipsilateral palate and vocal cord weakness
- > Ipsilateral face hemi-anesthesia
- Contralateral body hemi-anesthesia

Lacunar Strokes

- > Due to hypertension
- > Occlusion of very small arterioles
- > Over time they form "cysts" in the brain
- >Pure hemiplegia
- >Pure hemisensory
- Multiple bilateral frontal lobe "lacunes" can cause pseudobulbar palsy

Work up:

History

Computerized Tomography Brain

CBC with platelets

Troponin

Electrolytes, Glucose, Bun, Cr,

Coagulation profiles

ECG

Trans-thoracic Echocardiogram

Carotid Ultrasound/Trans-cranial Doppler Consider MRI/MRI Diffusion/Angiography



Stroke and Multiple Sclerosis Ischemic Stroke Treatment

- -Thrombolysis-Alteplase(only need CT/Glucose)
 - ->18 yrs old with an ischemic stroke Dx
 - Onset time 3 hours(3-4.5 with caveats)
- -Treat BP-gradually IV <180/105
- -Aspirin/Antiplatelets
- -Oxygen >94%
- -Surgical Intervention evaluation LVO
 - -intra-arterial therapy
 - -mechanical thrombectomy

CONTRAINDICATIONS TO ALTEPLASE (tPA)

Absolute-

Intracranial hemorrhage on CT

Clinical Presentation suggests subarachnoid hemorrhage

Neurological surgery, serious head trauma, or previous stroke past 3 months Uncontrolled hypertension(>185 mmHg SBP or >110 mm Hg DBP)

History of intracranial hemorrhage

Seizure at stroke onset Known AVM, neoplasm, or aneurysm Active internal bleeding Suspected/confirmed endocarditis Known bleeding diasthesis: plts<100,000, heparin with elevated PTT, oral anticoagulants and INR>1.7, thrombin inhibitors

Abnormal blood glucose(<50 or >400 mg/dl)

Relative –

Only minor or rapidly improving stroke symptoms Patient has had major surgery or serious trauma excluding head trauma in previous 14 days History of GI/Urinary hemorrhage in last 21 days Recent arterial puncture at a noncompressible site Recent lumbar puncture Post myocardial infarction pericarditis Pregnancy

Additional WARNINGS to tPA > 3-4.5 hr onset-

Age >80 History of prior stroke and diabetes Any active anticoagulant use (even with INR <1.7) NIHSS>25

Stroke and Multiple SclerosisPost Acute Care Therapy

Antiplatelets

ASA* (160-300 mg) *24-48 hours after acute intervention

Plavix(Clopidogrel)

Warfarin for valvular atrial fibrillation

Dabigatran, Apixaban, Rivaroxaben- (non valvular Atrial Fibrillation)

Manage underlying causes:

Cardiac- per ACC for angina or coronary syndromes HTN- JNC guidelines- <130/80 Diabetes- HbA1C <6.5-7.0 Tobacco abuse management Hyperlipidemia- LDL <70 If >70% carotid stenosis- surgery in 48 hrs-7 days

Score for Atrial Fibrillation Stroke Risk:

Congestive Heart Failure	1pt
Hypertension	1pt
Age>75	1pt
Diabetes Mellitus	1pt
Stroke or TIA Symptoms	2pt

Score >2 High Score >1 <2 Moderate Score 0 Low oral anticoagulant oral anticoagulant or ASA ASA 160-325mg

Stroke and Multiple Sclerosis Intracerebral Hemorrhage

Amyloid Angiopathy

- > Commonly causes recurrent bleeds
- > >65 yrs old
- Subcortical , rarely affects deep structures
- > Can cause multi-infarctional dementia
- Also found in alzheimers patients- unclear association
- Occasionally can be associated with subarachnoid

Intracerebral Hemorrhage

- Hypertension
- Gradual and smooth onset of symptoms
- Putamen>Thalamus>Pons>Cerebellum
 - > Putamen
 - Contralateral hemiparesis/sensory loss/hemianopsia
 - Acts just like a middle cerebral infarct
 - > Thalamus
 - Contra hemiplegia/hemianesthesia/sensory>motor
 - > Pons
 - *Coma/pinpoint pupils/complete paralysis*
 - Can have decerebrate posturing bilaterally
 - > Cerebellum
 - Acute dizziness/ataxia/vomiting
 - No mentation change or loss of consciousness

Stroke and Multiple Sclerosis Subarachnoid Hemorrhage

- Cerebral saccular aneurysm bleed
 - -Usually Circle of Willis
 - -*IC*=40%/AC=35%/MC=20%
- > Hypertensive hemorrhages with ventricular rupture
- > A-V Malformations
- > Symptoms
 - Acute/Severe headache (thunderclap)-unresponsive to meds
 - May be alert/confused /comatose
 - No focal neurological signs
 - Neck stiffness is classic- but not always present

Stroke and Multiple Sclerosis Hemorrhagic Stroke Work Up

Computerized Tomography

(CT misses 10% of Bleeds)

>Lumbar Puncture

• Xanthochromic supernatent is diagnostic

- If LP (-) can be hours before blood gets in CSF
- >Cerebral Angiography
- > Can re-bleed in 24 hours due to vasospasms

Treatment

- -Neurosurgery consult/Intervention
- -ABC'S/ Intracranial Pressure monitoring

-Hemodynamic and edema management/Nimodipine/Mannitol/Glycerol/Saline

-Seizure management

Multiple Sclerosis

Myelin deterioration- demyelination

- Brain
- Spinal Cord
- Optic Nerve

Pathophysiology

10x more common in northern latitudes May be viral in origin— Female2:1 Males Autoimmune but does have genetic components Onset 20-50 yrs of age

Plaques

- Cause a mononuclear inflammation
- Demyelination with axonal sparing
- Oligodendrogial cell loss and astrocyte proliferation
- Long standing lesion Astrogliosis

Symptoms

- Mononeuropathy +/- multiplex
- Optic neuritis
- Ophthalmoplegia/Ophthalmoparalysis-
- Intermittent Diplopia
- Extremity weakness
- Tremors
- Lhermitte sign-

(Paresthesias radiating down the spine into extremities on neck flexion)

Multiple Sclerosis-H&E STAIN



Types of Multiple Sclerosis

Clinically Isolated Syndrome(CIS)

No reoccurrence after initial

Relapsing-remitting

Most common Has attacks followed by none then reoccurs

Primary-Progressive

Men Gradual decline few plateaus

Secondary-progressive

Stage II relapsing-remitting. No periods of remission

Progressive-relapsing

Rare. Progressive form until the end

Malignant (Marburg Variant)

Very rare. Decline to death in few months

McDonald Criteria: (attack must last 24 hours and 30 day interval)

Diagnosis of Multiple Sclerosis:

Attacks 2 or more	Lesions 2 or more	Additional Information
2 or more	1	Dissemination in space or further attack
1	2	Dissemination in time or further attack
1	1	Dissemination space/time or further attack
0		1 yr of disease progression and 2 of below: -Positive MRI Brain -Positive MRI Spinal Cord -Positive CSF

Diagnostic Tests:

MRI – TEST OF CHOICE-Brain/Spinal Cord

-White plaques lesions

Evoked Action Potentials

-Silent lesions

Lumbar Puncture

-Increased IgG/Oligoclonal IgG bands in CSF

-Elevated protein





Stroke and Multiple Sclerosis Treatment*

- Acute Phase/Initial
 - Steroids 500mg daily x 5 days
 - Plasma exchange for severe deficits with poor response to steroids
- Oral Immunomodulator-
 - Fingolimod(Gilenya), Ampyra, Aubagio, Tecfidera
- Relapsing-Remitting- most common
 - Beta-interferons(1-a,1-b)-
 - -Avonex/Rebif/Betaseron/Extavia/Plegridy
 - Monoclonal Antibodies-
 - -Ocrevus,Rituxin,Tysarbi
 - -Alemtuzumab (Lemtrada)- HIV negative
 - Copolymer-
 - -Copaxone/Glatoba
- Primary Progressive
 - -Ocrevus(ocrelizumab)
- Chronic/Advanced
 - Novantrone(mitoxantrone)- IV

*Ambulation difficulties treatment is Ambyra (helps with MS ambulation only)

- 34 yr old presents with:
- ataxia
- ophthalmoplegia
- paresthesia of the legs intermittently
- massive weight loss over the past few months.
- history is significant for HIV
- On gancyclovir and protease inhibitors and T-cell counts have remained <200.
- His mentation is going quickly and he has no memory and has stopped eating.
- What is your diagnosis?



Answer

PML

Progressive Multifocal Leukencephalopathy

PML is caused by the JC Virus but there are some drugs that can create a reversible leukoencephalopathy as in this case drug induced



Central Pontine Myelinolysis(CPM)

- >Occurs in patients with severe hyponatremia
- >Their sodium is corrected too aggressively
- >Quadraparesis
- ≻Mutism
- Pseudobulbar palsy
- Swallowing dysfunction
- Treatment:

Correct Na slowly and treat underlying cause