Management of Stroke Due to Infective Endocarditis (IE)

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No Disclosures

Objectives

- Recognize patients with stroke due to infective endocarditis.
- Understand the risks and benefits of anticoagulation or thrombolytic therapy for patients with stroke due to infective endocarditis.
- Know the factors necessary for developing a treatment plan for patients with stroke due to infective endocarditis.
Neurological Complications of Infective Endocarditis

- Overall 20%-40% of patients with IE.
  - Ischemic Stroke.
  - Hemorrhagic Stroke.
  - Cerebral Infection.
  - Seizures.
  - Headache.
  - Encephalopathy.
  - Spinal Cord Infarction or Abscess.
  - Dizziness.
  - Retinal Ischemia.
  - Cranial and Peripheral Neuropathies.

Ischemic Stroke due to Infective Endocarditis

- Occurs in 17%-30% of patients with IE and accounts for 50%-75% of all neurological complications of IE.
- Septic and non-septic emboli.

Hemorrhagic Stroke due to Infective Endocarditis

- 2%-17% of patients with IE (typically intraparenchymal or subarachnoid).
- Primary
  - Usually results from septic emboli leading to septic necrosis and rupture of vessel wall.
  - Less commonly due to rupture of a mycotic aneurysm.
- Secondary
  - Typically hemorhagic transformation of ischemic stroke from septic embolism.
  - Occurs in 20%-40% of patient with infective endocarditis and ischemic stroke.
### Suspicion of Infective Endocarditis

- Febrile illness and
  - New murmur suggestive of regurgitation.
  - Pre-existing cardiac lesion, and no clinically obvious site of infection.
- Valvular heart disease with stenosis or regurgitation.
- Valve replacement.
- Structural heart disease even if surgically corrected (except ASD; fully repaired VSD or patent ductus arteriosus).
- Hypertrophic cardiomyopathy.
- Recent intravascular intervention and bacteremia (especially with predisposing condition).
- CHF.
- New cardiac conduction disturbance.
- Embolic (stroke, conjunctival hemorrhage, splinter hemorrhages, Janeway lesions) or immunological phenomenon (Roth spots, Osler Nodes).
- Abscess of unknown cause (renal, splenic, cerebral, vertebral).

### Suspicion of Infective Endocarditis (cont.)

- Protracted history of sweats, weight loss, anorexia, and an pre-existing cardiac lesion.
- Any new unexplained embolic event (cerebral or limb).
- Unexplained, persistently positive blood cultures with predisposing condition.
- Catheter-related blood stream infection persistently positive 72 hours after catheter removal.

### Diagnosis of Infective Endocarditis: Duke Criteria

**Major Criteria**

- Two separate positive blood cultures (or persistently positive*) for Infective Endocarditis
  - Strep. Vindera
  - Strep. Bovis
  - HACEK (Haemophilus, Actinobacillus, actinomycetemcomitans, Cardiobacterium hominis, Eikenella species, and Kingella kingae)
  - community-acquired Staphylococcus aureus or enterococci, in the absence of a primary focus

- Positive echocardiogram for IE
  - mobile intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation, or
  - abscess, or
  - new partial dehiscence of prosthetic valve

*Two >12 hours apart, or three of 3 or 4 within an hour
### Diagnosis of Infective Endocarditis: Duke Criteria

<table>
<thead>
<tr>
<th>Minor Criteria</th>
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<tr>
<td>• Predisposing heart condition or intravenous drug use</td>
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<td>• Temperature &gt; 38.0°C (100.4°F)</td>
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<td>• Vascular phenomena (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions)</td>
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<td>• Immunologic phenomena (glomerulonephritis, Osler’s nodes, Roth spots, rheumatoid factor)</td>
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<td>• Microbiological evidence (positive blood culture but not a major criterion, or serological evidence of active infection with organism consistent with IE)</td>
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<td>• Echocardiographic findings consistent with IE but not a major criterion</td>
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### Emboli: Janeway Lesions

- Non-tender, often hemorrhagic, lesions occurring mostly on the palms and soles. Usually septic emboli.

### Emboli: Conjunctival Hemorrhages

- Septic or thrombotic emboli
Emboli: Splinter Hemorrhages

- Usually thrombotic but may be septic emboli

Osler Nodes

- Red-purple, slightly raised, tender lumps, often with a pale center, typically found on fingers and/or toes
- Due to immune complex mediated vasculitis.
- Pain often precedes the development of the visible lesion by up to 24 hours.
- They can occur at any time during the course of endocarditis (usually subacute) and last from hours to several days.

Roth Spots

- Due to immune complex mediated vasculitis
Diagnosis of Infective Endocarditis: Duke Criteria

Diagnosis requires:
• Two major criteria, or
• One major and three minor criteria, or
• Five minor criteria

Risk Factors for Neurologic Complications

• Left side rather than right side valve involvement
• “Virulent” organisms
  – Staphylococcus aureus
  – Enterococci
  – Escherichia coli
  – Streptococcus bovis
  – Fungi
  – Enterobacteriaceae
  – Anaerobic bacteria

Risk Factors for Neurologic Complications (cont.)

• Within 1-2 weeks of infection
• Valve vegetations
  – Present
  – Change in size or consistency on serial echocardiography
  – Presence of spontaneous echo-contrast
• Antiphospholipid antibodies
Anticoagulation in Patients with IE

- Hemorrhagic complications are more common in anticoagulated patients:
  - Hart et al found one-third of patients with endocarditis and subsequent intracerebral hemorrhage were either anticoagulated or had an underlying bleeding diathesis. Stroke 18:1048, 1987
  - Pruitt and colleagues found 23% of all intracerebral hemorrhages occurred in the 3% of anticoagulated patients. Medicine 57:329, 1978
  - Le Cam et al reported 50% of all intracranial hemorrhages in patient with IE occurred in the 13% of patients that were anticoagulated. Eur Heart J 5, suppl C:97, 1984

Anticoagulation in Patients with IE: Native Valves

- Paschalis et al:
  - No difference in the incidence of cerebral embolism between patients on long-term anticoagulation (due to pre-existing prosthetic valve) and those not anticoagulated.
    - Long-term anticoagulation: 30% cerebral embolism.
    - No anticoagulation: 29% cerebral embolism.

Anticoagulation in Patients with IE: Prosthetic Valves

- Emboli occur in 50%-88% of patients with prosthetic valve infective endocarditis.
  - Wilson et al reported that in patients with prosthetic valves:
    - 3 of 38 (8%) who received anticoagulation had neurological complications
    - 10 of 14 (71%) who received inadequate anticoagulation or did not receive anticoagulation had neurological complications.
  - Johnson reported 50% incidence of intracranial hemorrhage in patients with prosthetic valve IE treated with anticoagulation.
Anticoagulation in Patients with IE

- Thus, consensus opinion:
  - Avoid anticoagulation in patients with native valve endocarditis.
  - Use caution anticoagulating patients with prosthetic valve endocarditis.
  - Use caution anticoagulating patients with DIC, thrombocytopenia, or vitamin K deficiency.

Thrombolytics in Patients with IE

- Junna et al:
  - 56 year-old man with left MCA distribution stroke (NIHSS: 15).
    - IV tPA: 156 minutes after symptom onset.
    - Head CT (24 hours post tPA): evolving left MCA stroke but no hemorrhage.
    - NIHSS (48 hours post tPA): 4.
    - Blood cultures: beta hemolytic Strep.
    - TEE: 0.8 cm x 0.8 cm vegetation on the anterior mitral leaflet with regurgitation and flail leaflet.

- Bhuva et al:
  - 46 year-old man with right MCA (NIHSS: 15).
    - IV tPA: 110 minutes after symptom onset of symptoms with deterioration an hour after the infusion.
    - Head CT: Occipital, and frontal lobe intracerebral hemorrhage (ICH).
    - Blood cultures: Corynebacterium.
    - Head CT (hospital day 7): hemorrhagic transformation of the right MCA infarct, midline shift, and uncal herniation leading to death.
    - Autopsy: vegetations on the mitral and aortic valves.

- 65 year-old woman with left MCA distribution stroke (NIHSS: 21).
  - IV tPA: 120 minutes after symptom onset.
    - Head CT 24 hours post tPA: subarachnoid hemorrhage (SAH) over the left frontal lobe and small ICH in the right precentral gyrus and cerebellum.
    - Blood cultures: Streptococcus viridans.
    - TTE vegetations on both mitral valve leaflets and the aortic valve.

- 61 year-old man with left MCA distribution stroke (NIHSS: 17).
  - IV tPA: 90 minutes after symptom onset. IA attempted but no arterial blockage found.
    - Head CT about 24 hours after IA: multiple bilateral cerebral and cerebellar hemorrhages, and SAH in the posterior fossa.
    - Blood cultures: methicillin-sensitive Staphylococcus aureus.
    - TEE: small vegetation on the anterior mitral leaflet.
Antibiotic treatment for IE
(J Antimicrob Chemother 2012; 67: 269–289)

- Chronic or subacute presentation:
  - Three sets of blood cultures, 2-6 hours apart, prior to commencing antimicrobial therapy.

- Suspected IE and severe sepsis or septic shock:
  - Two sets of blood cultures, within 1 hour, prior to commencement of empirical therapy (avoid undue delay in commencing empirical antimicrobial therapy).

- When the causative microorganism has been isolated, the MIC of the chosen antimicrobial should be established by a standardized laboratory method to ensure susceptibility.

Antibiotic treatment for IE
(J Antimicrob Chemother 2012; 67: 269–289)

Surgical treatment for IE
(Circulation 2005; 111: e394-e434)
Objectives

- Recognize patients with stroke due to infective endocarditis
  - Fever.
  - Sweats, weight loss, anorexia, and an pre-existing cardiac lesion.
  - IV drug abuse.
  - Hypertrophic cardiomyopathy/CHF.
  - New murmur.
  - Recent intravascular intervention and bacteremia (especially with predisposing condition).
  - New cardiac conduction disturbance.
  - Conjunctival hemorrhage.
  - Splinter hemorrhages.
  - Janeway lesions.
  - Roth spots.
  - Osler Nodes.
  - Renal, splenic, cerebral, or vertebral abscess of unknown cause.
  - Unexplained embolic events.
  - Unexplained, persistently positive blood cultures with predisposing condition.
  - Catheter-related bloodstream infection persistently positive 72 hours after catheter removal.

Objectives

- Understand the risks and benefits of anticoagulation or thrombolytic therapy for patients with stroke due to infective endocarditis.
  - For patients with IE, most intracranial hemorrhages occur in those on anticoagulation.
  - No clear evidence that anticoagulation reduces the risk of cerebral embolism.
  - Patients with prosthetic valves are high risk for embolization but also at high risk of intracranial hemorrhage. Careful evaluation including head CT, brain MRI, and/or angiography is warranted.
  - There is insufficient evidence for or against the use of thrombolytics for patients with acute ischemic stroke due to IE. Extreme caution is warranted.

Objectives

- Know the factors necessary for developing a treatment plan for patients with stroke due to infective Endocarditis.
  - Empiric antibiotic therapy may be started in patients with acute presentation, sepsis, or septic shock.
    - Subacute presentation usually does not require empiric treatment.
  - However, identification of the organism and its sensitivity is required for choice and duration of antibiotic treatment.
  - Surgical intervention should be considered for those with:
    - Large or persistent vegetation.
    - Repeated embolization.
    - Valve dysfunction.
    - Perivalvular extension.