Cardiogenic Emboli: Part IV-CHF, Low EF, & Related Topics

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Case

- This 54 yo man presented > 12 h after the onset, first, of L face and thumb weakness and then, later, dysarthric speech
Embolic stroke, cardiogenic or atherogenic source
Embolic stroke, cardiogenic or atherogenic source?
PMHx included
- Cardiomyopathy w/ EF 20-30% (NSR)
- Smoker, dyslipidemia

Meds included
- ASA
Case: Summary

- 54 yo w stroke in the setting of low EF/CHF
  - *Were these areas of infarction due to a single embolus that fragmented?*
  - *Were they due to multiple emboli?*
  - *Were these in relation to the low EF/CHF?*
Cerebral Embolism Task Force

- PRIMARY features
  - Abrupt onset, maximal deficit
  - **Presence of a potential embolic source**
  - Multiple brain infarcts involving the cortex or cerebellum in multiple vascular territories
SECONDARY features

- Hemorrhagic infarct by imaging
- Absence of atherosclerotic vascular disease by angio
- Angio evidence of "vanishing" clot
- Evidence of embolism to other organs
Cardiac Disorders and IS

- **AFIB**
  - 4 to 5 fold increase risk of IS

- **CHF**
  - 2 to 3 fold increase risk of IS
Stroke 2011;42:2977-2982
A distinction can be made between SYS and DIA dysfunction, the latter affecting ~1/3 of all pts w/ CHF

- EF is decreased w/ SYS dysfunction
- EF is normal in those w/ DIA dysfunction, characterized by elevated end-DIA ventricular pressure
Epidemiology of CHF

- Major RFs for CHF
  - HBP, MI, valvular disease, DM, AFIB

- Lifetime prevalence for CHF
  - 1 in 5 in those older than 40-y
CHF represents the most common reason for hospitalization in those older than 65-y

- 5-y survival is ~35%
- SYS dysfunction
  - Overall annual mortality of 15% to 19%
- DIA dysfunction
  - Overall annual mortality of 08% to 09%
- Once there is CHF-associated limitation of moderate exercise
  - 1-y survival rate is 55%
- Symptoms at rest
  - 1-y survival rate is as low as 5%
Prevalence of accompanying AFIB in CHF pts
- ~10% to 17%
- Increases w/ left atrial diameter and functional class, reaching almost 50% in pts w/ the most limitation
- This is relevant because AFIB is associated w/ increased stroke risk and mortality in CHF pts
Stroke as a consequence of CHF

- Increased thrombus formation
- Increased prevalence of LV dysfunction
- Decreased LV EF%
- Increased prevalence of AFIB
- Increased blood viscosity
- Increased coagulation
  - Increased D-dimer concentration
  - Increased thrombin-antithrombin complex levels
  - Increased thrombin concentration
  - Decreased tissue plasminogen activator
  - Increased fibrin cleavage products
- Decreased fibrinolysis
  - Increased plasminogen activator inhibitor-1 level
- Increased thrombocyte aggregation
  - Increased P-selectin level
  - Increased beta-thromboglobulin concentration
- Increased endothelial dysfunction
  - Increased von Willebrand factor concentration
  - Increased soluble thromboglobulin concentration
  - Increased E-selectin level
Increased large artery atherosclerosis
- Increased prevalence of HBP and DM
Increased small vessel occlusion
- Increased prevalence of HBP and DM

? Borderzone infarction
- Increased malfunctioning of cerebral autoregulation
Prevalence of stroke in pts w/ CHF

- ~10% to 24% of all stroke pts have CHF
- CHF is thought to be the likely cause of stroke in ~9%
- Framingham: risk of IS is 2 to 3 times for pts w/ CHF than it is w/o CHF
- w/in 1-mo after the Dx of CHF
- Stroke risk is highest (HR=5.8)
9% to 10% risk of recurrent stroke per year in stroke pts w/ CHF according to retrospective studies

OR=2.1 of having another stroke compared to stroke pts w/o CHF
Warfarin and Antiplatelet Therapy in Chronic Heart Failure (WATCH)

- N=1587 pts w/ CHF, an LVEF 35% or <, and persisting NSR
  - WARF was associated w/ fewer nonfatal strokes than was either ASA or CLOP (0.6% v 2.3%) during an average f/u of 21-mo
  - However, study terminated early because of slow enrollment
- Additional RFs for stroke pts w/ CHF
  - Survival and Ventricular Enlargement (SAVE) study
  - RR of 1.2 per 5% LVEF reduction
  - Framingham
  - CHF does not account for increased risk of stroke w/ advanced age
  - The presence of AFIB was associated w/ a 2-fold increased stroke risk in those w/ CHF
Studies of Left Ventricular Dysfunction (SOLVD)
- N=5457 male pts w/ CHF
  - Stroke risk was increased w/ age, Hx of HBP, DM, and prior stroke
- N=958 female pts w/ CHF
  - Stroke risk was increased w/ DM and decreased EF

Reasons for Geographic And Racial Differences in Stroke (REGARDS)
- Hypotension may be a RF for stroke
Stroke and CHF: death or disability

Retrospective cohort studies have demonstrated a more than doubled risk of death after stroke for CHF pts

- Stroke-induced amplification of cardiac failure due to autonomic dysregulation
- Stroke-induced neurologic deficits are more severe in CHF pts
- Stroke pts w/ CHF have longer hospital stays
Do we recognize only the tip of the iceberg?

~20% to 42% of all CHF pts showed cerebral ischemic lesions on MRI compared with 0% to 12% in healthy controls of similar age
~25% to 80% of all pts w/ CHF experience neuropsychological changes, including decreased attention and concentration, memory loss, diminished psychomotor speed, and decreased executive function.

There is also a higher mortality in CHF pts w/ cognitive impairment.
Some Conclusionary Comments

- AFIB is associated with increased stroke risk and increased mortality in CHF pts
It seems likely that CHF-related strokes are primarily embolic, but concurrent subtypes of stroke have to be taken into account.
Case

- 77 yo man experienced dizziness, generalized weakness and difficulty walking X 2-d
- Awoke w/ difficulty getting OOB w/ moderate L-sided weakness
- PMHx included CHF, AFIB, and prior SDH
- Meds included dose-adjusted WARF (INR in ED=1.38 “as we were keeping him low”)
Head CT #1 = no acute changes

Mild CHF, BP 100-116 SYS
Rapidly resolving RMCA syndrome except for persistent L VF loss

MRI = next slide

MRA = negative
MRI ~24-hours after onset: DWI (top row) and T2GRE images of multi-focal hemorrhagic infarction
Are these embolic strokes?

Or are these borderzone strokes?

Or a single embolus that fragmented?
CT @ ~48-h post-onset: evident area of hemorrhagic transformation of a bland infarct into a partially hemorrhagic one
- WARF held
- CHF easily treated
- *How do we move forward?*
Patients with CHF have a 2- to 3-fold increased risk of ischemic stroke compared with pts w/out CHF
Available evidence for additional “vascular” stroke RFs in CHF pts is inconsistent

- Additional RFs
  - Men: prior stroke, HBP, and DM
  - Women: AFIB, DM, and extent of LV dysfunction
  - Advanced age does not appear to be an additional RF
Available evidence indicates a higher mortality and morbidity after ischemic stroke in patients with CHF.
Clinically silent strokes occur frequently in pts w/ CHF and are likely to contribute to cognitive impairment, frequently appearing in pts w/ CHF.
There is no current evidence of a clinical benefit of anticoagulation compared with antiplatelet therapy with regard to stroke prevention in CHF pts with persisting NSR.
In pts w/ CHF and AFIB, anticoagulation (target INR range 2.0 to 3.0) is superior to antiplatelet agents and is clearly indicated