CONGRATS
to Dr. Wang on completing enrollment in the Resolute PAS study!

STUDIES WHERE MHIF RANKS IN TOP 5 IN THE WORLD FOR ENROLLMENT

• CONCERT (1st) - Traverse
• dal-GenE - Knickelbine
• LOWER (1st) - Knickelbine
  • PRECEPT - Melby
• Radiance-HTN (1st) - Wang
• SENECA (1st) - Traverse
  • SMILE - Eckman
• TAILOR-PCI - Chavez
• VENTRIX (1st) - Traverse
• Zenith p-Branch - Manunga

16
Studies in the pipeline to start soon

465
Patients enrolled to date in 2017

THANK YOU
Dr. Alsidawi for keeping research top of mind and open communication with the Valve Research Coordinators!
Case Carrousel

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MINNEAPOLIS HEART INSTITUTE FOUNDATION CARDIOVASCULAR GRAND ROUNDS

Disclosures:

- None
Agenda

- Case review
- Highlight important points
- Comments

Case 1

- 82 year old male patient.
- First contact with your healthcare system, receives his care through the VA system. No records available on Care Everywhere.
- Lives in a VA skilled nursing facility.
- Nurse who usually cares for him was on vacation, comes back on a Tuesday at 7am for his shift and reports that the patient is not acting like his usual self (decreased LOC and possible right sided facial droop).
- 911 was called to transfer to the ED.
- There is also reports of a mechanical fall the preceding Saturday.
**HPI**

- Reports left hip pain that has been present since his fall.
- Falls asleep while ED providers are trying to get a history and is unable to provide any additional useful information (“mumbling”), intermittently becomes agitated.
- Unable to provide information regarding PMHx or medications.
- NH staff and daughter contacted for additional data gathering, report he has required help with feeding and urinating, unable to ambulate, inappropriate speech (at baseline he is ambulatory, able to set up his meds and requires very little assistance with ADLs).

**PMHx**

- Dementia, mild, unspecified
- Bipolar disorder
- Anxiety and PTSD
- DM type 2, “diet controlled”
- HTN
- Hypothyroidism
- COPD
- GERD
Medications

- ASA 81mg daily PO
- Formoterol 12mcg bid inhaled
- Gabapentin 300mg bid PO
- Gabapentin 1200mg HS PO
- Levothyroxine 62.5mcg daily PO
- Lithium 450mg HS PO
- Quetiapine 25mg tid PO
- Quetiapine 300mg HS PO
- Tamsulosin 0.8mg HS PO
- Omeprazole 20mg bid PO

Also, completed a 7 day course of ciprofloxacin 500mg bid PO two days prior to admission after being diagnosed with a UTI.

Social

- Resides in a VA nursing home
- Veteran of the Navy
- Now retired, “odd jobs” after leaving the armed forces
- Remote history of tobacco use
- EtOH use disorder, now in remission for 8 years
- No recreational drug use including no IVDU
- Daughter very involved in his care and is his healthcare agent
Exam

- BP: 162/79 mmHg
- HR: 91 bpm
- Temp: 38.9°C
- Resp: 19 x min
- SpO2: 97%

Initial work up

Constitutional: He appears well-developed and well-nourished.
HENT
   - Head: Normocephalic and atraumatic.
   - Eyes: Conjunctivae are normal. Pupils are equal, round, and reactive to light.
Cardiovascular: Normal rate and normal heart sounds.
   - Occasional irregular beat.
   - Pulmonary/Chest: Effort normal and breath sounds normal. No respiratory distress. He has no wheezes. He has no rales. He exhibits no tenderness.
Abdominal: Soft. Bowel sounds are normal. There is no rebound.
   - Generalized abdominal discomfort.
Musculoskeletal: Normal range of motion. He exhibits no edema.
Neurological: He is alert. Patient does not follow commands, simply mumbling when asked questions or asked to do anything. Disoriented.
   - Pulls both arm away when holding arm. Face moving symmetrically with expression. Resists movement of both legs.
Skin: Skin is warm and dry. No rash noted.
Psychiatric:
   - Appears confused and can become agitated intermittently but redirectable.
Cont.

**CMP**
- Glucose: 197 (H)
- Sodium: 134 (L)
- Potassium: 4.2
- Chloride: 104
- CO2: 24
- Creatinine: 0.94
- GFR, Non-African American: 82
- AnGap: 7 (L)
- ICA, Actual: 4.50
- ICA pH Corrected: 4.57
- Albumin: 2.8 (L)
- Lactate: 2.0
- Lipase: 49
- Total Protein: 6.7

**CBC**
- Hgb: 13.5
- Plt: 132 (L)
- WBC: 19.19 (H)
- Abs Neutrophil: 16.89 (H)
- Alk Phos: 90
- ALT (SGPT): 35
- AST (SGOT): 40
- Bili Direct: <0.2
- Bili Total: 0.5
- TSH: 0.6

**UA**
- WBC Ur: 0-5
- RBC Ur: 4-20 (A)
- Nitrite Ur: NEGATIVE
- Leuk Est: NEGATIVE
- Specific Gravity: 1.010
- PH Urine: 7.5 (H)
- Protein Ur: 30 (A)
- Ketones: NEGATIVE
- Appearance: CLEAR
- Bili UA: NEGATIVE
- Blood Ur: MODERATE (A)
- Color: YELLOW
- Mucus: 1+
- Urine Glucose: 100 (A)
- Urobilinogen: 0.2

Cont.

- Troponin level of 0.609 ug/L
- Blood culture drawn prior to starting antibiotics and pending
- CXR done, possible left basilar atelectasis, otherwise clear
- CTabd/pelv done, no acute pathology of the abdomen or pelvis
- CTC-spine: No fracture or subluxation of the cervical vertebrae, degenerative changes present
- CThead: No acute pathology, old lacunar infarct in the posterior limb of the left internal capsule
- Attempted LP failed due to agitation
- Planned admission to medicine for management and work up
But then...

- Mental status continued to worsen
- Became persistently tachycardic to the low 100s bpm
- BP down to 120s mmHg systolic (was 160mmHg on arrival)
- Lab called providers with critical result of gram positive cocci present in both blood culture samples

Cont.

- Decision was made to intubate
- Already received acyclovir, vancomycin and meropenem in the ED
- Had borderline BP values with RSI, and sedation, normalized after 3L of normal saline
- LP completed after sedation
- Admitted to medical ICU team
Next day

- Stable overnight after antibiotics and IVF resuscitation, not requiring pressors, easily ventilated on minimal settings
- Records from VA arrived, prior urine culture had grown Enterococcus faecalis
- ID consulted
- Troponin level trended: 0.747, 0.763, 1.280
- Lactate trended down after IVFs (1.1 then 0.8)
- CSF studies reassuring
- ID recommended echocardiogram and possible cardiology consult given Enterococcus bacteremia
- Transitioned to ampicillin and ceftriaxone
**Report**

- Technically limited study
- Normal left ventricular size, estimated LVEF is 65% no WMA identified
- Fibrocalcific process of the mitral valve annulus
- Mobile mass attached to the LA aspect of the posterior MV leaflet and/or mitral annulus, It is very suspicious for a vegetation
- Aortic stenosis (mild) with an 11.2 mmHg mean gradient
- Tricuspid regurgitation jet is not adequate for estimation of PA systolic pressure
- TEE is recommended in this pt for better imaging of the mitral valve.

**TEE, first images on the screen after esophageal intubation**
TEE contd.

TEE contd.
Fistula

In conclusion

- TEE reported multiple large vegetations, mobile, mainly in the LA aspect of both the anterior and posterior mitral valve leaflets.
- An abscess was reported as well, with fistulous connection between the LA and LV.
- CVS and cardiology were involved.
- After discussion with his healthcare agent, decision was made to transition to end of life cares with focus on comfort.
Endocarditis

- Infection of the endocardial surface of the heart
- Usually involving one or more heart valves
- Includes intracardiac device infection
- Precise incidence is difficult to ascertain
- Should have high index of suspicion in patients at risk
- Duke criteria
- Requires multi-disciplinary approach

Risk Factors

- Age (>60yo)
- Male gender
- IVDU
- Poor dental hygiene
- Structural heart disease
- Hardware/device or prosthetic valves
- Chronic hemodialysis
- HIV or other immunosuppression
- Prior episode of endocarditis

**Duke criteria**

### Major criteria

- Positive blood cultures for IE (two of the following):
  - Typical microorganisms consistent with IE from two separate blood cultures:
    - Staphylococcus aureus
    - Viridans streptococci
    - Streptococcus pneumoniae (and other streptococci, including nutritional variant strains (S. viridans, S. sanguinis), and other non-streptococcal streptococci)
    - Microaerophilic and anaerobic bacteria
    - Pseudomonas aeruginosa
    - Other enteric species
  - Peripherally positive blood cultures:
    - For organisms that are typical causes of IE (at least two positive blood cultures from blood samples drawn >12 hours apart)
    - For organisms that are more commonly skin contaminants: "Presence of a majority of at least two positive blood cultures (with first and last drawn at least one hour apart)"

### Minor criteria

- Positive blood cultures for cardiac infection or phase 3 IgM antibody titer >1.50\*P
- Evidence of endocardial involvement (one of the following):
  - Embolus or microembolus
  - Vegetation (reflecting thrombosis or necrosis of a valve or on supporting structures, in the path of regurgitant jets, or on implanted material, in the absence of another etiologic explanation)
  - Abscess
  - Necrotic debris of endocardial valve
  - New valvular regurgitation
  - Increase in or change in existing murmur not sufficient

### Definite IE is established in the presence of any of the following:

**Pathologic criteria**

- Pathologic lesions: vegetation or intracardiac abscess demonstrating active endocarditis on histology
- Microorganisms: demonstrated by culture or histology of a vegetation or intracardiac abscess

**Clinical criteria**

- Using specific definitions listed in Table B:
  - 2 major clinical criteria OR
  - 5 minor clinical criteria
- Possible IE:
  - Presence of 1 major and 1 minor clinical criteria OR presence of 3 minor clinical criteria
- Rejected IE:
  - A firm alternate diagnosis is made OR
  - Resolution of clinical manifestations occurs after 54 days of antibiotic therapy OR
  - No pathologic evidence of infective endocarditis is found at surgery or autopsy after antibiotic therapy for four days or less
  - Clinical criteria for possible or definite IE not met
**Imaging**

- Echo is paramount; TTE is ok as an initial test but TEE will usually be required.
- CT: helpful in paravalvular extension and detection of abscess or pseudoaneurysm.
- FDG PET/CT: Useful for evaluation of prosthetic valve endocarditis.

Treatment

Antimicrobial therapy: principles and methods
The treatment of IE relies on the combination of prolonged antimicrobial therapy and – in about half patients – surgical eradication of infected tissues.

Prolonged therapy with a combination of bactericidal drugs is the basis of IE treatment. Drug treatment of PVE should last longer (at least 6 weeks) than that of native valve endocarditis (NVE) (2–6 weeks).

In both NVE and PVE, the duration of treatment is based on the first day of effective antibiotic therapy, not on the date of surgery. A new full course of treatment should only start if valve cultures are positive, the choice of antibiotic being based on the susceptibility of the latest recovered bacterial isolate.

The indications and pattern of use of amoxicillin-sulbactam have changed. They are no longer recommended in staphylococcal NVE because their clinical benefits have not been demonstrated but they can increase renal toxicity; and, when they are indicated in other conditions, amoxicillin should be given as a single daily dose in order to reduce nephrotoxicity.

Main complications of left-sided valve IE and their management
Surgical treatment is used in approximately half of patients with IE because of severe complications.

Early consultation with a cardiac surgeon is recommended in order to determine the best therapeutic approach. Identification of patients requiring early surgery is frequently difficult and is an important scope of the ‘Heart Team’.

In some cases, surgery needs to be performed on an emergency basis (within 24 h), urgent basis (within a few days, <7 days), irrespective of the duration of antibiotic treatment. In other cases, surgery can be postponed to allow 1 or 2 weeks of antibiotic treatment under careful clinical and echocardiographic observation before an elective surgical procedure is performed.

The three main indications for early surgery in IE are its 3 main complications, i.e., HF, uncontrolled infection, and prevention of embolic events.

### 2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)
Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

### ACC/AHA Guideline

<table>
<thead>
<tr>
<th>I</th>
<th>B</th>
<th>Decision about timing of surgical intervention should be made by a multidisciplinary Heart Valve Team of cardiology, cardiothoracic surgery, and infectious disease specialists (255).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>B</td>
<td>Early surgery during initial hospitalization before completion of a full therapeutic course of antibiotics is indicated in patients with left-sided IE caused by S. aureus, fungal, or other highly resistant organisms (261-268).</td>
</tr>
<tr>
<td>Ia</td>
<td>C</td>
<td>Early surgery during initial hospitalization before completion of a full therapeutic course of antibiotics is indicated in patients with IE complicated by heart block, aneurysm or aortic abscess, or destructive penetrating lesions (281, 268-273).</td>
</tr>
<tr>
<td>Ia</td>
<td>B-NR</td>
<td>Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) for IE is indicated in patients with evidence of persistent infection as manifested by persistent bacteremia or fever lasting longer than 5 to 7 days after start of appropriate antimicrobial therapy (261, 263, 268, 274-276).</td>
</tr>
<tr>
<td>Ib</td>
<td>B</td>
<td>Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients with valvular IE caused by S. aureus or fungi, even without evidence of device or lead infection (277-280).</td>
</tr>
<tr>
<td>Ib</td>
<td>C</td>
<td>Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is reasonable in patients with IE who present with recurrent embolism and persistent vegetations despite appropriate antibiotic therapy (281, 283).</td>
</tr>
<tr>
<td>Ib</td>
<td>B</td>
<td>Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) may be considered in patients with native valve endocarditis who exhibit mobile vegetation greater than 10 mm in length (with or without clinical evidence of embolic phenomena) (281, 283).</td>
</tr>
</tbody>
</table>
TABLE 1 Indications for Surgery in AHA and ESC Guidelines

<table>
<thead>
<tr>
<th>Condition</th>
<th>AHA Guidelines 2016 (18)</th>
<th>Class, Level of Evidence</th>
<th>ESC Guidelines 2016 (18)</th>
<th>Class, Level of Evidence</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocarditis in patients with IE, who present with valve dysfunction resulting in symptoms or signs of MI</td>
<td>1B</td>
<td>Aortic or mitral VRE, or PVE with severe acute valvular dysfunction, or fatal valve failure due to valvular dysfunction, need for valve replacement, or severe obstructive valvular disease</td>
<td>1B</td>
<td>Emergency</td>
<td></td>
</tr>
<tr>
<td>Endocarditis in patients with IE with severe valvular dysfunction, or need for valve replacement, or severe obstructive valvular disease</td>
<td>1B</td>
<td>Aortic or mitral VRE, or PVE with severe acute valvular dysfunction, or fatal valve failure due to valvular dysfunction, need for valve replacement, or severe obstructive valvular disease</td>
<td>1B</td>
<td>Urgent</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled infection (sepsis, abscess, endocarditis)</td>
<td>1B</td>
<td>Localized uncontrolled infection (sepsis, abscess, endocarditis)</td>
<td>1B</td>
<td>Urgent</td>
<td></td>
</tr>
<tr>
<td>Endocarditis in patients with IE with severe valve regurgitation and pronounced symptoms; no contraindications to surgery</td>
<td>1B</td>
<td>Infection caused by fungi or multiresistant organisms</td>
<td>1B</td>
<td>Urgent</td>
<td></td>
</tr>
<tr>
<td>Endocarditis in patients with IE who have failed IVE and have no contraindications to surgery</td>
<td>1B</td>
<td>Infection caused by fungi or multiresistant organisms</td>
<td>1B</td>
<td>Urgent</td>
<td></td>
</tr>
<tr>
<td>Prevention of infection</td>
<td>1B</td>
<td>Persistent positive blood cultures despite appropriate antibiotic therapy and absolute control of systemic causes of infection (biotics)</td>
<td>1C</td>
<td>Urgent/Effective</td>
<td></td>
</tr>
<tr>
<td>Endocarditis in patients who present with recurrent episodes and persistent endocarditis despite appropriate antibiotic therapy</td>
<td>1B</td>
<td>Persistent positive blood cultures despite appropriate antibiotic therapy and absolute control of systemic causes of infection (biotics)</td>
<td>1C</td>
<td>Urgent/Effective</td>
<td></td>
</tr>
<tr>
<td>Endocarditis in patients with severe valve regurgitation and no contraindications to surgery</td>
<td>1B</td>
<td>Persistent positive blood cultures despite appropriate antibiotic therapy and absolute control of systemic causes of infection (biotics)</td>
<td>1C</td>
<td>Urgent/Effective</td>
<td></td>
</tr>
<tr>
<td>Early surgery may be considered in patients with mobile vegetations &gt;10 mm, particularly those involving the mitral valve, and associated with other relative indications for surgery</td>
<td>1B</td>
<td>Aortic or mitral VRE, or PVE with persistent vegetations &gt;10 mm after 2 weeks of appropriate antibiotic therapy</td>
<td>1B</td>
<td>Urgent</td>
<td></td>
</tr>
</tbody>
</table>

*Defined as “surgery within hospitalization and before completion of a full course of antibiotics.” *Defined as “emergency surgery—performed within 24 h, urgent surgery—within a few days, elective surgery—after at least 2 weeks of antibiotic therapy.

HAE = Acinetobacter species; K. pneumoniae species; S. pneumoniae; S. epidermidis; S. aureus; S. epidermidis; S. aureus; VRE = vancomycin-resistant enterococci; other abbreviations as in Table 1.

Cahill et al. Challenges in Infective Endocarditis. JACC Jan 2017, 69 (3) 325-344; DOI: 10.1016/j.jacc.2016.10.066

TABLE 5 Studies of IE After TAVR

<table>
<thead>
<tr>
<th>First Author, Year (Ref. #)</th>
<th>No. of TAVR-IE Patients</th>
<th>1-YR Incidence of TAVR-IE</th>
<th>Microbiology</th>
<th>In-Hospital Mortality</th>
<th>1-YR Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aung et al., 2013 (150)</td>
<td>4 (cohort of 132)</td>
<td>3.0%</td>
<td>Enterococci (79%), oral streptococci (25%)</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Amat-Santos et al., 2015 (15)</td>
<td>53 (cohort of 7,844)</td>
<td>0.5%</td>
<td>CoNS (24%), Staphylococcus aureus (21%), enterococci (22%), oral streptococci (5.7%)</td>
<td>47%</td>
<td>66%</td>
</tr>
<tr>
<td>Bosmans et al., 2011 (151)</td>
<td>2 fatal cases (cohort of 326)</td>
<td>0.61%</td>
<td>Not reported</td>
<td>Not reported</td>
<td>100%</td>
</tr>
<tr>
<td>Latib et al., 2014 (152)</td>
<td>29 (cohort of 2,572)</td>
<td>0.89%*</td>
<td>Enterococci (21%), CoNS (17%), S. aureus (14%), oral streptococci (3.4%)</td>
<td>45%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Mangner et al., 2016 (153)</td>
<td>55 (cohort of 1,820)</td>
<td>2.25%*</td>
<td>S. aureus (38%), enterococci (31%), CoNS (9.9%), oral streptococci (3.6%)</td>
<td>64%</td>
<td>75%</td>
</tr>
<tr>
<td>Olsen et al., 2015 (154)</td>
<td>18 (cohort of 509)</td>
<td>3.1%</td>
<td>Enterococci (33%), S. aureus (17%), oral streptococci (17%), CoNS (11%)</td>
<td>11%</td>
<td>Not reported</td>
</tr>
<tr>
<td>PARTNER A, 2011 (155)</td>
<td>3 (cohort of 344)</td>
<td>0.87%*</td>
<td>Not reported</td>
<td>Not reported</td>
<td>33%</td>
</tr>
<tr>
<td>PARTNER B, 2010 (156)</td>
<td>2 (cohort of 178)</td>
<td>11.2%*</td>
<td>Not reported</td>
<td>Not reported</td>
<td>100%</td>
</tr>
<tr>
<td>Puls et al., 2013 (157)</td>
<td>5 (cohort of 180)</td>
<td>2.78%</td>
<td>Enterococci (40%), oral streptococci (20%), S. aureus (20%), E. coli (30%)</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td>Regueiro et al., 2016 (158)</td>
<td>250 (cohort of 20,066)</td>
<td>1.1% per person-year</td>
<td>Enterococci (25%), S. aureus (24%), CoNS (17%)</td>
<td>36%</td>
<td>66.7% (2-yr mortality)</td>
</tr>
<tr>
<td>Thomas et al., 2011 (159)</td>
<td>99.0% free of IE at 1yr (cohort of 1,033)</td>
<td>0.1%</td>
<td>Not reported</td>
<td>Not reported</td>
<td>3 deaths reported</td>
</tr>
</tbody>
</table>

*Calculated/estimated

CoNS = coagulase-negative staphylococci; IE = infective endocarditis; PARTNER = Placement of Aortic Transcatheter Valve; TAVR = transcatheter valve replacement.