

Infective Endocarditis

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Objectives

- Discuss the methods used in the diagnosis of infective endocarditis (IE)
- Recognize the criteria used to identify candidates for possible surgical intervention
- Review bacterial causes of endocarditis and current treatment recommendations
- Summarize new guidelines regarding prophylactic antimicrobial use for dental procedures

Patient Case

- MK is a 59 yo M who was referred to Skyridge Hospital on 2/13 by his hematologist for right knee effusion and warmth
- Other Complaints:
 - difficulty breathing
 - unexplained anemia requiring multiple transfusions over previous month (bone marrow biopsy negative)
 - possible CHF exacerbation
 - acute febrile illness ($T^{\circ} = 103$)
- Radiology: CT chest consistent with PE
- Elevated D-dimers

Patient Case (cont.)

- PMH:
 - HTN
 - HLD
 - CKD III
 - Renal artery stent 2010
 - CABG x 5 with mitral valve repair in 2010
 - Afib/Aflutter s/p ablation in 8/2014 with episodic reoccurrences
- Transferred to Erlanger for more extensive workup on 2/14

Patient Case - Erlanger Admission

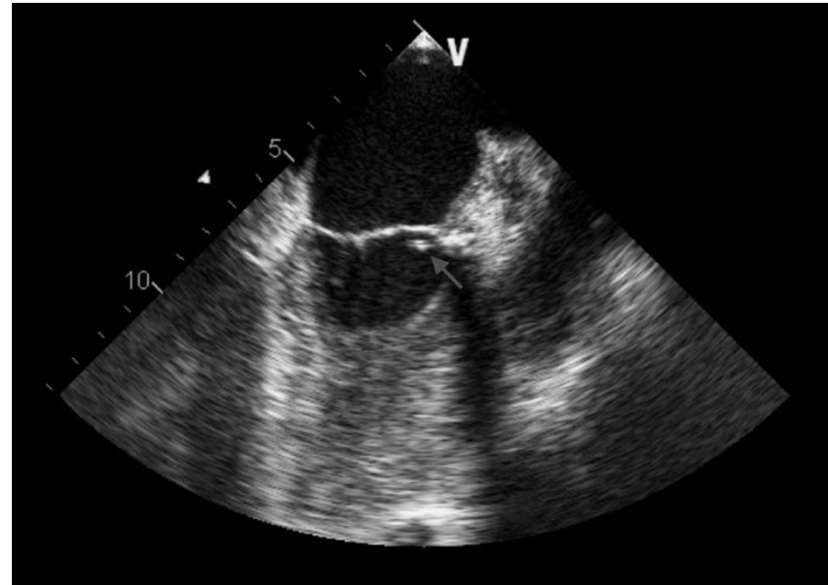
- On admit, patient had positive troponin/CPK consistent with NSTEMI
- Blood cx: positive for *E. faecalis*
 - Sensitive to Ampicillin, Penicillin, Streptomycin
 - Resistant to Gentamicin
- Radiology:
 - TTE – suggested mitral vegetations
 - TEE – large bulky mobile vegetations on anterior leaf of mitral valve with moderate mitral insufficiency and aortic valve vegetations
 - MRI – showed multiple focal cerebral infarctions secondary to septic emboli (patient denied neurological deficits)
- Diagnosis: infective endocarditis

Patient Case - Memorial Admission

- Transferred to Memorial on 2/19
- On 2/20 – Taken to cath lab and then directly to the OR
 - Mitral and aortic valve replacements
 - MAZE procedure
 - Aortic arch graft placement
- Antibiotic Regimen up to this point:
 - Skyridge – Rocephin
 - Erlanger – Vancomycin + Rocephin, then Vancomycin + Zosyn, then Ampicillin
 - Memorial – Vancomycin + Ampicillin post-op

Diagnosis of Endocarditis

- Modified Duke Criteria
- Imaging – complete <12 hr after initial evaluation
 - Should always be done in suspected endocarditis
 - Ideal study: TEE
 - TTE – used for low clinical suspicion or imaging will be of good quality (children)
 - TEE – used when imaging is difficult or poor (COPD, previous thoracic surgery, morbid obesity etc.)

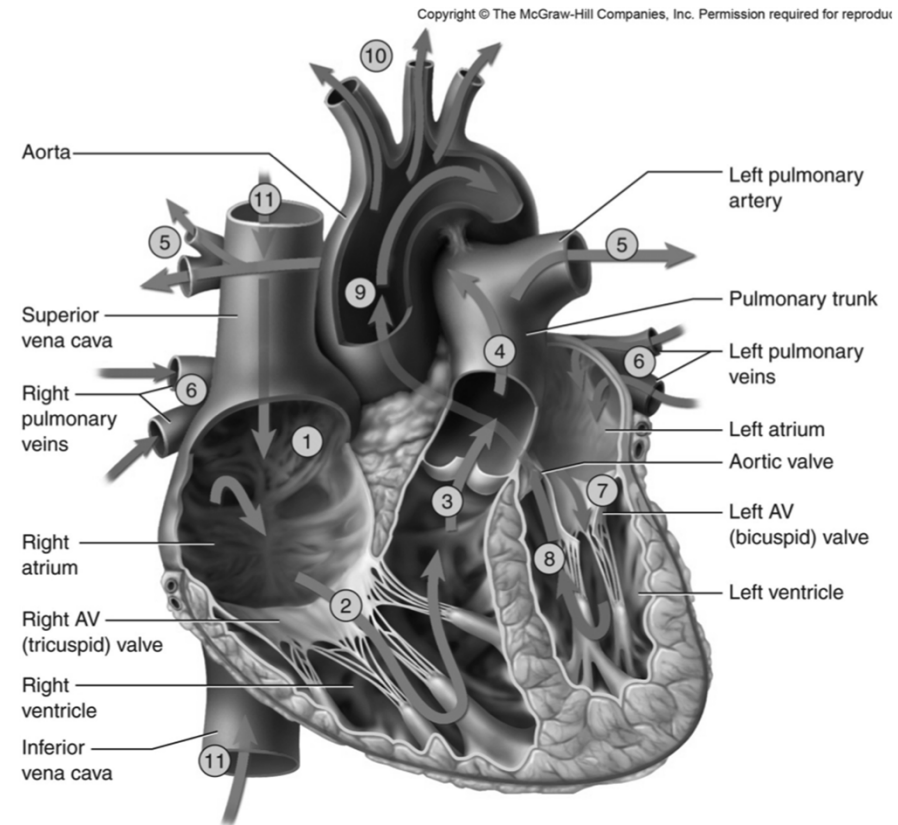


High Risk Patients

- The following are some features that identify patients in need of surgical intervention
 - Persistent vegetation after systemic embolization
 - Anterior mitral leaflet vegetation (esp. >10 mm)
 - ≥ 1 embolic events during first 2 weeks of treatment
 - Acute aortic/mitral valve insufficiency with signs of ventricular failure
 - Heart failure unresponsive to medical therapy
 - Valve perforation or rupture
 - New heart block
 - Large abscess or extension of abscess despite appropriate antimicrobial therapy

Bacterial Causes of Endocarditis

- 3 most common causes:
 - Staphylococci
 - Non-IV drug users – primarily left sided
 - Mortality rates 25-40%
 - IV drug users – primary involvement with tricuspid valve
 - Streptococci
 - More common in non-IV drug users
 - Enterococci
 - Cause in 10-14% of cases
 - Usually either *E. faecium* or *E. faecalis*



Enterococcal Endocarditis

- Tends to be more resistant to penicillin, ampicillin and vancomycin than streptococci
- Using only one antimicrobial agent will inhibit but not kill
- Treatment involves a combination of antibiotics to achieve synergy
 - Enterococci are relatively impermeable to aminoglycosides
 - Pair with cell-wall active agent to make a bactericidal combination

Treatment Recommendations

- Baddour LM, Wilson WR, Bayer AS et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications. *Circulation* 2005;111:e394-e434.
- Native/Prosthetic, strains susceptible to penicillin, gentamicin, vancomycin
 - Ampicillin or PenG + Gentamicin for 4-6 weeks
 - Vancomycin + Gentamicin for 6 weeks
 - Vancomycin should only be used for intolerance to Ampicillin or PenG

Treatment Recommendations (cont.)

- Native/Prosthetic, strains susceptible to penicillin, streptomycin, vancomycin and resistant to gentamicin
 - Ampicillin or PenG + Streptomycin (4-6 weeks)
 - Vancomycin + Streptomycin (6 weeks)
- Aminoglycoside resistance - plasmid-mediated
- *E. faecium* intrinsically resistant to amikacin, tobramycin
- *E. faecalis* often resistant to amikacin
- Streptomycin dosing in normal renal function:
 - 15 mg/kg divided every 12hrs
 - Trough <10, peak 20-35

Treatment Recommendations (cont.)

- Native/Prosthetic, strains resistant to penicillin and susceptible to vancomycin and aminoglycosides
 - β -lactamase producing strain
 - Augmentin + Gentamicin
 - Vancomycin + Gentamicin
 - Intrinsic penicillin resistance
 - Vancomycin + Gentamicin
- Therapy for both types = 6 weeks

Treatment Recommendations (cont.)

- Native/Prosthetic, strains resistant to penicillin, aminoglycosides and vancomycin
 - *E. faecium*
 - Zyvox or Synercid
 - *E. faecalis*
 - Primaxin + Ampicillin
 - Rocephin + Ampicillin
- Therapy for both strains = ≥ 8 weeks

High-level Aminoglycoside Resistance

- Ampicillin plus ceftriaxone is as effective as ampicillin plus gentamicin for treating *Enterococcus faecalis* infective endocarditis. *CID* 2013;56(9):1261-8.
- Observational, non-randomized, comparative multicenter cohort study
- Evaluated *E. faecalis* strains with both low and high-level aminoglycoside resistance
- Outcomes: death during treatment and at 3-month follow-up, adverse events requiring treatment discontinuation, treatment failure requiring change of agents and relapse
- Results: no difference in mortality, treatment failure or relapse
 - Greater risk of adverse events in ampicillin + gentamicin group (new RF)

Surgical Intervention

- Most beneficial in the early phase of endocarditis (when embolic rates are highest)
- Systemic embolization occurs in 22-50% of cases
 - Most events are during first 2-4 weeks of treatment
 - Risk higher with any size mitral vegetation (25%) compared with aortic vegetation (10%)
 - Among those with mitral vegetations, there is a higher risk of embolization with a vegetation on the anterior leaflet

Anticoagulation Considerations

- Controversial
- General recommendation: discontinue all anticoagulants for at least the first 2 weeks of treatment in patients with *S. aureus* prosthetic valve IE
 - Risk of hemorrhagic conversion in patients with recent systemic embolization
- Routine use of aspirin not recommended

Endocarditis Prophylaxis

- Nishimura, RA et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. *J Am Coll Cardiol.* 2014;63(22):e57-e185. doi:10.1016/j.jacc.2014.02.536
- Narrowed population who should receive prophylactic antibiotics prior to dental procedures
- Only those at high risk for IE
 - Prosthetic valve or valve repair with prosthetic material
 - Hx of endocarditis
 - Heart transplant with abnormal heart valve function
 - Certain congenital heart defects
- Prophylactic antibiotics not recommended for reproductive, urinary or GI tract procedures

Patient Case

- Continued Treatment Course

- Extensive mitral valve vegetations were seen in OR. Characterized as dense adhesions.
- Patient experienced post op pulmonary edema and internal hemorrhaging
- Taken back to OR twice for bleeding issues
- Developed right lobe infarction
- Placed on ECMO
- Hypovolemic shock, volume overload → CRRT

Antibiotic Treatment Course

- Initial post-op:
 - Ampicillin + Vancomycin with plan to start streptomycin when delivered to pharmacy
- Streptomycin 7.5 mg/kg Q12 hrs started on 2/23 in combo with Ampicillin + Vancomycin
 - Peak and trough drawn on 2/25
 - Vancomycin discontinued on 2/26
 - Continued course with Ampicillin + Streptomycin until levels back on 3/2
 - Trough = 33, Peak = 37

Antibiotic Treatment Course (cont.)

- Streptomycin discontinued and Teflaro started at 400 mg Q12 hrs for synergy with Ampicillin
 - 2nd trough sent out on 3/2 at the next scheduled dose
 - Trough = 12.07
- Teflaro vs. Rocephin
 - Supposed better gram + coverage than Rocephin
 - However, every time E-tested to *E. faecalis*, the bacteria have overgrown the plate
 - Data behind using Rocephin + Ampicillin
 - Rocephin not ideal in this patient because of liver issues

Patient Case (cont.)

- 2/28 – TEE showed diffuse widespread pericardial clot
 - Taken to the OR and clot evacuated
- 3/4 – taken off CRRT and extubated in AM
 - Later that evening: respiratory hypoxemia, coded for 2 min
 - Re-intubated
- 3/6 – performed tracheostomy

Conclusions

- If patient suspected of having IE, the modified Duke Criteria and imaging, preferably with a TEE, should be used within the first 12 hours to help confirm diagnosis
- Once blood cultures drawn, antimicrobial therapy should be immediately started and then narrowed per C&S results
- Patient is at greatest risk of systemic embolization during first 2-4 weeks of antimicrobial treatment
- Surgical intervention may be necessary in high risk patients and is most beneficial early in the course of IE
- Prophylactic antibiotic use for endocarditis was significantly narrowed to only include high risk patients

References

- Ampicillin plus ceftriaxone is as effective as ampicillin plus gentamicin for treating *Enterococcus faecalis* infective endocarditis. *CID* 2013;56(9):1261-8.
- Baddour LM, Wilson WR, Bayer AS et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications. *Circulation* 2005;111:e394-e434.
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