Valvular Heart Disease & Cardiac Neoplasms

Lecture Outline

- Bicuspid aortic valve
- Aortic valve stenosis
- Mitral valve prolapse
- Infective endocarditis
- “Noninfective” endocarditis
- Select cardiac neoplasms

Valvular Heart Disease

- Semilunar valves
  - Aortic and pulmonary valves
  - 3 cusps
  - Function depends on integrity and coordinated movements of cusps and attachments
Valvular Heart Disease

- Atrioventricular valves
  - Tricuspid and mitral
  - Competency depends on integrity of valve “apparatus”
    - Leaflets + annulus, chordae tendinae, papillary muscles, ventricular wall

Valve Histology

Connective tissue core: varies in density
(spongiosa, fibrosa, reticularis)
Collagen
Elastic fibers

Valvular Heart Disease

- Single or multiple valves
- Acute or chronic
- Physiologically unimportant to significant
- Regurgitant (insufficient) or stenotic
- Murmurs
- Congenital or Acquired
Bicuspid Aortic Valve

- Prevalence 1%
- 2 cusps
  - One larger with midline raphe
  - Incomplete embryonic separation
- Aortic Stenosis (50’s-60’s)
  - Infective endocarditis
- Underlying aortopathy

Calcific Aortic Degeneration

- Most common cause of AORTIC STENOSIS
- “Wear and tear”
- Dystrophic calcification
  - Deposition of calcium at sites of cell injury and necrosis
- Recent studies
  - Chronic injury – hyperlipidemia, HTN, inflammation
    - Sounds like atherosclerosis risks

Calcific Aortic Stenosis

Calcified masses within aortic cusps
Prevent cusp opening
Outflow obstruction
Increased pressure gradient across valve
Concentric LVH
Symptoms = poor prognosis
- Congestive heart failure
- Myocardial ischemia
- Syncope

Marked concentric LVH from pressure overload

Courtesy Ralph Leischner, MD

Mitral Valve Prolapse
(Myxomatous Degeneration of Mitral Valve)

- Enlarged, redundant, floppy leaflets
- Balloon into atrium during systole

Robbins, 10th edition, Figure 11-18
Mitral Valve Prolapse (Myxomatous Degeneration of Mitral Valve)

- Pathogenesis
  - Unknown
  - Developmental defect of connective tissue
    - Feature of Marfan Syndrome
    - Fibrillin-1 mutations

- 3% of population
  - Young women
- Majority asymptomatic, incidental finding
  - Midsystolic click
- Minority with nonspecific symptoms
  - Chest pain, dyspnea, fatigue, depression, anxiety
**Mitral Valve Prolapse**  
*(Myxomatous Degeneration of Mitral Valve)*

- Rare, serious complications (3% of patients)
  - Infective endocarditis
  - Mitral insufficiency
  - Stroke/systemic infarct
    - Embolism of leaflet atrial thrombi
  - Arrhythmias

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**Infective Endocarditis**

- Destructive inflammation of cardiac valves and endocardium
- Infection
  - Bacterial most common
“Vegetation”
Merriam-Webster

- Main Entry: **vegetation**
  - an abnormal outgrowth upon a body part;
  - specifically: any of the warty excrescences on the valves of the heart that are composed of various tissue elements including fibrin and collagen and that are typical of endocarditis

Vegetations of Infective Endocarditis

- Thrombotic debris, fibrin, inflammatory cells, microorganisms
- Large, bulky
- Destructive
- Erosive
- Friable
  - Embolize

Courtesy Ralph Leischner, MD

Robbins Pathologic Basis Disease, 7th edition, Figure 12-26

- Abscess
- Fibrin
- Inflammatory Cells
- Valve destruction
Spectrum of Infective Endocarditis

- **Acute**
  - Highly virulent micro-organisms
  - Usually previous normal valve
  - Rapid, severe destruction of valve
  - 50% mortality
  - Classic organism - *Staphylococcus aureus*

- **Subacute**
  - Low virulence organism
  - Affect previously deformed valve
  - Recovery with appropriate treatment
  - Classic Organism - *Streptococcus viridans*

Infective Endocarditis

- **Patients at risk**
  - Valvular disease
  - Prosthetic valves
  - Immune deficient
  - Diabetic
  - Intravenous drug abusers
  - Alcoholics

- **Portals of entry**
  - Infection elsewhere
  - Dental or surgical procedures with bacteremia
  - Injection of contaminated material into bloodstream
  - Occult source
    - gut, oral cavity, trivial injury

Infective Endocarditis

- **Diagnosis (Duke Criteria)**
  - Clinical suspicion
  - Blood cultures
  - Echocardiogram
**Infective Endocarditis Complications**

- **Cardiac**
  - Valve insufficiency
  - Abscess
  - Valve dehiscence or paravalvular leak in prosthetic valves

**Infective Endocarditis Complications**

- **Emboli**
  - Brain
  - Kidney
  - Spleen
  - Lungs
- **Immunologic**
  - Glomerulonephritis

Robbins, fig 12-16

**Infective Endocarditis**

- **Treatment**
  - IV antibiotics, usually prolonged course
  - Surgery
- **Prophylaxis with antibiotics for those at high risk**
LUMC patient

22F IV drug user, transferred from outside hospital today for h/o infective endocarditis. Blood and urine cultures are positive for Staph aureus, susceptibilities are pending. Echo with evidence of large tricuspid valve vegetation. From review of outside records, pt presented to the outside hospital with 8-day history of flu-like symptoms (left sided flank and back pain, high fevers at home for 1 week), severe enough that she had to treat herself with IV opiates. On exam in ED she was hypotensive 70/40s not responding to IVF boluses. Exquisite lumbar spine tenderness. Concern for septic emboli to spine and kidneys (given urine culture positive for S. Aureus as well as Bld Cx with GPC in clusters.) Pt was admitted to ICU overnight, given IVF with BP this morning 95-112/40-60s. This afternoon noted to be tachypneic 37 and tachycardic 120-130s. Transferred via Lifestar this afternoon. Upon arrival noted to be tachycardic in 130s, hypotensive 90-100s and somnolent. Bedside echo revealed hyperdynamic LV, large 1.6 x 1.8 cm tricuspid valve vegetation and small pericardial effusion. Central venous catheter placed in right femoral vein.

LUMC Patient

• FINDINGS AND CONCLUSIONS:
  LV EJECTION FRACTION: 49 %
  Large tricuspid valve vegetation. Moderate tricuspid regurgitation with an RV-RA gradient of at least 47 mm Hg, which suggests right ventricular hypertension. Right atrium and right ventricle are slightly enlarged. The left ventricle is normal in size and probably mildly hypokinetic. The other valves are structurally normal and not significantly insufficient or stenotic. Small pericardial effusion.

NONINFECTED Vegetations

• Acute Rheumatic Fever
• Endocarditis of System Lupus Erythematosus)
  (Liebman-Sacks Endocarditis)
• Nonbacterial Thrombotic Endocarditis
  (Marantic Endocarditis)
Rheumatic Fever
- Few weeks (10 days to 6 weeks) after Group A (B-hemolytic) streptococcal pharyngitis
- Acute Systemic manifestations
- Chronic Rheumatic Heart (valve) Disease

Acute Rheumatic Fever
- Pathogenesis
  - Immune response to group A Streptococi which CROSS-REACT with host tissues
    - Antibodies directed against M proteins of strep cross-react with self-antigens in the heart
    - CD4+ T cells specific for streptococcal peptides react with cardiac self proteins
      - Produced cytokines activate macrophages

Acute Rheumatic Fever
- Major Manifestations
  - Migratory polyarthritis, large joints
  - Carditis (Pancarditis)
  - Subcutaneous nodules
  - Erythema marginatum of skin
  - Sydenham chorea (involuntary purposeless, rapid movements, St. Vitus’ dance)
- Minor Manifestations
  - Fever
  - Arthralgia
  - Elevated acute-phase reactants
Acute Rheumatic Fever

Jones Criteria
Preceding group A Strep infection +
2 Major Manifestations or
1 Major and 2 Minor Manifestations

Acute Rheumatic Fever

• Heart
  – Pancarditis
  • Pericarditis
  • Myocarditis
  • Endocarditis

Rheumatic Fever Endocarditis
1-2 mm verrucae/vegetations
left sided heart valves

Adapted from
Robbins, 7th edition, Figure 12-24
Inflammation

- Aschoff Bodies
  - T lymphocytes
  - plasma cells
  - macrophages
    - Anitschkow cells (caterpillar cells)
  - Multinucleated cells

Robbins, 10th edition, Figure 11-19

What happens then?

- Organization of inflammation
- Fibrosis
- Obliteration of normal leaflet structure

Turbulence induced by ongoing valve deformities → additional fibrosis

Rheumatic Fever

- Chronic Rheumatic Valvular Disease
  - Valve leaflet fibrosis, fusion
    - Fish mouth or buttonhole stenosis
  - Cords short, thick, fused
Robbins, figure 11-19

**Rheumatic Fever**

- Chronic Rheumatic Valvular Heart Disease
  - Mitral valve most commonly involved
    - Alone in 65-70%
    - Aortic and mitral valves - 25%
    - Tricuspid, pulmonary valves - rare

**Endocarditis of System Lupus Erythematosus**

*Libman-Sacks Endocarditis*

- Systemic Lupus Erythematosus
- Sterile vegetations
  - Mitral and tricuspid valves, chords
  - Small
- Consequence of immune complex deposition and associated inflammation
- “Valvulitis”
  - leads to subsequent fibrosis, valve deformity
Nonbacterial Thrombotic Endocarditis (Marantic Endocarditis)

• Sterile thrombi (vegetations)
  – Small
  – Non-destructive
  – Loosely attached

Nonbacterial Thrombotic Endocarditis (Marantic Endocarditis)

• Marantic - Greek marantikos = “wasting away”
• Patients prone to hypercoagulable states
  – Sepsis
  – Cancer
    • Mucinous adenocarcinomas
      – Tumor derived mucin or tissue factor
  – Burns
  – Indwelling catheters
    • Lead to endocardial trauma
Nonbacterial Thrombotic Endocarditis (Marantic Endocarditis)

- **Clinical sequelae**
  - Local - Little effect on valve itself (no inflammation)
  - Systemic
    - Emboli
    - Infarcts

- Can serve as a nidus for bacterial colonization → infective endocarditis

Vegetation Review

Valve Pathology Summary

- **Calcific aortic stenosis** incidence increases with age
  - Develops earlier with bicuspid aortic valve
- **Myxomatous degeneration of mitral valve** usually without serious sequelae
  - Can lead to valve insufficiency, emboli, endocarditis
- **Infective endocarditis** can be aggressive with rapid valve destruction, or can be indolent
- **Chronic rheumatic valve disease** is a result of post-inflammatory scarring
  - SLE (Liebman Sacks) endocarditis similar sequelae
- **Nonbacterial thrombotic endocarditis** occurs in ill, hypercoagulable
  - Embolization most important complication
Neoplastic Heart Disease

Myxoma

- Most common primary tumor of the heart, adults
- 90% atria
  - L>>>R

Myxoma

- Gelatinous-appearing tumor

Myxoma

- Sulfur-rich globular cells
- Mucopolysaccharide matrix
- Abnormal blood vessel structure
Myxoma

• Ball-valve obstruction
  – Pedunculated lesions move into or through AV valves during systole
  – Position dependent
• Fever and malaise
  – Elaboration of Interleukin-6
• Embolization

Rhabdomyoma

• Most common primary pediatric heart tumor
• Obstructs valvular orifice or cardiac chamber
• May spontaneously regress

• Associated with Tuberous Sclerosis

Video

Cardiac Metastases

- Most common malignancy of heart
- Most common primary sites: Lung, lymphoma, breast, leukemia, melanoma, hepatocellular, colon

- Pericardial metastases:
  - Pericardial effusions, tamponade

- Venous extension:
  - Liver, kidney neoplasms
  - Obstruct venous return to heart

Questions

A 55-year-old woman without known chronic medical problems presents for annual health maintenance exam. On cardiac auscultation, there is midystolic click. Within 5 years she has increasing dyspnea. Echocardiography now shows mitral regurgitation from prolapse of a leaflet. Which of the following pathologic changes is most likely present in this valve?

A. Dystrophic calcification
B. Large, destructive vegetations
C. Myxomatous degeneration
D. Rheumatic fibrosis
E. Two leaflets