Case Scenarios in Acquired Heart Disease

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Presentation Objectives

At the end of this presentation, the attendees will be able to:

1. Define and recognize atypical Kawasaki disease
2. Understand the limitation of the Kawasaki criteria
3. Identify cases of Kawasaki disease likely to be resistant to IVIG therapy
4. Identify cases of myocarditis and limitations of treatment
5. Keep high index of suspicion for infective endocarditis cases
5 month old Brannon

- Brannon presented to a local Hospital ED with 4 day history of high grade fever

- He is fussy and difficult to console.

- There are no URTI symptoms.
Examination

- Fussy, very difficult to examine
- Febrile with 39.6°C. No rash seen
- No red eyes, no meningeal signs
- No cervical LAP
- Normal mucus membranes
- Hands and feet are normal
- He’s tachycardic and a flow murmur is heard.
Work-up

- CBC showed elevated white cell (24,300) count with 85% left shift. Hg is 8.8 g/dl

- CRP and ESR are very elevated

- Albumin 2.9 g/dl, Na 129

- platelets are 467,000

- LFTs were mildly elevated (in the 100-200 range)

- Urinalysis is normal

- Chemistry shows hyponatremia (132 meq/L)
Hospital course

- The baby was admitted and was started on IV ceftriaxone.
- After no resolution of fever after 4 days, ID consult was obtained.
- Lumbar puncture was done which was normal.
- CRP and ESR are still elevated.
- There is no resolution of fever 24 hr post broadening of antibiotics to vancomycin and Piperacillin/tazobactam.
Would you treat this patient as Kawasaki disease?

Ehh, What's up Doc... with that 5 Days of Fever Alarm?
Diagnostic criteria

- Fever > 5 days (must have)
- And 4 out of 5:
  1. Polymorphous rash
  2. Cervical lymphadenitis (>1.5 cm)
  3. Changes in the lips and mucus membranes
  4. Extremity skin changes (redness, swelling, peeling of the skin)
  5. Non-purulent bulbar conjunctivitis
Incomplete Kawasaki disease

- Following the strict criteria for Kawasaki disease resulted in missing 10-15% of patients who have Kawasaki disease.

- Not a small percentage of those patients ended up developing coronary artery aneurysms.

- So what to do in-order not to miss those patients?
Evaluation of suspected Kawasaki disease

- Child* with a fever for ≥5 days† without an alternative explanation

- How many clinical diagnostic criteria‡ are met?
  - 0 or 1 clinical criteria
    - Is the child ≤6 months old§ with a fever ≥7 days?
      - Yes
        - CRP <3.0 mg/dL and ESR <40 mm/hour
          - Assess for supplemental laboratory criteria§ and obtain echocardiogram
            - <3 supplemental laboratory criteria and negative echocardiogram
              - Possible KD
                - Treat and obtain baseline echocardiogram
            - ≥3 supplemental laboratory criteria OR positive echocardiogram¶
              - KD unlikely; however, perform serial clinical and laboratory re-evaluation if fever persists and obtain echocardiogram* if typical periungual desquamation develops even if fever has resolved
              - KD likely (categorized as "incomplete" since patient has only two or three clinical criteria)
                - Start treatment‡
      - No
        - CRP ≥3.0 mg/dL and/or ESR ≥40 mm/hour
          - Consistent with KD
            - Start treatment and obtain baseline echocardiogram
  - 2 or 3 clinical criteria and a strong clinical suspicion of KD
    - Suspected incomplete KD
      - Assess CRP/ESR
  - ≥4 clinical criteria¶
    - Consistent with KD
      - Start treatment and obtain baseline echocardiogram
Kawasaki Disease

- Also called mucocutaneous lymph node syndrome
- Likely caused by an abnormal immune system response to an infectious agent
- Most common between 1-2 years of life
- Cases below 3 months or more than 8 years are rare
Pathology

- During the acute phase of the illness, microvasculitis occurs with predilection to the coronary arteries

- Coronary artery aneurysms develop in 15-25% of untreated patients

- Diffuse pancarditis can happen leading to cardiac dysfunction, AV valve regurgitation, conduction abnormalities and pericarditis.

- During the late phases, fibrosis can result in narrowing of the coronary arteries leading to stenosis and possible myocardial infarctions

- Elevated platelet count increases the risk of MI
Other manifestations

- Sterile pyuria
- Elevation in liver enzymes
- Arthritis or arthralgia
- Gallbladder hydrops
Acute Phase (First 10 days)

- Abrupt onset of high fever and irritability. Conjunctivitis resolves quickly. Redness of mucus membranes, fissuring, ulcerations, strawberry tongue. Rash can be of different kinds. Cervical LAP happens in 50% of patients. Fever duration 11-12 days average, but resolves quickly with treatment.

- Leukocytosis, thrombocytosis, high inflammatory markers, sterile pyuria, elevated LFTs, lipid abnormalities.

- Coronaries can get affected during this stage.
Subacute Phase

- Desquamation and peeling of the fingers and toes
- Rash, fever and LAP disappear
- Most of cardiovascular manifestations occur in this phase
- Worsening of thrombocytosis
Convalescent Phase

- This phase lasts till all inflammatory markers and platelets return to normal levels
- Beau’s lines appear during this phase
Complications

- Cardiac manifestations dictate the prognosis
- Coronary aneurysms, thrombosis, stenosis
- Cardiac dysfunction, AV valve damage, dilation of the ascending aorta, effusion, heart block
- Peripheral artery aneurysms and stenosis
Management

- Admission
- High dose ASA (30-100 mg/kg/day)
- Anti-pyretics
- IVIG (2 g/kg IV infusion) +/- oral steroids. Repeat IVIG if no improvement
- Pulse steroids IV for non-responders
- Infliximab for resistant cases
Management

- Switch ASA to low-dose before discharge, some recommend not before at least 14 days of illness
- Stop ASA after platelets are normal, or 6-8 weeks after illness, whatever longer
- If coronary abnormalities persist, patient will be always on ASA
- In case of aneurysms, clopidogrel or even warfarin can be added
Would you start our patient on steroids along with IVIG and ASA when the patient presented?
The Kobayashi score

- Sodium less than 133 mmol/L (2 points)
- AST >100 Units/L (2 points)
- CRP >10 mg/dl (1 point)
- Neutrophils >80% of WBC (2 points)
- Platelets less than 300,000/mm³ (1 point)
- Days of illness at initial treatment less than 5 (2 points)
- Age less than 12 months (1 point)
Take home messages

- You don’t have to fulfill 4 criteria to diagnose Kawasaki disease

- Infants less than 6 months with fever for more than 7 days, consider strongly treating as Kawasaki disease

- In patients with risk of IVIG treatment failure, start steroids at the same time of IVIG and ASA
Case 2
12 year old Nihad

- 12 year old previously healthy, presented with fatigue, shortness of breath and pallor

- She is tachycardic and there is a 3/6 pansystolic murmur at apex

- There are lung crackles and her liver is enlarged
12 year old Nihad

- She was admitted to the PICU.
- CBC was non-specific, Electrolytes showed hyponatremia
- Liver enzymes were mildly elevated
- CRP and ESR were mildly elevated
Myocarditis

- Inflammation of the myocardium
- Viruses are most often the culprits, esp. Parvovirus, HHV6, enteroviruses, EBV etc.
Presentation

- Chest pain, shortness of breath, easy fatigability, palpitations, syncope

- Patients will usually have a pansystolic murmur of mitral regurgitation, S3 gallop, increased JVP, hepatomegaly and LL edema
Investigations

- ECG shows ST segment changes, T-wave inversions, tachycardia, decreased QRS voltage, ectopy and various degrees of heart block

- CXR shows cardiomegaly

- Echo shows dysfunction, heart dilation, MR, AI.

- MRI shows edema, scarring, dysfunction

- Biopsy shows inflammation and a causing virus sometimes could be identified. Although fell out of fashion for a while, now it is having a come back.
Management

- Mainly supportive
- Circulation support
- Be very careful with fluid administration
- IVIG?
- Anticoagulation
- Ventricular support (VAD, ECMO)
- Heart transplantation
Complications

- Severe heart failure
- Ventricular tachycardia, fibrillation
- Thrombo-embolism
- Chronic dilated cardiomyopathy
- Death
Our patient

- Patient condition continued to get worse despite milrinone, diuretics
- She was intubated
- Despite lack of evidence, IVIG was given
- Patient was started on Lidocaine for intermittent VT
- Patient passed away after an episode of VF that she couldn’t be resuscitated from
Case 3
Ahmed is a 16 year old male with history of TOF. He recently had surgical replacement of his RV-PA conduit 7 months ago.

He was admitted to an outside hospital with fever, chills and sweats, diagnosed as pneumonia.

He was transferred to our hospital after 4 days of ceftriaxone.
16 year old Ahmed

- CBC showed high WBC 19500, Hg of 8.6, high CRP and ESR
- Blood culture is pending
- CXR showed new left upper lobe and right middle lobe opacification
- Urinalysis, eye examination is normal
- Echo showed dehiscence of the RV-PA conduit with pseudo-aneurysm and pericardial effusion
What do you think is the diagnosis?
Infective Endocarditis

- **Definition:** Microbial infection of the inner endocardium and valve tissue

- **Incidence varies over time because of changing definition and change in the incidence of risk factors like drug abuse and infective endocarditis**
Risk Factors

- Male sex
- Age > 60
- Injection drug abuse
- Poor dental hygiene
## Comorbid conditions

- Congenital and structural heart disease
- Valvular heart disease
- Prosthetic heart valves
- History of infective endocarditis
- Presence of intravascular devices/stents
- Chronic hemodialysis
- HIV infection
Organisms

- Staphylococcus aureus
- Viridans grp streptococcus
- Coagulase negative staph
- Enterococcus
- Streptococcus bovis
- Non-HACEK gram –ve
- Fungi
- HACEK group gram -ve
Clinical manifestations

- Fever is the most common symptom
- B type symptoms like chills, night sweats
- Anorexia, fatigue, weight loss, abdominal pain, chest pain
- Hematuria
Signs

- New heart murmur or change in the quality of an existing murmur
- Vascular and immunologic phenomena like Osler’s nodes, Janeway lesions, Roth spots, splinter hemorrhages are rare in pediatrics
- Symptoms and signs of embolic phenomena (Stroke, spleen or kidney infarct)
- Splenomegaly
Modified Duke criteria for diagnosis of infective endocarditis - Table A

<table>
<thead>
<tr>
<th>Definite IE is established in the presence of any of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pathologic criteria</strong></td>
</tr>
<tr>
<td>Pathologic lesions: vegetation or intracardiac abscess demonstrating active endocarditis on histology OR</td>
</tr>
<tr>
<td>Microorganism: demonstrated by culture or histology of a vegetation or intracardiac abscess</td>
</tr>
<tr>
<td><strong>Clinical criteria</strong></td>
</tr>
<tr>
<td>Using specific definitions listed in Table B:</td>
</tr>
<tr>
<td>2 major clinical criteria OR</td>
</tr>
<tr>
<td>1 major and 3 minor clinical criteria OR</td>
</tr>
<tr>
<td>5 minor clinical criteria</td>
</tr>
<tr>
<td><strong>Possible IE</strong></td>
</tr>
<tr>
<td>Presence of 1 major and 1 minor clinical criteria OR</td>
</tr>
<tr>
<td>presence of 3 minor clinical criteria</td>
</tr>
<tr>
<td><strong>Rejected IE</strong></td>
</tr>
<tr>
<td>A firm alternate diagnosis is made OR</td>
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<tr>
<td>Resolution of clinical manifestations occurs after ≤4 days of antibiotic therapy OR</td>
</tr>
<tr>
<td>No pathologic evidence of infective endocarditis is found at surgery or autopsy after antibiotic therapy for four days or less</td>
</tr>
<tr>
<td>Clinical criteria for possible or definite IE not met</td>
</tr>
</tbody>
</table>

IE: infective endocarditis.
* The category of possible IE represents a modification from the previous published Duke criteria.

### Modified Duke criteria for diagnosis of infective endocarditis - Table B

#### Major criteria

**Positive blood cultures for IE (one of the following):**

- Typical microorganisms consistent with IE from two separate blood cultures:
  - *Staphylococcus aureus*
  - Viridans streptococci
  - *Streptococcus gallolyticus* (formerly *S. bovis*), including nutritional variant strains (*Granulicatella* spp and *Abiotrophia* defectiva)
  - HACEK group: *Haemophilus* spp, *Aggregatibacter* (formerly *Actinobacillus actinomycetemcomitans*), *Cardiobacterium hominis*, *Eikenella* spp, and *Kingella* kingae
  - Community-acquired enterococci, in the absence of a primary focus; OR

**Persistently positive blood culture:**

- 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: Three or a majority of ≥4 separate blood cultures (with first and last drawn at least one hour apart)

**Single positive blood culture for *Coxiella burnetii* or phase 1 IgG antibody titer >1:800**

#### Evidence of endocardial involvement (one of the following):

**Echocardiogram positive for IE:**

- Vegetation (oscillating intracardiac mass on a valve or on 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

**New valvular regurgitation**

- Increase in or change in preexisting murmur not sufficient

#### Minor criteria

**Predisposition:** Intravenous drug use or presence of a predisposing heart condition (prosthetic heart valve or a valve lesion associated with significant regurgitation or turbulence of blood flow)

**Fever:** Temperature ≥38.0°C (100.4°F)

**Vascular phenomena:** Major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, or Janeway lesions

**Immunologic phenomena:** Glomerulonephritis, Osler nodes, Roth spots, or rheumatoid factor

**Microbiologic evidence:** Positive blood cultures that do not meet major criteria OR serologic evidence of active infection with organism consistent with IE

(Endocardographic minor criteria eliminated)*

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IE: infective endocarditis; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.

* Modifications from the previous published Duke criteria are noted by the asterisk.

Treatment

- Depends on the status of the patient, microbiology and underlying condition (artificial valves etc)

- Get blood cultures ASAP so you can start empirical antibiotics

- Patients who fail medical therapy might be candidates for surgical intervention
Treatment

- Depending on the underlying organism, antibiotic therapy will be tailored.

- Monitoring of therapy using drug levels, repeated echocardiographic imaging and blood cultures
Surgical intervention

- Infection causing valve dysfunction and heart failure
- Extensive penetrating infection causing annular or erosion, abscess or heart block
- Fungal endocarditis (other than neonatal) or drug resistant organisms
- Resistant infection (more than 7 days) after the start of appropriate therapy
- To prevent systemic embolism (there is criteria for this)
Prevention

• Indications for IE prophylaxis changed significantly in 2007:
  • Prosthetic heart valves, including bioprosthetic and homograft valves
  • A prior history of IE
  • Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
  • Completely repaired congenital heart defects with prosthetic material or device during the first six months after the procedure (whether placed by surgery or by catheter intervention)
  • Repaired congenital heart disease with residual defects at the site or adjacent to the site of the prosthetic patch or prosthetic device
  • Valve regurgitation due to a structurally abnormal valve in a transplanted heart
Prevention

- Ok, the patient is high risk, but when give antibiotics?
  1. Dental procedures that involve the gingiva, peri-apical region or injuring the mucosa
  2. Skin infections
  3. Respiratory procedure that is part of treatment of an existing infection
  4. GI or UTI infection
Complications

- IE in children carries a 5% mortality
- Cyanotic heart disease and IE caused by Staph aureus carry higher risk
- Heart failure, severe valve damage. Graft or surgical material damage
- Abscess formation. Fistula.
- Arrhythmia, heart block.
- Metastatic infection
- Glomerulonephritis
Thank You