Kawasaki Disease
1:45 – 2:30 p.m.

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Disclosures

We have no relevant financial relationships to disclose.
Objectives

• Describe the characteristic signs and symptoms of Kawasaki disease

• Understand the process of diagnosing Kawasaki disease

• Discuss the cardiac manifestations, appropriate cardiac imaging and testing, and potential cardiac sequelae of Kawasaki disease
Kawasaki Disease

• Second most common vasculitis of childhood
• Most common cause of acquired heart disease in childhood
• Worldwide distribution
• All ethnic groups; bias toward East Asian children
• Seasonality and occasional epidemics
• Etiology remains unknown
Kawasaki Disease

• 85% younger than 5 years

• Peak age 18-24 months

• Infants and those > 5 years less common but have increased risk of CAAs
Kawasaki Disease

• Clinical Features
  • Fever $\geq 5$ days
  • Rash
  • Mucous membrane changes
  • Conjunctivitis
  • Extremity changes
  • Cervical adenopathy

Diagnosis: No diagnostic test
Fever and 4/5 additional criteria

Challenge: Incomplete Cases
Kawasaki Disease

• Coronary artery aneurysms
  - 15-25% of untreated patients
  - Giant aneurysms (≥ 8 mm) most concerning
  - IVIG decreases incidence to < 5%

• Pericarditis, myocarditis may also occur early in disease
Kawasaki Disease: Fever

- Daily, high, spiking
- Remits transiently with antipyretics
- 39-40 degrees
- Untreated, median duration 11 days
- Treated, ≤ 2 days
Kawasaki Disease: Conjunctivitis

- Bilateral
- Bulbar > Palpebral
- Spares limbus
- No exudate
- Painless
Kawasaki Disease: Mucous membranes

- Erythema, dryness, fissuring or peeling of lips
- Diffuse erythema of pharynx
- “Strawberry” tongue

Discrete oral lesions or ulcers and exudate not seen
Kawasaki Disease: Rash

- No single distinct form
- Most common: diffuse maculopapular erythematous
- Others:
  - Urticaria-like
  - Scarlatiniform
  - Erythema multiforme
  - Generalized erythroderma
- More prominent in perineum with early desquamation here

Bullae or vesicles do not occur
Kawasaki Disease: Extremities

- **Early**
  - Erythema of the palms and soles
  - Induration diffusely of dorsa of hands and feet

- **Late (2-3 weeks)**
  - Desquamation of fingers and toes
Kawasaki Disease: Adenopathy

- Least common main clinical feature
- Unilateral
- Anterior
- At least one lymph node > 1.5 cm
- Firm, non-fluctuant
- Minimal or no erythema or tenderness

Generalized adenopathy unusual
Kawasaki Disease

Other Clinical Findings:
- Arthralgia or arthritis
- Abdominal pain, diarrhea, vomiting
- Hydrops of gallbladder
- Extreme irritability
- Aseptic meningitis
- Urethritis or meatitis
- Anterior uveitis

- Cardiac disease
# Clinical Manifestations of Kawasaki Disease

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<th>Acute</th>
<th>Subacute</th>
<th>Convalescent</th>
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<tr>
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<td>aneurysms</td>
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<tr>
<td><strong>Skin</strong></td>
<td></td>
<td>red palms/soles</td>
<td>desquamation</td>
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<tr>
<td><strong>Lips, Mucosa, Conjunctiva</strong></td>
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<tr>
<td><strong>Cervical Adenitis</strong></td>
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<td><strong>Thrombocytosis</strong></td>
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Kawasaki Disease: Laboratory Findings

• Leukocytosis (neutrophil predominant)
• Elevated inflammatory markers (ESR, CRP)
• Mild anemia
• Thrombocytosis (2nd week) (thrombocytopenia may be seen early)
• Low albumin
• Elevated transaminases
• Sterile pyuria
• CSF pleocytosis
Kawasaki Disease: Differential Diagnosis

- Viral infection (adenovirus, EBV, enterovirus, measles)
- **Group A strep** infection (scarlet fever)
- Staphylococcal scalded skin syndrome
- **Drug reactions** (e.g. Stevens-Johnson Syndrome)
- Toxic shock syndrome
- Bacterial cervical lymphadenitis
- Rocky Mountain Spotted Fever
- Leptospirosis
- Mercury hypersensitivity (acrodynia)
- Systemic-onset JIA
What about incomplete cases?
Evaluation of Suspected Incomplete Kawasaki Disease (KD)¹

Fever ≥ 5 days and 2 or 3 clinical criteria²

Assess Patient Characteristics³

Consistent with KD

Inconsistent with KD

Persistent Fever

Assess Laboratory Tests

CRP < 3.0 mg/DL and ESR < 40 mm/hr

Follow Daily

No Peeling

Typical Peeling⁵

Fever continues for 2 days

Fever resolves

≤ 3 Supplemental Laboratory Criteria⁴

≥ 3 Supplemental Laboratory Criteria⁴

Echo

Echo -

Echo +⁶

Fever Persists

Fever Abates

Treat⁷

Repeat Echo Consult KD Expert

KD Unlikely

CRP ≥ 3.0 mg/DL and/or ESR ≥ 40 mm/hr

Urine > 10 WBC/hpf

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Kawasaki Disease

Exception: Infants

< 6 months old with prolonged fever (7 days) should have laboratory testing and echocardiogram....even in absence of any other clinical features
Kawasaki Disease

• Treatment
  – Optimal to treat before 10 days of fever
  – IVIG 2 g/kg over 10-12 hrs
  – Aspirin
    • 80-100 mg/kg/d every 6 hrs while febrile
    • Reduce dose to 3-5 mg/kg/d as single dose once defervesced
    • Continue aspirin for at least 6-8 weeks
  – If fever persists or recurs:
    • Second IVIG, corticosteroids, others
Kawasaki Disease

• Cardiac manifestation keys:
  – All thought to be the result of an inflammatory process
  – Typically the inflammation is a transient process
  – May result in ischemic injury
Kawasaki Disease: Cardiac Manifestations

- Coronary Artery Lesions
  - Aneurysms seen in ~17% of KD in 1983 when treatment was only aspirin
  - Mortality rate in children in 1974 was above 1%, currently 0.01%
  - Lesions
    - Dilation (ectasia)
    - Aneurysm
    - Stenosis
    - Intimal proliferation
Kawasaki Disease: Coronary Artery Lesions

• Lesions occur during initial acute phase
• If no coronary findings by 4-8 weeks, then unlikely to develop
• Most commonly the lesions regress in the first 30 days
• Of those that persist, most regress in size over years
Kawasaki Disease: Coronary Artery Lesions

• Aneurysms
  – Size
    • Small ~3-5 mm
    • Medium 5-8 mm
    • Giant >8 mm
  – Sites (most common to least)
    • Proximal LAD
    • Proximal RCA
    • LMCA
    • LCx
    • Distal RCA
Kawasaki Disease: Coronary Artery Lesions

Heart with Normal Coronary Arteries
(in red)

Heart with Coronary Artery Aneurysms
(in red)

normal coronary artery

fusiform aneurysm
saccular aneurysm
Coronary Aneurysms by ECHO
Kawasaki Disease: Coronary Artery Lesions

- Natural history of aneurysms
  - Smaller and more distal aneurysms more likely to regress
  - More than half will regress in first 1-2 years
  - Giant aneurysms have worse prognosis
Kawasaki Disease: Coronary Artery Lesions

- Aneurysms create area for thrombosis to develop
- Focus of therapy
- Acute occlusion by thrombosis is different than adults with coronary artery disease
  - Doesn’t involve plaque rupture
  - Occurs very rapidly and thrombus burden can be very large
Kawasaki Disease: Coronary Artery Lesions

• **Stenosis**
  – Late sequelae of aneurysm formation
  – Mechanisms:
    • Recanalization (neo-revascularization)
    • Post-regression stenosis
Kawasaki Disease: Coronary Artery Lesions

- As regression occurs there is neo-intimal proliferation
- Even without stenosis can result in fibrous intimal thickening despite normal caliber vessel
- Intravascular imaging demonstrates impaired relaxation despite normal appearing vessel
Intravascular Ultrasound
Kawasaki Disease: Other Cardiac Findings

• Non-coronary Cardiac Lesions
  – Pericardial effusion
  – Pericarditis
  – Myocarditis
    • Occurs during the acute phase
    • May see decrease in ventricular function acutely
    • Severity does not predict development of aneurysms
  – Hemodynamic instability
Kawasaki Disease: Other Cardiac Findings

• Valve disease
  – Typically affects mitral or aortic valve
  – Onset in acute phase
  – Rarely persists

• Other vasculature
  – Rarely see aneurysms of other large vessels
  – May lead to necrotic extremities, infarction, vascular rupture, or stroke
Kawasaki Disease: Cardiac Imaging

• Echocardiography
  – Time of diagnosis
  – 2 weeks
  – 6-8 weeks after onset
  – If normal, then imaging at 1 year is optional
Kawasaki Disease: Cardiac Imaging

• Other non-invasive imaging
  – Cardiac MRI
    • MRA
    • Tissue characterization
  – CT heart
  – Stress imaging
    • Echo
    • MRI
    • Nuclear testing
Kawasaki Disease: Cardiac Imaging

• Coronary angiography
  – Recommended for risk level 4 (large/giant/multiple coronary aneurysms) or 5 (coronary obstruction)
  – First at 6-12 months post infection
  – Further testing if other testing suggests abnormal perfusion
  – Use to assess therapeutic options
Kawasaki Disease Recommendations

• Physical activity
  – No limitation if normal coronary arteries or transient ectasia
  – If aneurysms present then guide physical activity with stress/perfusion imaging
  – Avoid contact sports if bleeding risk
Kawasaki Disease Medical Therapy

• High dose aspirin initially until afebrile
• Low dose aspirin:
  – for first 6-8 weeks as long as changes are transient
  – Long term for risk level 3 (small aneurysms) and above
• Combine anti-platelet with anti-thrombotic for risk level 4 or 5
Kawasaki Disease

Questions???
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