Kawasaki Disease

Jennifer Esau, DO
Via Christi Family Medicine Residency
CC: Fever
HPI: A 5 month old Caucasian male presents to clinic with a 4.5 day history of fever. He was seen 2 days ago in the ED and started on antibiotics for otitis media. Mother states his fever is persistent despite use of Advil and Tylenol. She additionally noted a rash over his groin, hands, and chest which began yesterday.
ROS: +Rhinitis, diarrhea, decreased oral intake, red cracked lips.
PMH: Eczema
Birth history: Full term NSVD
Immunizations: Has received 4 month vaccines
Medications: Advil
Allergies: NKDA
Case Presentation

Physical Exam
* VS: Temp **103.7**, BP 115/72, Pulse 207, RR 56, O2Sat 98%
* General: Alert, irritable
* NECK: Supple, no LAD
* PULM: CTAB
* CV: Tachycardia
* ABD: Soft, NTTP, +bowel sounds
* SKIN: *Polymorphous erythematous rash on chest, feet, groin.*
* NEURO: No gross motor deficits.
Definition

* Acute, self-limiting vasculitis of infancy and early childhood characterized by
  * Fever
  * Rash
  * Conjunctivitis (bilateral non-exudative)
  * Inflammation of mucous membranes
  * Cervical lymphadenopathy
  * Erythematous induration of hands and feet
80% of cases occur in children <5 years

Boys:Girls – 1.5:1

Incidence for Children in the US

- 32.5 per 100,000 in Asian decent
- 16.9 per 100,000 in African Americans
- 11.1 per 100,000 in Hispanics
- 9.1 per 100,000 in Whites
Etiology

* Unknown
* Clinical Features suggest an infectious process
Leading cause of acquired heart disease in children

- Coronary artery aneurysms or ectasia occur in 15-25% of untreated children which may lead to myocardial ischemia, sudden death, or ischemic heart disease

- Standard treatment reduces this risk to <5%
Diagnostic Criteria

- Fever of unknown cause lasting 5 days or more AND at least 4 of the 5 following criteria
  - Bilateral non-exudative conjunctivitis
  - Changes of the lips and oral cavity; Diffuse reddening, dryness and fissuring; Protuberance of tongue papillae (strawberry tongue)
  - Redness and indurative edema of palms and soles
  - Polymorphous exanthem without vesicles or crust
  - Acute nonpurulent swelling of cervical lymph nodes of 1.5cm or more
Acute Phase

- Fever, oropharyngeal erythema, swelling of hands, cervical lymphadenopathy
- Fever and rash fade after 10-12 days

Subacute Phase

- Lip cracking and fissuring
- Desquamation of skin over tips of fingers and toes
- Onset of arthralgia and/or arthritis
- Cardiac disease

Convalescent Phase

- Begins after 25 days. Absence of clinical signs but persistence of residual inflammation
Conjunctivitis in Kawasaki disease

Cracked, red lips seen in Kawasaki disease

Strawberry tongue
Indurated edema of the dorsum of the hands as seen in Kawasaki disease (acute phase)

Characteristic periungual desquamation of the hands and feet seen in Kawasaki disease
Atypical Kawasaki Disease

- Consider in infants and children with fever >5 days and 2-3 principal diagnostic criteria
- Infants <6 months may only have fever
  - High risk for coronary abnormalities
  - Consider echo if unexplained fever >7 days and laboratory evidence of systemic inflammation
- In patients with fever >5 days and 2-3 criteria met, CRP and ESR should be measured. (Evidence Level C)
Evaluation of Suspected Incomplete Kawasaki Disease (KD)¹

Fever ≥ 5 days and 2 or 3 clinical criteria²

Assess Patient Characteristics³

Consistent with KD
Assess Laboratory Tests

CRP <3.0 mg/DL and ESR <40 mm/hr
Follow Daily
Fever continues for 2 days
No Peeling
No f/u
Echo⁶
Repeat Echo Consult KD Expert
KD Unlikely

Fever resolves
Typical Peeling⁸
Echo⁶
Fever Persists
Fever Abates
Echo + ⁶
Treat⁷

Inconsistent with KD
Persistent Fever
KD Unlikely

CRP ≥3.0 mg/DL and/or ESR ≥40 mm/hr

<3 Supplemental Laboratory Criteria⁴
Echo
Echo –
Fever Persists
Fever Abates
Treat⁷

≥3 Supplemental Laboratory Criteria⁴
Echo + ⁶
Treat⁷
Goals of Treatment

* Acute Phase
  * Decrease inflammation in coronary artery wall and prevent coronary thrombosis
* Long-term Phase
  * Prevent myocardial ischemia in patients with coronary artery aneurysms
Treatment

* High dose IVIG 2 g/kg in single infusion (evidence Level A)
* High dose aspirin 80-100mg/kg/d (evidence Level C)
* Begin low dose aspirin (3-5 mg/kg/d) when high-dose aspirin is discontinued. Continue until 6-8 weeks after onset of illness and no evidence of coronary aneurysms (evidence Level C)
* Ibuprofen should be avoided in children with coronary aneurysms taking aspirin for its antiplatelet effect (evidence Level B)
* Steroid treatment should be limited to children in whom IVIG has been ineffective in alleviating fever. (evidence Level C)
**Case Presentation**

* Lab
  * WBC 20.6 K/uL, sed rate >140 mm/hr, albumin 3.2 g/dL, ALT 81 U/L, AST 63 U/L
* Treatment
  * Received high dose IVIG and high dose aspirin. Fever and conjunctival erythema resolved. He remained afebrile for 48 hours, was changed from high dose to low dose aspirin and discharged home.
* Follow-up
  * Echocardiogram was negative, will follow-up with Cardiologist again in 6 weeks
  * Follow-up with PCP. Will monitor CRP and CBC. When acute phase reactants are within normal limits, aspirin will be stopped.
  * 6 month MMR vaccine will be delayed for 11 months.
Follow-up

* Physical activity- directed by cardiologist for patients with coronary artery abnormalities
* Repeat echocardiogram at 6-8 weeks
* Live virus vaccines should be postponed for 11 months
  * Passively acquired antibodies persist following IVIG administration and may interfere with vaccine immunogenicity.
* Influenza vaccine recommended for all children >6mo who require long-term aspirin therapy due to possible increased risk of Reye syndrome
<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Pharmacological Therapy</th>
<th>Physical Activity</th>
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<tbody>
<tr>
<td>I (no coronary artery changes at any stage of illness)</td>
<td>None beyond 1st 6–8 weeks</td>
<td>No restrictions beyond 1st 6–8 weeks</td>
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<tr>
<td>II (transient coronary artery ectasia disappears within 1st 6–8 weeks)</td>
<td>None beyond 1st 6–8 weeks</td>
<td>No restrictions beyond 1st 6–8 weeks</td>
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<tr>
<td>III (1 small-medium coronary artery aneurysm/major coronary artery)</td>
<td>Low-dose aspirin (3–5 mg/kg aspirin per day), at least until aneurysm regression documented</td>
<td>For patients &lt;11 y old, no restriction beyond 1st 6–8 weeks; patients 11–20 y old, physical activity guided by biennial stress test, evaluation of myocardial perfusion scan; contact or high-impact sports discouraged for patients taking antiplatelet agents</td>
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<tr>
<td>IV (≥1 large or giant coronary artery aneurysm, or multiple or complex aneurysms in same coronary artery, without obstruction)</td>
<td>Long-term antiplatelet therapy and warfarin (target INR 2.0–2.5) or low-molecular-weight heparin (target: antifactor Xa level 0.5–1.0 U/mL) should be combined in giant aneurysms</td>
<td>Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations guided by stress test/evaluation of myocardial perfusion scan outcome</td>
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<tr>
<td>V (coronary artery obstruction)</td>
<td>Long-term low-dose aspirin; warfarin or low-molecular-weight heparin if giant aneurysm persists; consider use of β-blockers to reduce myocardial O₂ consumption</td>
<td>Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations guided by stress test/myocardial perfusion scan outcome</td>
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<tr>
<td>Risk Level</td>
<td>Follow-Up and Diagnostic Testing</td>
<td>Invasive Testing</td>
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<tr>
<td>I (no coronary artery changes at any stage of illness)</td>
<td>Cardiovascular risk assessment, counseling at 5-y intervals</td>
<td>None recommended</td>
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<tr>
<td>II (transient coronary artery ectasia disappears within 1st 6–8 weeks)</td>
<td>Cardiovascular risk assessment, counseling at 3– to 5-y intervals</td>
<td>None recommended</td>
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<tr>
<td>III (1 small-medium coronary artery aneurysm/major coronary artery)</td>
<td>Annual cardiology follow-up with echocardiogram + ECG, combined with cardiovascular risk assessment, counseling; biennial stress test/evaluation of myocardial perfusion scan</td>
<td>Angiography, if noninvasive test suggests ischemia</td>
</tr>
<tr>
<td>IV (≥1 large or giant coronary artery aneurysm, or multiple or complex aneurysms in same coronary artery, without obstruction)</td>
<td>Biannual follow-up with echocardiogram + ECG; annual stress test/evaluation of myocardial perfusion scan</td>
<td>1st angiography at 6–12 mo or sooner if clinically indicated; repeated angiography if noninvasive test, clinical, or laboratory findings suggest ischemia; elective repeat angiography under some circumstances (see text)</td>
</tr>
<tr>
<td>V (coronary artery obstruction)</td>
<td>Biannual follow-up with echocardiogram and ECG; annual stress test/evaluation of myocardial perfusion scan</td>
<td>Angiography recommended to address therapeutic options</td>
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Kawasaki disease is the leading cause of acquired heart disease in children.

- Treatment may be initiated if fever <5 days and classic diagnostic criteria met. (Evidence Level C)
- In patients with fever >5 days and 2-3 criteria met, CRP and ESR should be measured. (Evidence Level C)
- High dose IVIG 2 g/kg should be given as first line therapy. (Evidence Level A)
- High dose aspirin 80-100 mg/kg/d (divided QID) should be given with IVIG. (Evidence Level C)
- Avoid live virus vaccines for 11 months after IVIG
References


* UpToDate. Kawasaki Disease: Clinical Features and Diagnosis