UC DAVIS HEALTH | CHILDREN'S HOSPITAL

The Care of Children with Kawasaki Disease

Evaluation of the child with suspected Kawasaki Disease:

Laboratory studies	CBC with differential, ESR, CRP, CMP (includes ALT and albumin), GGT, urinalysis (can be clean catch or bag specimen). Could also consider sending other tests to rule out infectious etiology (i.e. blood cultures, urine culture from appropriately collected specimen, RVP, lumbar puncture, especially in <6 month old infant).
Imaging (depending on symptoms)	Chest X-ray, Abdominal ultrasound (can have acalculous cholecystitis), Neck ultrasound (if large cervical LAD)
Cardiac studies	EKG, Echocardiogram
Consultations	Please page or contact Pediatric Cardiologist On-Call to obtain approval for Pediatric Complete Echocardiogram. Also consider consulting Pediatric Infectious Disease (help with treatment and diagnosis), Pediatric Rheumatology (if ddx includes autoimmune disease), Ophthalmology (if concern for uveitis)

Diagnosis of Kawasaki Disease:

Classic KD is diagnosed in the presence of fever for at least 5 d (the day of fever onset is taken to be the first day of fever) together with at least 4 of the 5 following principal clinical features. In the presence of ≥4 principal clinical features, particularly when redness and swelling of the hands and feet are present, the diagnosis of KD can be made with 4 d of fever.
1. Erythema and cracking of the lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
2. Bilateral bulbar conjunctival injection without exudate
3. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like
4. Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in the subacute phase
5. Cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral
A careful history may reveal that ≥1 principal clinical features were present during the illness but resolved by the time of presentation.
Patients who lack full clinical features of classic KD are often evaluated for incomplete KD (see Figure 1 below). If coronary artery abnormalities are detected, the diagnosis of KD is considered confirmed in most cases. Note that while coronary artery abnormalities strongly support the diagnosis of KD, a normal echocardiogram does not exclude Kawasaki disease.
Laboratory tests typically reveal normal or elevated white blood cell count with neutrophil predominance and elevated acute phase reactants such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) during the acute phase. Low serum sodium and albumin levels, elevated serum liver enzymes, and sterile pyuria can be present. In the second week after fever onset, thrombocytosis is common.

Diagnosis of incomplete KD: (Prolonged unexplained fever, fewer than 4 of the principal clinical findings, and compatible laboratory or echocardiographic findings):

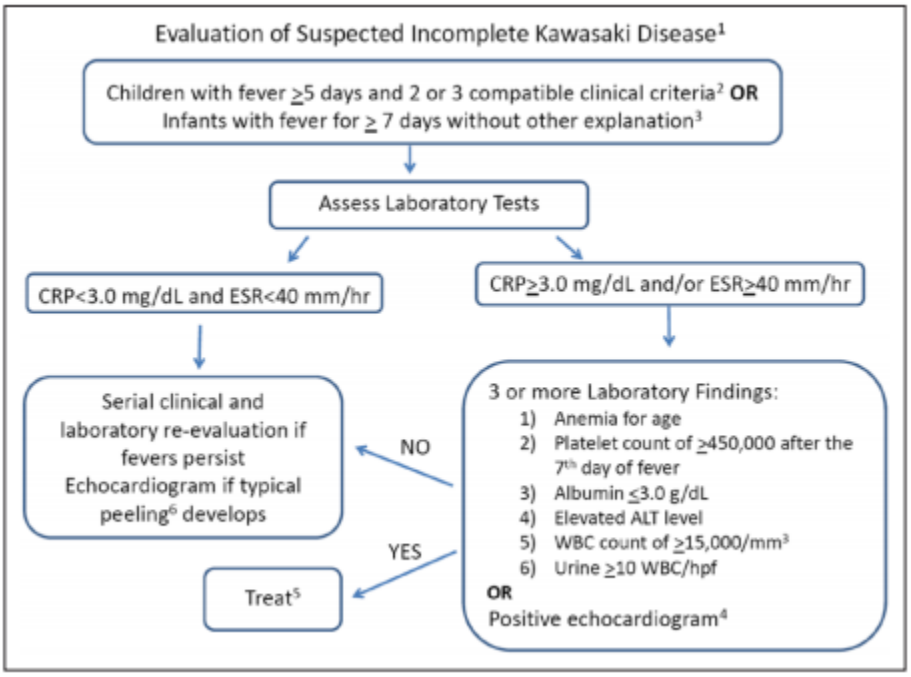

Figure 1. Evaluation of suspected incomplete Kawasaki Disease. From "Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease. A Scientific Statement for Health Professionals from the American Heart Association." McCrindle et al, *Circulation* 2017.

Initial treatment for all patients with Kawasaki Disease:

1. IVIG 2g/kg as a single infusion given over 10-12 hours
    a. Side effects include infusion reactions, anaphylaxis (avoid if known IgA deficiency, but routine screening not recommended), Coombs-positive hemolytic anemia, aseptic meningitis, renal impairment, thromboembolic events
    b. Ensure adequate hydration prior to administration of IVIG
2. Aspirin (30-50mg/kg/day divided every 6 hours) for the acute phase. Continue aspirin at this dose until afebrile for 36-48 hours, then transition to low-dose aspirin (3-5 mg/kg/day, rounded to either 0.5 or 1 baby aspirin) until discontinued by cardiology.
    a. Side effects include allergy, tinnitus, GI bleeding, Reye syndrome (associated with varicella and influenza infections)
3. For fever, only use acetaminophen at standard dosing. Do not use ibuprofen (contraindicated while on aspirin).
4. All children ≥ 6 months should receive a seasonal influenza vaccine, as should their family members. Only inactivated vaccine should be administered while the child is receiving aspirin therapy. This should be done prior to discharge form the hospital.
5. Patients should be monitored until afebrile for at least 36 hours from the completion of the IVIG infusion. If patient has a temperature ≥38.0 after 36 hours, then consider repeat treatment for IVIG-resistant KD (see below).

Treatment of a patient with Kawasaki Disease and coronary artery abnormalities (z-score >= 2.5) on initial echocardiogram:

1. In addition to IVIG and moderate-dose aspirin, give augmented initial therapy with **infliximab 10 mg/kg IV over 2 hours** if the following criteria are met:

a. patient has received primary vaccine series for Hepatitis B Virus
b. there are no risk factors for tuberculosis (e.g. prior residence or prolonged stay in endemic area; known contact; exposure to adults who are HIV+, experiencing homelessness, incarcerated, or people who inject drugs)
c. if criteria (a) and (b) above are not met, steroids are another option. Contact Peds ID to discuss

2. Discuss timing and location (inpatient versus outpatient) of follow-up echo with Peds Cardiology prior to discharge
3. Continue moderate-dose aspirin until afebrile for 36-48 hours or until time of discharge (whichever is sooner), then transition to low-dose aspirin until cardiology follow up.
4. If patient has another fever greater than 36 hours after the end of second line therapy, please consult Pediatric Infectious Diseases if not done previously for further treatment recommendations.

Treatment of a patient with IVIG-resistant Kawasaki Disease *(remains febrile 36 hours – 7 days after end of first IVIG infusion):*

1. Obtain repeat labs including CBC with differential, CRP, CMP and repeat echocardiogram. Do not repeat ESR as this is falsely elevated following IVIG.
2. Give second line treatment with **infliximab 10mg/kg IV over 2 hours** if the following criteria are met:
    a. patient has received primary vaccine series for Hepatitis B Virus
    b. there are no risk factors for tuberculosis (e.g. prior residence or prolonged stay in endemic area; known contact; exposure to adults who are HIV+, experiencing homelessness, incarcerated, or people who inject drugs)
    c. if criteria (a) and (b) above are not met, steroids are another option. Contact Peds ID to discuss
3. Alternative second line therapy (criteria for infliximab not met or treating physician preference): second dose of IVIG 2g/kg IV over 10-12 hours.
4. Continue moderate-dose aspirin until afebrile for 36-48 hours or until time of discharge (whichever is sooner), then transition to low-dose aspirin until cardiology follow up. See above for further discharge considerations.
5. If patient has another fever greater than 36 hours after the end of second line therapy, please consult Pediatric Infectious Diseases if not done previously for further treatment recommendations.

Discharge planning for patients hospitalized and treated for Kawasaki Disease:

1. Prior to discharge, please discuss the following with the families:
    a. Please call back to the hospital (916-734-2011) and ask to speak with Pediatric Hospitalist physician on call if temperature ≥38.0 in the first week following treatment.
    b. Continue aspirin daily until cardiology follow-up.
    c. Do not administer ibuprofen at home while on aspirin.
    d. Postpone routine live vaccines (such as MMR and varicella) for 11 months after treatment for KD.
    e. Please contact your child's physician if the child develops any symptoms of GI bleeding (side effect of aspirin), such as dark stools, pallor, or dizziness.

Reference:

"Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease. A Scientific Statement for Health Professionals from the American Heart Association." McCrindle et al, *Circulation* 2017;135:00-00. DOI: 10.1161/CIR.0000000000000484.

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Miyata K, Bainto EV, Sun X, Jain S, Dummer KB, Burns JC, Tremoulet AH. Infliximab for intensification of primary therapy for patients with Kawasaki disease and coronary artery aneurysms at diagnosis. Arch Dis Child. 2023 Oct;108(10):833-838. doi: 10.1136/archdischild-2023-325639. Epub 2023 May 31. PMID: 37258054

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