May 5, 2020

Kawasaki Disease Guidelines

Background:

- Kawasaki disease(KD) is relatively rare - 4000-5500 cases reported in the US every year.
- Peak age of occurrence in United States is between 18 and 24 months.
    - Fifty percent of patients are younger than 2 years
    - 80% are younger than 5 years
- Cases are uncommon in children older than 8 years, but rare cases occur even in adults.
- More cases, including clusters, occur during winter and spring.
- No evidence indicates person-to-person or common-source spread, although the incidence is tenfold higher in siblings of children with the disease than in the general population.

Diagnosis:

- In our experience, the majority of cases are incomplete/atypical, and diagnosis can be particularly challenging (see algorithm for atypical cases in next page).
- Consult Infectious Disease for all patients as there is a need for post-hospital follow up and all cases are discussed within the Infectious Disease group.
    - High risk patients are even more likely to benefit – Please see below for definition and treatment recommendations
- Diagnosis of concurrent viral upper respiratory infection sometimes is present in a patient with Kawasaki disease and, even if confirmed by virus detection, should not delay treatment.
- The following mucocutaneous or laboratory findings should prompt a search for an **alternative diagnosis**:
    - bullous, vesicular, or petechial rash
    - oral ulcers
    - pharyngeal or conjunctival exudates
    - generalized lymphadenopathy or splenomegaly
    - leukopenia or relative lymphocyte predominance.

Laboratory testing:

- Always check ESR and CRP when considering the diagnosis of KD.
- Once treated with IVIG do not use ESR for follow up.
- Please send midstream urine specimen/bag specimen if midstream is not practical, do not catheterize as the cause of pyuria is urethritis.
- Lab workup includes CBC, ESR, CRP, CMP, urinalysis and urine culture and echocardiogram

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Kawasaki Disease Guidelines

Diagnosis of Classic KD (AHA guidelines 2017)

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, although experienced clinicians who have treated many patients with KD may establish the diagnosis with 3 d of fever in rare cases:

1. Erythema and cracking of 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 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.

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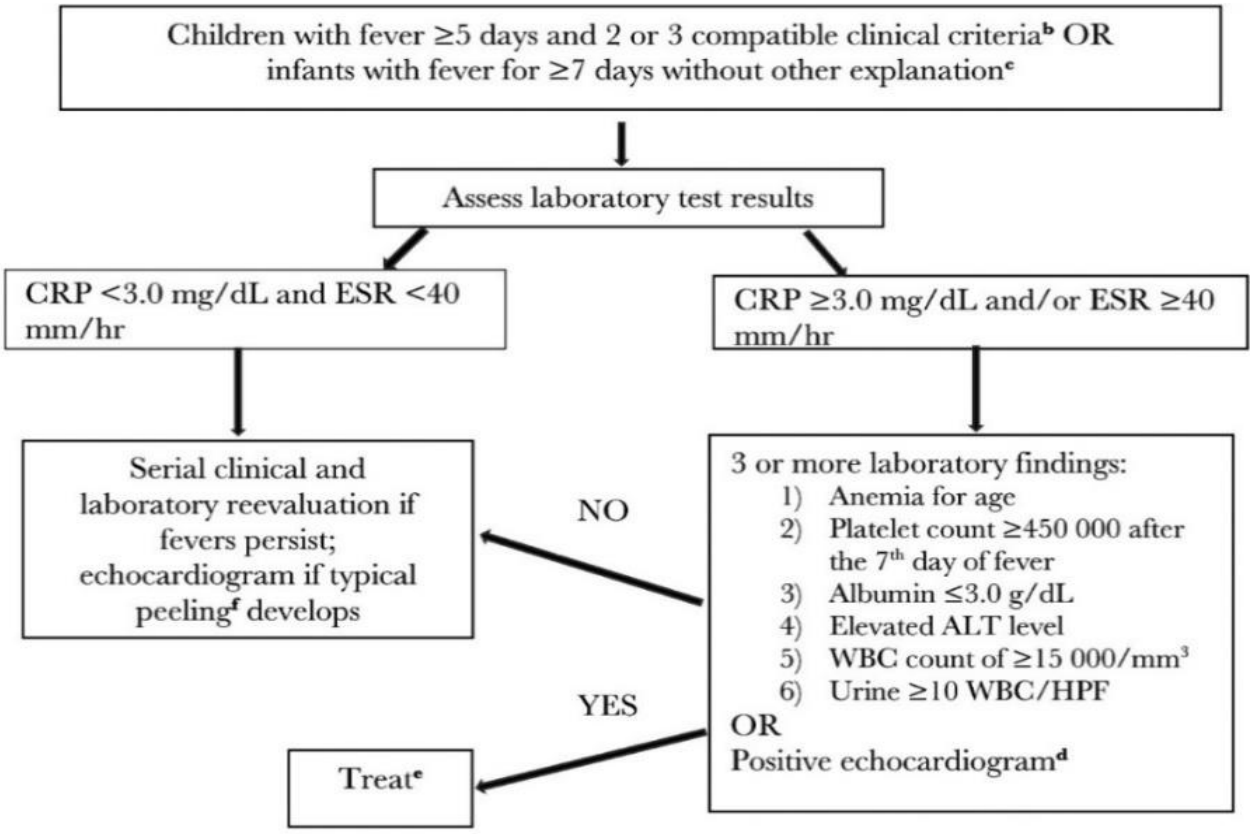
Kawasaki Disease Guidelines

Patients who lack full clinical features of classic KD are often evaluated for incomplete KD

Algorithm for evaluation of atypical Kawasaki disease (source: Redbook 2018)



CRP indicates C-reactive protein; ESR, erythrocyte sedimentation rate; ALT, alanine transaminase; WBC, white blood cell; HPF, high-powered field.

[a]In the absence of a "gold standard" for diagnosis, this algorithm cannot be evidence based but rather represents the informed opinion of the expert committee. Consultation with an expert should be sought anytime assistance is needed.

[b]See text for clinical findings of Kawasaki disease.

[c]Infants ≤6 months of age are the most likely to develop prolonged fever without other clinical criteria for Kawasaki disease; these infants are at particularly high risk of developing coronary artery abnormalities.

[d]Echocardiography is considered positive for purposes of this algorithm if any of 3 conditions are met: z score of left anterior descending coronary artery or right coronary artery ≥2.5; coronary artery aneurysm is observed; or ≥3 other suggestive features exist, including decreased left ventricular function, mitral regurgitation, pericardial effusion, or z scores in left anterior descending coronary artery or right coronary artery of 2 to 2.5.

[e]Treatment should be given within 10 days of fever onset. See text for indications for treatment after the tenth day of fever.

[f]Typical peeling begins under the nail beds of fingers and toes.

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Kawasaki Disease Guidelines

Risk stratification:
This is considered increasingly important. In the absence of a universally agreed algorithm, the following represents a consensus from our group guided by recent data and expert opinion

High risk Criteria –

1. Infants under 6 months of age
2. Those with coronary abnormalities on baseline ECHO – Z score of ≥2.5 in RCA or LAD/ aneurysms.
3. Those with resistance to primary treatment with IVIG
4. Additional criteria – **need ≥3 of the following if not already met above**
    - Male
    - CRP level >10 mg/dl
    - Age 7-12 months or > 8 years
    - WBC >20,000 with neutrophil predominance
    - Platelet count <150,000
    - Sodium <133
    - Albumin <2.8
    - Hemoglobin <9
    - ALT>100
    - Fever for more than 10 days

Treatment guidance including repeat ECHO cardiogram:

Standard risk patients –

- IVIG 2 grams/kg once, plus high dose aspirin at 80-100 mg/kg/day in 4 divided doses until discharge from hospital (document negative flu test before high dose aspirin in the flu season).
- At discharge, transition to low dose aspirin 3-5 mg/kg/day for 42 days - until the 6-week ECHO.

High risk patients –

- IVIG 2 grams/kg once plus Methylprednisolone 2mg/kg/day divided TID until afebrile (usually between 3-5 days) plus high dose aspirin at 80-100 mg/kg/day in 4 divided doses until discharge from hospital (document negative flu test before high dose aspirin in the flu season). Then transition to PO prednisolone at 2mg/kg/day once daily until the CRP is <5. After that, wean to 1mg/kg/day once daily and then 0.5 mg/kg/day once daily over 2-3-weeks
- At discharge transition to low dose aspirin at 3-5 mg/kg/day for 42 days - until the 6-week ECHO

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Kawasaki Disease Guidelines

Echocardiography and cardiovascular complications:

- Cardiac imaging with standard echocardiography can assist in establishing diagnosis in "atypical cases" and provide comprehensive evaluation of cardiovascular complications of KD in "typical cases".
- Initial echocardiogram should be performed as soon as the diagnosis is suspected or the treatment with IVIG therapy is initiated. Do not wait for echocardiogram to start treatment if index of suspicion for KD is high.
- Verbal coordination with cardiology service is critical to assess the need for sedation as well as the timing of the study as these children are typically irritable and uncooperative. Standard risk patients get Echocardiogram at initial diagnosis followed by repeat study at 2 weeks and at 2 months (6 to 8 weeks). It is extremely uncommon to develop coronary artery complications after 6 to 8 weeks.
- For high risk patients, more frequent imaging may be required. Depending upon the findings on the initial echocardiogram, treating physician may request repeat echocardiogram either on day 3 or even weekly to monitor the progression of cardiovascular complications and guide management. If serial echocardiograms show worsening of Z scores or development of coronary aneurysms, discuss with cardiology service for consideration for advanced noninvasive testing with cardiac MRI or CT coronary angiography. This may be pursued in complicated cases with extensive coronary involvement on case to case basis.
- Invasive testing with coronary angiography is considered after thorough discussion at the weekly Cath conference in the Heart center. This is reserved for severe cases with multiple large aneurysms and/or coronary thrombi to evaluate the extent of the distal coronary involvement and guide management. We typically wait for 3 to 6 months before doing any invasive testing.
- Continued long term follow up focusing of heart healthy lifestyle with preventive cardiology is suggested on annual basis.

Relevant facts

- 80% of patients with Kawasaki disease who ultimately developed coronary artery disease had abnormalities (z score ≥2.5) on an echocardiogram obtained during the first 10 days of illness.
- Despite prompt treatment with IVIG and aspirin, approximately 2% to 4% of patients develop coronary artery aneurysms even when treatment is initiated before the onset of coronary artery abnormalities.

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Kawasaki Disease Guidelines

- Approximately 30% of patients who receive IVIG, 2 g/kg, plus aspirin have fever within the first 36 hours after completing the IVIG infusion, which is not an indication of therapeutic failure. However, 10% to 20% of treated patients have recrudescent or persistent fever beyond 36 hours after completion of their IVIG infusion and are termed IVIG-resistant.

Follow up:

- All patients diagnosed with KD need follow up at 2 weeks and 6 weeks post hospital discharge
- This should include an ECHO cardiogram to look for the coronary artery abnormalities
- High risk patients may need earlier follow up and ECHO based on physician discretion
- All patients with KD need to go home on low dose aspirin at 3-5 mg per kg per day for 42 days until the 6-week ECHO is complete. Additional decisions for those with abnormalities will be made in conjunction with cardiology
- Low dose aspirin does not seem to pose risk of Reyes syndrome

Document prepared by Shankar Upadhyayula, MD Supadhyayula@akronchildrens.org

Kelly Williamson, PharmD. Kwilliamson@akronchildrens.org

Ashish Saini, MD ASaini@akronchildrens.org

Reviewed by Order Set Committee on June 2, 2020

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