Paediatric Clinical Practice Guideline

Diagnosis and management of Kawasaki Disease (KD)

Author: Dr C Bevan / Dr M Lazner / Dr P Venugopalan / Dr K Fidler / Mr C Chadwick. Ratified by the Medicines Governance Group June 2019

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Pan-London consensus guidelines are in the process of being developed – this guideline reflects local agreements and is to be used in the meantime.

Quick flowchart

► Diagnosis (page 2)
Fever > 5 days + at least 4 of the following
A. LymphAdenopathy
R. Polymorphous Rash
D. Distal changes (of the extremities)
I. Conjunctival Injection (bilateral, non-purulent)
O. Oral mucosa and lip changes

► Investigations (page 4)
- Admit to Medical ward
- Blood Tests as per Guideline
- Imaging as per Guideline
- Arrange cardiac echo ideally within 7 days of presentation.

► Treatment (page 5) – start even before baseline cardiac echo
1. IVIG
   2 grams/kg IV infusion

2. Aspirin
   Total 50 mg/kg/day in 4 divided doses for 14 days after fever has been resolved for 48 – 72 hours
   then
   3 - 5 mg/kg OD (max 75 mg/day) until OPD FU in 6-8 weeks (prescribe full course until outpatient appointment)

► Discharge and follow up (page 6)
- If no coronary artery changes on presentation, arrange FU in 6-8 weeks with CoW consultant plus repeat cardiac echo / ECG before OPD by referral to Dr Venu.
- If coronary artery changes at any point on Cardiac Echo, discuss with and refer to Paediatric cardiology at ECH for management and follow up in the Kawasaki clinic.
  Email referral to Paraskevi.Theocharis@gstt.nhs.uk.
Background

Acute Febrile Mucocutaneous Syndrome = vasculitis of unknown aetiology, characterised by multisystem involvement and inflammation of small-medium sized arteries resulting in aneurysm formation

- Commonest cause of acquired heart disease in the UK
- Children 6 months – 5 years old (peak : 1-3 years old, rare in > 7 years old
- < 6 months are at high risk of developing coronary artery aneurysms.

Assessment

Typical Symptoms and Diagnosis

**High Fever for ≥ 5 days**
- Typically > 39 degrees
- Unaffected by antibiotics and common antipyretics.
- No apparent focus
- Miserable and unwell

+ 4 or more of the following:

**Mucus Membrane changes:**
1. Injection/Erythema of the oropharynx
2. Dry/fissured/erythematous lips
3. ‘Strawberry tongue’.

**Bilateral non purulent Conjunctivitis**

**Changes of extremities:**
1. Erythema / oedema of palms
2. Digital swelling
3. Desquamation fingers-toes / inguinal (after 2nd-3rd week)

**Rash:** Polymorphous, non-vesicular / truncal / inguinal area

**Lymphadenopathy:** anterior cervical, >1.5 cm, unilateral

Note: In the presence of established coronary anomalies, diagnosis can be made with less than 5 major criteria (3 out of 5).

Other features strongly suggestive of KD:
- **Irritability** – Almost universal esp. in infants.
- **Erythema and induration of BCG scar**
Atypical or Incomplete Kawasaki:

= Incomplete presentation of the disease, regardless of the presence of coronary complications.

- More common in < 1 year old, > 6 year old - high Index of suspicion in infants.
- Higher incidence of coronary artery aneurysm formation.
- Fever > 5 days **plus 2 or more** of the principal clinical features.
- Diagnosis should be made with the combination of clinical and laboratory findings including a cardiac echo.
- Discuss cases with Paediatric Cardiologist.

Clinical Manifestations

### Acute Phase (week 1 – 2)

- Fever
- Bilateral, non-purulent conjunctivitis
- Mucosal changes
- Cervical Lymphadenopathy (70%)
- Polymorphous Rash (80%)
- Oedema of hands and feet.

**Also:**

- Extreme Irritability esp. in infants
- Abdominal pain / Diarrhoea / Vomiting.
- Gall bladder Hydrops, increased ALT
- Arthritis of medium-large size joints.
- Facial nerve palsy.
- Aseptic Meningitis.
- Carditis:
  - tachycardia, SOB, congestive heart failure
- Hearing loss (rarely persistent).

### Sub-acute phase (week 3 – 4)

- Begins with gradual resolution of the fever and the other symptoms
- Desquamation of the skin: fingers / toes / inguinal area / generalised
- Formation of Coronary Artery Aneurysms:
  - Risk Factors:
    1. Prolonged fever
    2. Prolonged elevation of inflammatory markers
    3. Age <1 or >8 years old.
    5. Incomplete response to IVIG.

### Convalescent phase (week 6 – 8)

- Begins with disappearance of symptoms
- Continues until ESR normal
- Beau lines of fingernails

Differential diagnoses to consider:

- Scarlet fever
- Viral exantham
- Stevens Johnson Syndrome
- Juvenile idiopathic arthritis
- Staphlococcal scalded skin / toxic shock syndrome
Investigations

FBC ** Repeat FBC in 2nd week to look for thrombocytosis**
- Leucocytosis and Neutrophilia (50%) / occasional neutropenia.
- Thrombocytosis
  - In acute phase: normal or slightly raised
  - 2nd week: often > 1000
ESR, CRP: often CRP > 50, ESR > 80
U+E’s
LFT’s: Abnormal (40%) – Mildly raised transaminases / Hypoalbuminaemia
ASOT, antiDNAse B
VZV serology
Blood Culture
Urine MC+: sterile pyuria very common.
Viral / Bacterial Throat swab

LP – discuss with consultant
- CSF pleocytosis

ECG
- Non-specific ST and T-wave abnormalities, arrhythmias, prolonged PR interval, prolonged QT.
- Needs to be performed as baseline and then repeated with the cardiac Echo.

Cardiac echo – mandatory but should not delay treatment.
- Look for: Coronary Aneurysms / Mitral Regurgitation / Global Function.

Baseline echo at presentation (Within 1 week):
- For uncomplicated patients, repeat echo in 6 – 8 weeks after treatment (before Consultant routine FU).
- If coronary artery changes, D/W Paediatric Cardiologist and refer to Rapid Access Clinic at Evelina Children’s Hospital (ECH) London for review.

To arrange contact either:

- Dr Venu, Paediatric Consultant at RACH
- Adult Cardiac Physiologists
ext. 4573, fax: 01273 684554 or via switchboard
- Evelina Children’s Hospital London, paediatric cardiology department

MRI / Coronary Angiogram / Exercise test / Nuclear imaging (Arranged by KD specialist centres).
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Management

Intravenous Immunoglobulin (IVIG)

1. 2 gram/kg intravenous infusion
   - Pharmacist to be contacted to provide brand-specific advice on the rate and titration of the infusion.

Should be started as early as possible within first 10 days of fever onset.

May still be given after 10 days if evidence of ongoing inflammation. Not to be given in children whose fever has resolved, lab values are normal and echo is negative.

Needs Immunoglobulin request form (available on Pharmacy website)

For patients with persistent fever after 1st dose:
   - Review diagnosis.
   - Consider a second dose of IVIG (2 g/kg).
   - Consider steroids after discussion with tertiary centre.

Aspirin

2. Anti-inflammatory dose: **Total 50 mg/kg/day in 4 divided doses** for 14 days after fever has been resolved for at least 48-72 hours.
   - Antiplatelet dose: **3 - 5 mg/kg/day in one daily dose (max 75mg/day)** for 6-8 weeks.

Stop ibuprofen as may antagonize antiplatelet effect of aspirin.

Hypoglycaemia can occur with high dose aspirin in cases of Reyes syndrome. In any child with sudden change in level of consciousness, check Glucose and LFT’s and treat appropriately.

Other treatments after discussion with tertiary centre:

3. **Corticosteroids**
   - **Prednisolone 2 mg/kg OD** for 14 days after normalisation of CRP.

4. **Clopidogrel**
   - Consider as add on in children with high risk for coronary artery thrombosis.
   - 1 mg/kg/day (max 75 mg/day).

5. **Low Molecular Heparin or warfarin**
   - Indicated in children with rapidly expanding coronary artery aneurysms or very large aneurysms. Target INR usually 2.0 – 3.0.
Further Management and follow up

Depends on echo findings:

- If echo normal – arrange follow up with CoW consultant at 6 – 8 weeks and refer to Dr Venu for a repeat echo PRIOR to clinic appointment.

- No coronary artery changes at any stage
  - No antiplatelet therapy after 6 weeks.
  - Discharge to GP at 6 months
  - At 1 year post diagnosis, GP to do: BP / lipid profile / BMI / smoking, diet and activity assessment.

- Cardiac Echo abnormal on presentation or in FU OPD (6 – 8 weeks)
  - Continue low dose aspirin.
  - Discuss with and refer patient to the Paediatric Cardiologist for further management.

  Email referral to Kawasaki clinic at ECH Paraskevi.Theocharis@gstt.nhs.uk.

Immunisations

- Defer all immunisations (live or otherwise) for at least 6 months after treatment with IVIG.
- Delay MMR / varicella immunisations for 11 months after administration of IVIG as may have inadequate response.
- All children should receive the inactivated seasonal flu vaccine (see below).
- NB If live vaccinations are given within 14 days before IVIG they will need repeating at least 11 months afterwards.

Varicella exposure

- Reye’s syndrome is a risk for patients taking high dose aspirin during influenza or varicella infection. Parents should be told to contact RACH if the child develops symptoms of or is exposed to either influenza or varicella.

Ibuprofen

- Ibuprofen should be avoided in children taking aspirin as it may antagonize the antiplatelet effect of aspirin.

References