KAWASAKI DISEASE: A CASE SERIES

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When the doctor hits a wall: The tragic story of Ian Bore
OBJECTIVES

- Highlight the cases of Kawasaki Disease (KD) as seen in Aga Khan Hospital 2012-2017

- Underline the diagnostic criteria for complete and incomplete KD

- Discuss evidence-based approach to management of KD
OUTLINE:

- Introduction
- Diagnostic Criteria
- Findings:
  - Demographic Data
  - Signs and Symptoms
  - Lab Findings
  - ECHO Findings
- Approach to management
**DEFINITION:**

- **Vasculitides of childhood with predilection for the coronary arteries**
  - Up to 20-25% affected if untreated

- **Highest incidence reported in Asian children**
  - Annual incidence rate of 264.8 per 100,000 population aged 0-4 years reported in 2012
DIAGNOSTIC CRITERIA:

- Fever $\geq$ 5 days + at least four of:
  - Conjunctivitis
  - Oral mucous membrane changes
  - Peripheral extremity changes
  - Polymorphous rash
  - Cervical lymphadenopathy

*without an alternative explanation*
**Kawasaki Disease**

*Classic Symptoms*

- Conjunctivitis (spares limbus)
- Rash ~ all body parts (flakes) -> desquamation
- Adenopathy ~ enlarged lymph nodes (cervical)
- Strawberry tongue ~ red + mouth & throat
- Hands & feet ~ swollen + rash
Figure 166-4 Indurative edema of the hands in mucocutaneous lymph node syndrome (Kawasaki disease). (Courtesy of Tomisaku Kawasaki, MD. From Hurwitz S: Clinical pediatric dermatology, Philadelphia, 1993, Saunders.)

Figure 166-5 Desquamation of the fingers in a patient with mucocutaneous lymph node syndrome (Kawasaki disease). (Courtesy of Tomisaku Kawasaki, MD. From Hurwitz S: Clinical pediatric dermatology, ed 2, Philadelphia, 1993, Saunders.)
患者发热至少5天且<4项主要标准

- 可诊断为KD，当冠状动脉异常被检测到

- 在没有这种情况的情况下，可以诊断为不完全的KD

- 评估ESR/CRP

- 评估其他支持实验室
Child with a fever for ≥5 days without an alternative explanation

How many clinical diagnostic criteria are met?

0 or 1 clinical criteria

- Is the child ≤6 months old with a fever ≥7 days?
  - Yes
  - CRP < 3.0 mg/dL and ESR < 40 mm/hour
  - Possible KD
    - Treat and obtain baseline echocardiogram
  - No
  - CRP ≥ 3.0 mg/dL and/or ESR ≥ 40 mm/hour
  - Suspected incomplete KD
    - Assess CRP/ESR
    - ≥3 supplemental laboratory criteria and positive echocardiogram
      - KD likely (categorized as "incomplete" since patient has only two or three clinical criteria)
      - Start treatment
  - KD unlikely; however, perform serial clinical and laboratory re-evaluation if fever persists and obtain echocardiogram if typical periungual desquamation develops even if fever has resolved

2 or 3 clinical criteria and a strong clinical suspicion of KD

- Suspected incomplete KD
  - Assess CRP/ESR
  - <3 supplemental laboratory criteria and negative echocardiogram
    - KD unlikely; however, perform serial clinical and laboratory re-evaluation if fever persists and obtain echocardiogram if typical periungual desquamation develops even if fever has resolved
  - ≥3 supplemental laboratory criteria OR positive echocardiogram
    - KD likely (categorized as "incomplete" since patient has only two or three clinical criteria)
    - Start treatment

≥4 clinical criteria

- Consistent with KD
  - Start treatment and obtain baseline echocardiogram
## DEMOGRAPHIC DATA

- 13 patients seen from Jan 2013 to Dec 2017

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>Male (n 7, 53.8%)</th>
<th>Female (n 6, 46.1%)</th>
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<tbody>
<tr>
<td>Gender</td>
<td></td>
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<tr>
<td>Nationality</td>
<td>Kenyan (n 10, 76.9%)</td>
<td>Other African nationality (n 3, 23.1%)</td>
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<tr>
<td>Age</td>
<td>Mean ( 2 yrs )</td>
<td>Range ( 11 months- 5 years)</td>
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<tr>
<td>Duration of symptoms at presentation</td>
<td>Mean ( 7.1 days)</td>
<td>Range ( 1- 10 days)</td>
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<tr>
<td>Duration of admission</td>
<td>Mean (4.6 days)</td>
<td>Range ( 2 days - 7 days)</td>
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Most patients were between 1 and 2 years of age.

Infants ≤6 months of age with KD more likely to lack clinical features of KD other than fever and at increased risk for coronary artery aneurysm.
Most Common Presenting Symptoms

- Limb swelling
- GI symptoms (vomiting, diarrhoea)
- URTI symptoms (painful throat, cough)
- Rash
Clinical Signs Present

- Fever
- Cervical Lymphadenopathy
- Polymorphous rash
- Peripheral Extremity changes
- Oral mucosa changes
- Conjunctivitis
Figure 166-1 Clinical symptoms and signs of Kawasaki disease. A summary of the clinical features from 110 cases of Kawasaki disease seen in Kaohsiung, Taiwan. LAP, lymphadenopathy in head and neck area; BCG, reactivation of bacille Calmette-Guérin inoculation site; CAD, coronary artery dilation, defined by an internal diameter >3 mm. (From Wang CL, Wu YT, Liu CA, et al: Kawasaki disease: infection, immunity and genetics, Pediatr Infect Dis J 24:998–1004, 2005.)
61% (n 8) had complete KD with fever + at least 4 out of 5 of the diagnostic criteria

Incomplete KD:
- fever for more than 5 days and 2-3 compatible clinical criteria
- Infants with fever more than 7 days without any other explanation
Lab Findings

- Hyponatremia (Na < 135)
- Negative Blood Culture
- Deranged Liver function Tests
- Sterile pyuria (WBC > 5, urine...)
- Hypoabuminemia (Albumin (<38)
- Thrombocytopenia (Platelets > 450)
- Anaemia (Hb < 11)
- Leucocytosis (WBC > 15,000)
- Elevated CRP/ ESR
12 patients had ECHOs done during admission

Only one patient was found to have abnormal findings: coronaries dilated bilaterally, the LAD has saccular dilatations measuring 5 mm.

5 patients had at least one documented repeat ECHO
Figure 166-6  Coronary angiogram demonstrating giant aneurysm of the left anterior descending coronary artery (LAD) with obstruction and giant aneurysm of the right coronary artery (RCA) with an area of severe narrowing in a 6-year-old boy. (From Newburger JW, Takahashi M, Gerber MA, et al: Diagnosis, treatment, and long-term management of Kawasaki disease, Pediatrics 114:1708-1733, 2004.)
CAA (Coronary Artery abnormalities) develop in up to 25% of untreated patients in the 2nd to 3rd wk of illness.

- Myocarditis
- Cardiogenic shock (KD shock syndrome)
- Pericarditis
- Mitral regurgitation
- Axillary, popliteal, iliac, or other arteries may also become dilated
All 13 patients received IV Immunoglobulin-12 responded to treatment.

No adverse effects were reported after treatment.

One patient did not improve and needed a second dose of IVIg and Methyl prednisone (30mg/kg IV).
IVIG RESISTANT KD

- IVIG-resistant KD occurs in approximately 15% of patients
  - defined by persistent or recrudescent fever 36 hr after completion of the initial IVIG infusion.
  - These patients are at increased risk for CAA.
- Typically, another dose of IVIG at 2 g/kg is administered
- Corticosteroids have also been used as secondary or “rescue” therapy when fever persists.

All 13 patients received aspirin but dosing varied from high (80-90 mg/kg/day) to moderate (30-50 mg/kg/day) to low dose (3 mg/kg/day)

One patient on high dose aspirin was noted to have developed symptoms consistent with aspirin induced bronchospasm; changed to low dose
The American Academy of Pediatrics (AAP) and American Heart Association (AHA) have recommended a broad range of aspirin doses (30 to 100 mg/kg/day).

Several retrospective studies have examined different aspirin doses - no differences noted in the rate of coronary artery abnormalities.

One study however reported higher odds of IVlg resistance in the low dose aspirin cohort (odds ratio: 3.2, 95% CI 1.1-9.1).
9 patients were concurrently treated with IV antibiotics. Choice of antibiotics included: ceftriaxone, ciprofloxacin

One positive blood culture:
- Staph Hemolyticus susceptible to Clindamycin and Vancomycin
ADJUVANT THERAPY:

- 2 patients received 3 doses of Albumin at 0.5-1g/kg/ dose x 3/7
  - Had serum levels of 20 g/L, 23 g/L
  - Clinically had swelling of the extremities

- Hypoalbuminemia is a useful prognostic marker

- Albumin infusion has been performed in the early stage of acute KD, especially when edema is extensive, but effects of albumin infusion on KD outcome are untested.
High index of suspicion needed
- younger patients are more likely to have incomplete KD but are also at higher risk of coronary arteriopathy

Diagnosis is clinical. Investigations serve to:
- rule out differentials
- support diagnosis especially in incomplete KD
- monitor response
Morbidity mainly secondary to coronary artery pathology

- ECHO should be done at presentation and repeated 2-3 weeks and 4-6 weeks after treatment

- Low dose aspirin just as effective as high doses, less risk of adverse effects

- Up to a third of patients may have concurrent infections