Atypical presentations of Kawasaki disease

BY:

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Case 1
An 3 year old female child, suffered from fever and conjunctival injection and was misdiagnosed as Chickenpox.

then she developed strawberry tongue, mucosal injection and periungual desquamation; diagnosed then late (after 1 month of fever) as KD.

she received 2 doses of IVIG showing marked improvement and regression of the coronary aneurysms.
Before treatment
Case 2

A 2-year-old male infant

- **Complaint**: fever and irritability and poor feeding.

- **Moter Sought medical advice at several stage:**
  - D2 of fever: Poor feeding ::: tonsillitis → home treatment ((amoxicillin – clavulanic))
  - D5 of fever: Δ Irritability & Rash ::: viral otitis media → home treatment (( stop antibiotic ))
  - D7 of fever: Ecchymosis in groins ??? and Rash , Red eyes and non significant Cervical lymphadenopathy → Admission and investigation
### HEMATOLOGY REPORT

<table>
<thead>
<tr>
<th>Test</th>
<th>Relative count</th>
<th>%</th>
<th>Absolute count</th>
<th>K/uL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>24</td>
<td>20 - 50</td>
<td>1.01</td>
<td>1.5 - 8</td>
</tr>
<tr>
<td>Segmented Band</td>
<td>22</td>
<td>35 - 80</td>
<td>0.92</td>
<td>0.9 -</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>63</td>
<td>50 - 70</td>
<td>0.88</td>
<td>0 - 1.2</td>
</tr>
<tr>
<td>Monocytes</td>
<td>8</td>
<td>0 - 10</td>
<td>0.34</td>
<td>0.4 -</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>5</td>
<td>0 - 3</td>
<td>0.21</td>
<td>0.2 -</td>
</tr>
<tr>
<td>Basophils</td>
<td>0</td>
<td>0 - 1</td>
<td>0</td>
<td>0 - 0</td>
</tr>
</tbody>
</table>

**Comment:** Moderate hypochromic microcytic anemia with RBCs anisocytosis. Mild leucopenia with absolute neutropenia and relative lymphocytosis. Moderate thrombocytopenia.

- **CRP:** 344 mg/dl (less than 8)
- **ESR:** 160 mg/hr (less than 6)

### DPC: 55

- **Pancytopenia**
- **Viral**

### URINE ANALYSIS REPORT

- **Physical Examination:**
  - Urine: {value}
  - Color: {value}

- **Chemical Examination:**
  - Acid: Absent
  - Alkaline: Absent
  - Sugar: Absent
  - Albumin: Absent
  - Nitrate: Absent
  - Specific Gravity: 1.025
  - Blood: Absent
  - Leukocyte: Absent
  - Mucus: Absent
  - Tube: Absent
  - Cast: Absent

- **Microscopic Examination:**
  - Amorphous: Absent
  - Crystals: Absent
  - Fat: Absent
  - Pigment: Absent
  - Bacteria: Absent
  - WBC: Absent
  - RBC: Absent

**Normal urinalysis**
CMV Ig G, Ig M: negative
CMV PCR in urine: negative

- Course of IV antibiotics till blood culture result appear
  Blood culture: no growth
- Fever persistent ... 2 weeks
Fever persists inspite of antibiotics,

blood and urine cultures were negative.

On examination on D13 of fever:
Peeling of perianal area
investigations

- Echocardiography.. Normal coronaries
- Albumin 2.6
- ALT 70
- Urinalysis and culture: sterile pyuria

UA

**Urine Analysis Report**

- Physical Examination:
  - Volume: Random sample
  - Color: Amber Yellow
  - Odor: Aromatic
  - Aspect: Slightly turbid
  - Deposit: Absent

- Chemical Examination:
  - Reaction: Alkaline / pH 8
  - Protein: Absent
  - Sugar: Absent
  - Acetone: Absent
  - Nitrite: Absent
  - Specific Gravity: 1.015
  - Bilirubin: Absent
  - Urobilinogen: Normal
  - Leucocytes: Absent
  - Blood: Absent
  - pH: 4.5 - 6.5
  - Neutrophil Count: Absent
  - Absent
  - Absent
  - Absent
  - Absent
  - Absent
  - Absent

- Microscopic Examination:
  - RBCs: 0 - 10
  - WBCs: 1 - 2
  - Epithelial Cells: Absent
  - Casts: Absent
  - Crystal: Absent
  - Amorphous: Phosphates
  - Ova: Absent
  - Mucus: Absent
  - Urine Artifacts: Absent
  - Fungi: Absent
  - No growth

*Urine culture is recommended*
Conflict:

May be KD

→ Fever more than 5 days
+ only 3 features:
1. Red eyes
2. Rash and perineal desquamation.
3. Extremity changes.

But Low platelet count ???
**IVIG**

After IVIG

**ESR:**
1\(^{st}\) hr: 25 mg/hr (less than 6)
2\(^{nd}\) hr: 55 mg/hr
Kawasaki Disease

- Approximately 85-90% of cases occur in children less than five years of age, with a peak incidence under the age of 2 years.
- Epidemics of Kawasaki disease primarily occur in the late Winter and Spring.
- Mucocutaneous LN syndrome
- Infantile PAN

Dr. Tomisaku Kawasaki
Acute febrile phase: Fever, redness of eyes, strawberry tongue, redness of pharyngeal mucosa, unilateral cervical lymphadenopathy, dry cracked lips, edema over the extremities, extreme irritability, perineal desquamation, myocarditis, hydrops of gall bladder, sterile pyuria, and BCG site reactivation.

Subacute phase: Resolution of clinical findings seen during the acute phase, appearance of periungual desquamation, coronary artery abnormalities, and arthritis.

Convalescent phase: Disappearance of all clinical signs, ESR and CRP return to normal, and beau lines.

Clinical manifestations of Kawasaki Disease

- Acute
  - Fever
  - Arthritis
  - Cardiovascular
    - Myocarditis
  - Skin
    - Red palms/soles
  - Lips & Conjunctiva
  - Cervical Lymphadenopathy

- Subacute
  - Aneurysms
  - Desquamation

- Convalescent
  - Nail changes

Weeks: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9

ESR, CRP & platelets
Risk factors for coronary aneurysms

1. Male sex.
2. Age < 12 months or > 5 years.
3. Fever lasting > 10 days.
4. Low serum albumin and/or Hb.
5. Clinical signs of cardiac involvement (arrhythmias, pericardial effusion).

20% of untreated patients.

Mortality rate around 2%

Early manifestation

Fever + 4 of clinical criteria
Generalized Rash
Cervical Lymphadenitis

- Unilateral
- More than 1.5 cm

Mucositis
Tongue changes

(Bilateral - Painless - Non purulent)

Conjunctivitis

(Bilateral - Painless - Non purulent)
BCG site reactivation

Erythema and edema of extremities
Perianal desquamation

This is not all
Other Findings

- Extreme irritability, severe abdominal pain, diarrhea and vomiting are common.

- Urethritis with sterile pyuria (70% of cases)

- Hepatic dysfunction and jaundice (40% of cases)

- Arthritis or arthralgia (35%)

Gall bladder hydrops
 **Pericardial effusion or arrhythmias (20%)**

 **Gallbladder hydrops (<10%)**

 **Carditis with HF (< 5%).** This can occur at any time in the first 3 weeks, and usually resolves by 6 to 8 weeks.

 **Other arterial aneurysms (e.g. iliac, femoral, renal, axillary) may occur**
Atypical Kawasaki disease presenting as a retropharyngeal abscess

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Aseptic meningitis (25%)
Incomplete Kawasaki Disease

Fever and less than 4 principal clinical features of KD
Atypical Kawasaki Disease

clinical manifestations suggestive of KD along with some unusual features
E.g. seizures, stroke, nephritis, and acute hepatitis.
infants may present more commonly with atypical features and have increased predilection for CAD.
Supplementary Laboratory Information

- Albumin < 3 mg/L
- Anemia for age
- White cell count > 15,000
- Platelets after 7 days > 450,000
- Elevated ALT
- Urine White Cells > 10 per HPF

Positive Echocardiogram (any ONE of the following)

- Z score of RCA or LAD > 2.5
- **Japanese MOH criteria, Any 3 suggestive features:**
  1. Perivascular brightness
  2. Lack of tapering of coronary arteries
  3. Z score > 2.0
  4. Pericardial effusion
  5. Mitral regurgitation
  6. Impaired LV function
Peeling

Baue’s lines

(transverse grooves in nailbeds)
Differential Diagnosis

- Viral infections e.g. Measles, Adenovirus,...
- Scarlet fever
- Staphylococcal scalded skin syndrome
- Toxic shock syndrome
- Polyarteritis nodosa
- Bacterial cervical lymphadenitis
- Drug hypersensitivity reactions
- Stevens-Johnson syndrome
- Leptospirosis
- Mercury hypersensitivity
**Differential Diagnosis**

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<tbody>
<tr>
<td>Age group</td>
<td>Mostly below 5</td>
<td>All age groups</td>
<td>Mostly between 3-13 years</td>
<td>Most common in preschool children</td>
</tr>
<tr>
<td>Etiology/Causative organism</td>
<td>Unknown</td>
<td>Drugs (sulphonamides, anticonvulsants), Mycoplasma pneumonia</td>
<td>Streptococcus pyogenes</td>
<td>Measles virus</td>
</tr>
<tr>
<td>Nature of rash</td>
<td>Polymorphous, never vesicular</td>
<td>Atypical targets or purpuric macules, vesicles, tend to coalesce</td>
<td>Punctate erythema, “sunburn with goose pimples” or “sandpaper”</td>
<td>Macular, dull red papular, tend to coalesce</td>
</tr>
<tr>
<td>Distribution of rash</td>
<td>Begins on the trunk, spreads to extremities</td>
<td>Starts from the face and chest, spreads to whole body</td>
<td>First appears on upper trunk, generalizes within a few hours or over 3-4 days</td>
<td>Starts from the forehead and behind the ears, spreads downwards</td>
</tr>
<tr>
<td>Time of onset of rash</td>
<td>During first week of illness</td>
<td>7-10 days after drug exposure (range 5-28 days)</td>
<td>Within 24-48 hours after onset of symptoms</td>
<td>Develops on fourth day of fever</td>
</tr>
<tr>
<td>Other characteristics of rash</td>
<td>Non pruritic rash</td>
<td>Pruritis and cutaneous pain</td>
<td>Relative pallor around the mouth, desquamation after 7-10 days</td>
<td>Leaves fine desquamation of skin</td>
</tr>
</tbody>
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**Treatment**

Treatment aims to **rapidly “switch off” the inflammatory process** and minimize the risk of coronary artery inflammation / aneurysm formation.

- Specific therapy must be given **early** to be most effective, so it should be given when the diagnosis is **strongly suspected**.

- Intravenous immunoglobulin. If given with aspirin within 10 days of the onset of fever, IVIG relieves symptoms and reduces the risk of coronary aneurysm.
- The dose is **2 grams per kg, over 10 to 12 hours** - Evidence level A.
- In about 10% of children, the fever may not respond to the first dose of IVIG within 48 to 72 hours, or may recur. In this situation, a second dose of IVIG may be given.
- Be aware of the possibility of isoimmune hemolysis, particularly in blood group A patients.
- IVIG should still be given later than 10 days if there are signs of continuing inflammation (fever, high ESR) or evolving coronary artery disease.
Aspirin

- **Dose**: 30 - 50 mg/kg/day in 4 divided doses in the 1st week of the illness.
  
  There is no evidence that the dose of salicylate effects aneurysm formation. Level A evidence.

- Reduce the dose to 3 to 5 mg/kg/day (once daily) once the fever is under control.
  
  **If the coronary arteries are normal at 6 weeks, stop aspirin.**

- If there are coronary artery aneurysms, continue low-dose aspirin with or without warfarin or other antiplatelet medication.

Reye syndrome

Several children with KD have developed Reye syndrome while on high dose **Aspirin**.

It is important therefore to change to low dose Aspirin as soon as possible.

- **Warn the parents to discontinue Aspirin if the child develops influenza or chickenpox.**
Refractory Disease & High Risk Patients

- **Methylprednisolone** pulsed 30mg/kg/day once daily - 3 days
  If the child does not improve after 2x doses of IVIG, or in selected circumstances where the child is very unwell.

- Other treatment options for refractory Kawasaki Disease include a weaning course of oral prednisolone – starting at 2mg/kg/day and Infliximab (TNF alpha blocker) 5mg/kg as a single dose.

Subsequent Immunization

- Measles and other live virus vaccines (i.e. varicella) should be deferred for **11 months** following IVIG treatment.

- Alternatively, a child at high risk of measles could be vaccinated, then re-vaccinated at least 11months after the administration of IVIG.

- Other routine immunizations should not be interrupted.

- **Annual influenza vaccination** is recommended for children with coronary aneurysms on aspirin.
References

- Newburger J et al. Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Statement for Health Professionals From the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Pediatrics 2004;114;1708-1733


- AAP Red Book 2012 http://aapredbook.aappublications.org/content/1/SEC131/SEC205.body


THANK YOU
FOR YOUR ATTENTION 😊