Even Incomplete Kawasaki Can Completely Break a Heart

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Key Learning Objectives

- Infants are more likely than other age groups to present with atypical features of Kawasaki disease, resulting in delayed diagnosis.
- It is important to have a high clinical suspicion in infants with fever of unknown origin and consider KD early to initiate treatment and prevent coronary artery pathology.
- Respiratory viruses, including enterovirus, are often found in children with KD. The presence of a positive viral study does not rule out the possibility of Kawasaki disease.

Introduction

- There is no consensus definition for fever of unknown origin (FUO) in pediatrics, though it becomes a concern in children with daily fevers (>38.3C) for >8 days without an identified cause after outpatient/inpatient workup.[2]
- Prior to concluding a patient has a FUO, the following should be performed: a detailed history and physical, complete blood count, chemistry, liver function tests, chest x-ray, urinalysis, sedimentation rate, C-reactive protein, urine and blood cultures.
- Three general categories of illness account for the majority of FUO cases: infection, malignancy, and systemic rheumatologic diseases.[2]

Case Presentation

- A 5 month old boy presented with 15 days of fevers.
- Associated symptoms included intermittent cough, rhinorrhea, and diarrhea.
- He was treated for an ear infection with antibiotics 5 days into the course.
- The patient subsequently developed a transient erythematous rash on his abdomen, back, and lower extremities thought to be due to the antibiotics. The rash resolved prior to admission.
- His fevers persisted despite antibiotics, prompting presentation to the ED.
- He had no oral lesions or erythematous tongue, lymphadenopathy, extremity changes, or conjunctivitis.
- In the emergency room, initial labs revealed pancytopenia and he was admitted for malignancy workup.
- On exam, the infant was very well-appearing with normal vitals other than persistently elevated temperatures.

Workup

Cr: 0.24 mg/dL
Albumin: 2.8 g/dL
AST: 93 U/L
ALT: 72 U/L
ALP: 152 U/L
Tbili: 0.7 mg/dL
INR: 1
Ferritin: 322 ng/mL
Triglycerides: 429 mg/dl

WBC: 6.3 /dL
Hgb: 6.6 g/dL
Plt: 37 /dL
ANC: 1 /dL
ALC: 4.1 /dL
CRP: 54.3 mg/L
ESR: 44 mm/h
DAT: negative

Urinalysis: 19 WBC, 2 RBC, neg nitrite, negative culture
Resp viral panel: rhino/enterovirus+
Blood Enterovirus PCR +

Pertinent Negatives:

EBV & CMV PCR
HIV Ab/Ag
Adenovirus, Parvovirus PCR
Histoplasma Urine Ag
Quantiferon gold
Toxoplasma serologies
Flow cytometry and peripheral smear: pancytopenia with no blasts identified by morphologic assessment or flow

Coronary Artery Aneurysms

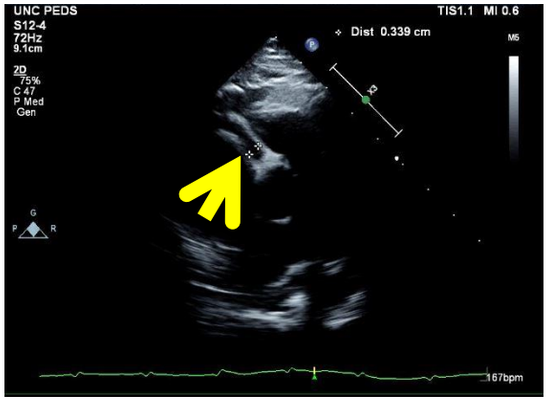

Figure 1: Transthoracic echocardiogram showed proximal coronary artery dilatation with the right coronary artery (yellow arrow) slightly larger than the left circumflex or left anterior descending arteries (not pictured). Distal coronary arteries were not well imaged due to patient non-cooperation.

Table 1: **Coronary artery aneurysm (CAA) z-scores**

Normal lumen diameter is represented by a z-score less than 2. Small aneurysms are represented by z-scores between 2.5 to 5, medium aneurysms 5-10, and giant aneurysms with z-scores >10. As shown in the table, our patient had both small and medium-sized aneurysms (source: Sundel 2019).

Table 1: Our Patient's CAA Z-scores

Artery	Z-score
Left main coronary	2.33
Left anterior descending	4.38
Circumflex	2.01
Proximal right coronary	5.20

Evaluation of Incomplete Kawasaki Disease

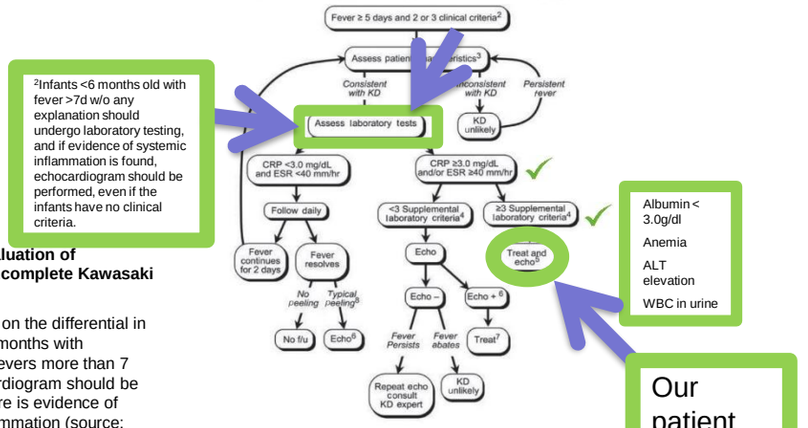

Figure 2: Evaluation of Suspected Incomplete Kawasaki Disease

KD should be on the differential in all infants <6 months with unexplained fevers more than 7 days. Echocardiogram should be pursued if there is evidence of systemic inflammation (source:

Discussion

- Kawasaki disease (KD) is a systemic vasculitis most commonly seen in the setting of conjunctivitis, mucositis, rash, extremity changes, and lymphadenopathy; however, not all children, particularly infants, present meeting the classical diagnostic criteria.[5]
- Many experts advise an echocardiogram be done in infants <6 months if there is evidence of systemic inflammation, even without clinical criteria **(Figure 2)**.
- Because of his age, our patient met incomplete criteria with elevated inflammatory markers, elevated ALT, sterile pyuria, and hypoalbuminemia **(Figure 2).**[5]
- Early diagnosis is important so treatment with IVIG can be initiated to prevent coronary artery aneurysms, a hallmark of the disease.
- Severity of coronary artery dilatation is measured by z-scores, which represent the number of standard deviations from the population mean coronary diameter adjusted for sex and body surface area **(Table 1).**
- Higher z-scores are associated with **delay in IVIG, age < 1 year** or >9 years, **male sex**, **fever > 14 days**, **hematocrit<35%,** WBC>12, and Na<135.[3]
- Diagnosis was delayed in our patient because of the atypical presentation, but also because of his blood cell line abnormalities, which raised significant concern for leukemia.

Kawasaki Disease + Viruses

- The etiology of Kawasaki disease is unknown, though it has been proposed that a preceding infection may trigger vasculitis in genetically susceptible individuals.[1]
- Multiple studies have found that children presenting with KD were more likely to test positive for common viruses compared to matched controls without KD. One study showed a higher incidence of KD in children with previous enterovirus infection.[4]
- Because of this association, a positive viral PCR cannot rule out the co-occurrence of Kawasaki disease.
- Our patient had a positive blood enterovirus PCR – this may have been the trigger for him developing KD.
- Disseminated enterovirus may also explain why our patient developed thrombocytopenia and leukopenia rather than thrombocytosis and leukocytosis, which are more commonly seen in KD.

References & Acknowledgments

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Thank you to Vince Gonzalez, MD for expertise and assistance in understanding the echocardiogram images!