Case Studies on COVID-19 in Children: Complication & MIS-C
Meet our Panelists

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Case Studies on COVID-19 in Children: Complications & MIS-C
Multisystem Inflammatory Syndrome in Children associated with COVID-19: An Update for Pediatricians

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Conflicts of Interests

• No conflicts of interest to declare

• All treatments for MIS-C are considered off label or under EUA
Learning Objectives

1. Describe the common clinical and laboratory findings among multisystem inflammatory syndrome in children associated with COVID-19 (MIS-C)

2. Discuss the proposed management strategies developed to identify and manage patients with MIS-C
Case Study

4-year-old female with conjunctival injection, vomiting, diarrhea & abdominal pain; altered mental status, lacy macular rash on extremities. Fever noted on day of admission. Shock Index: 2.3

CRP 13.7 mg/dl  ESR: 10 mm/hr
Na: 128 mg/dl  Albumin: 2.8 g/dl
ALC 882 cells/ul  Platelets: 154
CT abdomen/pelvis: Mesenteric adenitis.
CXR: normal heart size, perihilar infiltrates

Admitted with presumed diagnosis of acute viral gastroenteritis
Case Study

Received 20ml/kg NS bolus in the ED. Additional 20ml/kg bolus after admission.
Repeat CXR: pulmonary edema

Developed ↑ HR & RR; gallop rhythm & hypoxemia. Liver edge 5cm below the right ICM.
Transferred to PICU.

BNP 113, 990 pg/ml  Troponin: 212 (Ref Range: 0-14)
Shortening fracture declined from 33% to 5% despite vasoactive support.

ECMO team consulted. VA-ECMO initiated.
Coronavirus

• Enveloped +RNA viruses
• Genera: α, β, δ and γ
  – SARS-CoV-2 belongs to the Betacoronaviruses

Symptomatology
• Upper respiratory tract infection
• Lower RTI in immunocompromised patients and extremes of age
• SARS-CoV and MERS-CoV can cause GI symptoms
What is MIS-C?

• 1st reports from the UK: children with a post-inflammatory syndrome during COVID epidemic

• Subsequently in the USA (NY), France & Italy → the rest of the world

• ACUTE febrile illness with multisystem involvement

• Overlapping features with Kawasaki disease, Macrophage activation syndrome (MAS) and toxic shock syndrome
• Male 60% Female 40%
• Median Age (IQR): 9 (4 – 12 yrs)

Racial/Ethnic Predominance
• Hispanic/Latino: 29.3%
• African American, Non-Hispanic: 31.8%
• White, Non-Hispanic: 30.5%

• Incidence: 1 in 4000 children/adolescent after COVID-19

• Severity of acute illness is not predictive of developing MIS-C
## Clinical Presentations

<table>
<thead>
<tr>
<th>Systems / Symptoms</th>
<th>CDC Data (n=570)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fever:</strong> Subjective or Objective</td>
<td>100%</td>
</tr>
<tr>
<td><strong>GI:</strong> nausea/vomiting, diarrhea, abdominal pain; ileitis, colitis or appendicitis on imaging; elevated transaminases</td>
<td>91%</td>
</tr>
<tr>
<td><strong>Cardiovascular:</strong> shock, chest pain, acute CHF</td>
<td>87%</td>
</tr>
<tr>
<td>*included BNP, Trop-T</td>
<td></td>
</tr>
<tr>
<td>• LV dysfunction or Myocarditis</td>
<td>30 - 55%</td>
</tr>
<tr>
<td><strong>Pulmonary:</strong> cough, pulmonary edema or infiltrates on imaging</td>
<td>63%</td>
</tr>
<tr>
<td><strong>Derm/Mucocutaneous:</strong> conjunctival injection, mucositis, non-vesicular rash, palmar/plantar erythema or edema</td>
<td>71%</td>
</tr>
<tr>
<td><strong>Neurologic:</strong> Headache, confusion, focal neuro deficits, meningismus</td>
<td>38%</td>
</tr>
<tr>
<td><strong>Renal:</strong> Acute kidney injury</td>
<td>18%</td>
</tr>
<tr>
<td><strong>Cervical Lymphadenopathy:</strong> Unilateral, &gt;1.5cm</td>
<td>13%</td>
</tr>
</tbody>
</table>

Systems involved or symptoms included abnormal laboratory and imaging findings.
• Many common symptoms that overlap with common illnesses

• Think more severe or prolonged than expected for acute viral illness
## Laboratory Findings

<table>
<thead>
<tr>
<th>Lab</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/dl)</td>
<td>21.9 (15 – 30)</td>
</tr>
<tr>
<td>• CRP &gt; 5 mg/dl</td>
<td>99%</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>61.5 (43 – 77.5)</td>
</tr>
<tr>
<td>Procalcitonin (ng/dl)</td>
<td>6.2 (2.2 – 19.7)</td>
</tr>
<tr>
<td>Lymphopenia (%)</td>
<td>66%</td>
</tr>
<tr>
<td>ALC &lt; 1000 or &lt; 4500 cells/ul if age &lt; 8 months</td>
<td></td>
</tr>
<tr>
<td>Ferritin (mg/dl)</td>
<td>522 (305 – 820)</td>
</tr>
<tr>
<td>D-Dimer (mg/L)</td>
<td>2.4 (1.2 – 3.7)</td>
</tr>
<tr>
<td>Elevated NT-Pro-BNP</td>
<td>90%</td>
</tr>
<tr>
<td>Elevated Troponin</td>
<td>71%</td>
</tr>
</tbody>
</table>

Values displayed as either Median (IQR) or %
What is NOT consistent with MIS-C?

Consistent with MIS-C
- Complete or incomplete Kawasaki Disease
- Fever + GI symptoms + other system involvement
  - URI symptoms are much less commonly reported
  - Neurologic (Headache) or Cardiovascular (poor perfusion, shock)
- Fever + GI symptoms that are either:
  - Persisting longer than expected for a viral AGE
  - Severity is out of proportion as to that expected for a viral AGE
  - Can mimic appendicitis

NOT Consistent with MIS-C
- Chronic or relapsing symptoms
  - Unrelated or possibly “Long Haul COVID”
- Symptoms without fever
- Normal inflammatory markers
## Diagnostic Testing

<table>
<thead>
<tr>
<th>Serology</th>
<th>PCR</th>
<th># (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>−</td>
<td>+</td>
<td>10 (1.8%)</td>
</tr>
<tr>
<td>Unknown or Not Done</td>
<td>+</td>
<td>137 (24%)</td>
</tr>
<tr>
<td>+</td>
<td>−</td>
<td>263 (46.1%)</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>155 (27.2%)</td>
</tr>
<tr>
<td>Not Done</td>
<td>Not Done</td>
<td>5 (0.9%)</td>
</tr>
</tbody>
</table>
Akron Children’s Hospital – Interim Guidance for Management of Children with MIS-C
Does the patient meet ALL of the following?
1. Age ≤ 21 years
2. Fever ≥ 24 hours (objective or subjective)
3. Epidemiologic link to SARS-CoV-2 (not required)
4. At least 2 suggestive clinical features:
   1. GI symptoms
   2. Cardiovascular
   3. Mucocutaneous
   4. Non-vesicular rash
   5. Edema/erythema of the hands or feet
   6. Cervical Lymphadenopathy
   7. Neurologic

Initial Evaluation / Management for MIS-C

- History, exam, Vital signs with BP
- O₂ to keep sats > 90%
- PIV, fluid resuscitation – limit boluses to 5-10 ml/kg.
  - Check for rales, hepatomegaly & gallop after each bolus.
  - Use measuring tape to measure liver span & mark liver edge with a pen
- Exclude alternative diagnoses

Obtain MIS-C workup Priority 1 a
Abbreviated workup if suspicion for MIS-C low could include CMP, CBCD & CRP

- Well-appearing
- Vital signs normal for age

- Ill-appearing
- Hypotension, poor perfusion
- Signs of sepsis or shock

Obtain MIS-C workup Priority 1 & 2 a
- Give Ceftriaxone & Vancomycin after cultures obtained

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American Academy of Pediatrics
Dedicated to the health of all children
MIS-C interim guidance algorithm v 2.5 – 1/11/2021
Are both Criteria met?
1. CRP ≥ 5 mg/dl
2. At least 1 additional laboratory feature
   a. ALC < 1000/µL if older than 8 months (< 4500 if age < 8 mo)
   b. Platelet count < 150,000/µL
   c. Na < 135 mmol/L
   d. Neutrophilia
   e. Albumin < 3 g/dl

Lab results should not delay transfer to PICU if clinically indicated

• Obtain MIS-C workup Priority 1
  • Obtain MIS-C workup Priority 1 & 2
  • Give Ceftriaxone & Vancomycin after cultures obtained

No

• MIS-C less likely
• Re-evaluate in 1-2 days if symptoms do not improve or if new symptoms develop

MIS-C interim guidance algorithm v 2.5 – 1/11/2021
Are both Criteria met?
1. CRP ≥ 5 mg/dl
2. At least 1 additional laboratory feature
   a. ALC < 1000/uL if older than 8 months (< 4500 if age < 8 mo)
   b. Platelet count < 150,000/µL
   c. Na < 135 mmol/L
   d. Neutrophilia
   e. Albumin < 3 g/dl

Lab results should not delay transfer to PICU if clinically indicated

Are any of the following present?
• Shock/hypotension
• Cardiac dysrhythmias
• ↑ Troponin T
• Need for invasive or non-invasive respiratory support
• Concern for rapid progression

Severe Disease
• Admit to PICU

Mild or “Non-Severe” Disease
• Admit to Floor under Hospital medicine service
Inpatient management

• **Mild or “Non-Severe” disease:**
  – IVIG 2g/kg (max 100g) over 12-18 hours
  – Methylprednisolone 2mg/kg/day (60mg/day max) IV Q8H
  – PO steroids weaned over 2-3 weeks
  – Low dose Aspirin daily

• **Severe Disease:** IVIG as above
  – Methylprednisolone 30mg/kg/dose IV daily (max 1 gram)
  – PO Steroids weaned over 6-8 weeks with Endocrinology referral
  – If severe LV dysfunction present or need for vasoactive medications → Anakinra IV q6h (max 100mg/dose)
  – Lovenox while inpatient, then transition to aspirin before discharge
What should I do if I suspect a patient of having MIS-C?

• Refer to the ED for evaluation

• Consider CRP, CBC with diff & CMP for screening labs in a stable patient who has good follow up (order STAT if possible)

• Patients are at risk for rapid decompensation

• No risk factors identified for who will develop severe disease
Important Tips for PCPs to monitor for after discharge

• In the 2 weeks after discharge
  — **FEVER**
  — Recurrence of presenting symptoms
    • GI symptoms
    • Rash, conjunctival injection

• Instruct families to call managing specialist (ID, Cardiology, etc...). If there is concerns for shock, send to ED or call 911
ACH MIS-C Committee

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- **Emergency Medicine**
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  - Emily Scott, MD

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References


The heart after MIS-C: A cardiologist’s perspective

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Disclosure

- No conflicts of interest to disclose
- No off-label products will be discussed
History

• 11 y.o. male with a history of acute lymphoblastic leukemia (diagnosed age 3, off treatment 3 years later, cumulative doxorubicin dose 75 mg/m2, no cardiac complications during treatment), admitted January 2021 with MIS-C.
• HPI: 4 days of daily fevers, emesis, abdominal pain and diarrhea. No known exposure to COVID19 (family “very careful”)
• Hospital Course:
  – ED: afebrile but tachycardic and with rash, periorbital edema and conjunctival injection; hemodynamically stable on admission.
  – Troponin was elevated and echocardiogram showed LV systolic dysfunction (EF ~ 40%), so he was transferred to PICU and started on enalapril. Received solumedrol and IVIg and improved within 1-2 days.
  – He was discharged home on HD #4 on a steroid wean, aspirin and enalapril
Questions

• The patient is very active and is feeling well enough that he would like to get back to playing basketball with his friends, and perhaps play baseball in the spring. Is it safe to clear him for sports?
• At discharge, his echocardiogram and troponin were normal but his BNP remained elevated. Can we assume that his heart has “normalized”?
• What do we know about the long-term cardiac risks in children who have had MIS-C? Does the patient’s history of a hematologic malignancy affect the risk calculation, and, if so, how? What other factors may influence the long-term cardiac health for a young patient?
Why worry about inflammatory cardiac disease in a cancer survivor?

• Cardiac disease after cancer treatment is the most common non-malignancy related cause of mortality in this population.

• Commonly linked to:
  – Chemotherapy (especially anthracyclines)
  – Radiation to the chest wall

• Anthracyclines such as doxorubicin are still used in the treatment of most childhood cancers
  – Cardiotoxicity can manifest as either asymptomatic cardiac dysfunction or clinical heart failure.
  – While the risk of cardiotoxicity is dose dependent, it can occur at any dose.
Why I don’t like the term “sports clearance”

“Clearance” implies:

• A preseason ritual where you check some boxes
• Finite number of easily identifiable problems
• All you have to do is order the right tests
• Rule out the problem now, and you never have to worry about it again
• Other competing risks to the patient can be safely ignored
Sports don’t kill people. Disease kills people.
Which of these causes of sudden cardiac death might happen to a patient who has had MIS-C?

**FIGURE 5**
Causes of sudden cardiac death (SCD) among children and young adults 1 to 54 years of age, stratified by age groups.

*El-Assaad I Pediatrics. 2017;140(6):e20171438*
We know what happens to the heart acutely in MIS-C.

- Abnormal cardiac enzymes (>80%)
- Myocarditis (>50%)
  - LV dysfunction
  - Pericardial effusion
  - Mitral valve regurgitation
- Compensated shock (~50%)
  - responsive to fluids, inotropes
- Coronary artery abnormalities (10-20%)
  - dilatation
  - aneurysms
- Rhythm and conduction abnormalities
  - PVCs, VT
  - transient heart block
- Decompensated shock (<10%)
Myocardial/ coronary artery involvement: common in acute setting...

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MIS-C (n = 539)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe organ involvement³</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>432 (80.1)</td>
</tr>
<tr>
<td>Infiltrates on chest radiography</td>
<td>197 (36.5)</td>
</tr>
<tr>
<td>Lower respiratory infection</td>
<td>94 (17.4)</td>
</tr>
<tr>
<td>Asthma exacerbation</td>
<td>301 (55.8)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>170 (31.5)</td>
</tr>
<tr>
<td>Pediatric ARDS</td>
<td>57 (10.6)</td>
</tr>
<tr>
<td>Cardiovascular³</td>
<td>359 (66.7)</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>125 (24.9)</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
</tr>
<tr>
<td>&lt;35%</td>
<td>38 (7.6)</td>
</tr>
<tr>
<td>35%-&lt;45%</td>
<td>39 (7.8)</td>
</tr>
<tr>
<td>45%-&lt;55%</td>
<td>95 (18.9)</td>
</tr>
<tr>
<td>Coronary artery aneurysm</td>
<td>57 (13.4)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>46 (8.5)</td>
</tr>
<tr>
<td>Hematologic</td>
<td>256 (47.5)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>66 (12.2)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>50 (9.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MIS-C (n = 539)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical care interventions</td>
<td></td>
</tr>
<tr>
<td>Any respiratory support</td>
<td>303 (56.2)</td>
</tr>
<tr>
<td>Noninvasive positive pressure ventilation</td>
<td>192 (35.6)</td>
</tr>
<tr>
<td>Invasive mechanical ventilation</td>
<td>95 (17.6)</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>244 (45.3)</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation</td>
<td>18 (3.3)</td>
</tr>
</tbody>
</table>

| Clinical outcomes                    |                 |
| Length of admission, d (n = 1083)²   | 523             |
| No.                                  |                 |
| Median (IQR)                         | 7.0 (5.0 to 11.0)|
| Intensive care unit admission³       | 398 (73.8)      |
| Length of ICU stay, d (n = 639)      | 388             |
| No.                                  |                 |
| Median (IQR)                         | 4.0 (2.0 to 7.0)|
| Died                                 | 10 (1.9)        |

...but usually resolves....

Figure 4. Cardiovascular Outcomes of Patients With MIS-Ca

A Resolution of decreased left ventricular ejection fraction

B Resolution of coronary artery aneurysms

Cardiac Outcomes after MIS-C: NYC Cohort, 6 month longitudinal follow up

• 45 children admitted w/ MIS-C:
  – 76% ICU
  – 64% required inotropes
  – 44% had moderate-severe echocardiographic abnormalities at presentation

• On follow up:
  – 1 to 4 weeks: 18% had mild echocardiographic findings
  – 4 to 9 months, only 1 child had persistent mild dysfunction.

Long term cardiac consequences of MIS-C: 2 Helpful Models

**Myocarditis**

- Quiescent regulatory immune elements (myocytes and dendritic cells)
- Infectious or Noninfectious Inflammatory Trigger (frequently viruses)
- Acute myocarditis
  - Symptoms: Chest pain, Heart failure, Tachyarrhythmias, Acute cardiomyopathy
  - Pathogenesis:
    - Effector immune response
    - Antigen bearing cells
    - Auto-antigen specific T cells, macrophages and antibodies
- Regulatory elements restore tolerance:
  - Asymptomatic or mildly decreased cardiac reserve function
  - Possible myocyte hypertrophy or mild scarring
- Effector immune elements dominate:
  - Chronic recurrent chest pain
  - Progression to cardiomyopathy
  - Persistent cardiac inflammation with or without viral presence

**Kawasaki Disease**

- Natural History of Coronary Artery Architecture in Kawasaki Disease

Outcomes after acute myocarditis: recovery, cardiomyopathy or sudden death
Coronary artery aneurysms (CAA) may pose both short- and long-term risk to patients who have recovered from the acute illness.

What we know from Kawasaki Disease:

- For patients with CAA, highest risk of MI is within 6 weeks of hospital discharge
- Low annual incidence but high lifetime prevalence of coronary artery disease.

Pathophysiology of KD: Necrotizing arteritis. Is MIS-C the same thing?

## Long Term Outcomes from Kawasaki Disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population*</th>
<th>Duration of follow-up (years)</th>
<th>Comments</th>
<th>% giant aneurysms</th>
<th>% aneurysm pseudo-normalised</th>
<th>Thrombosis or stenosis (%)</th>
<th>Myocardial Infarction (%)</th>
<th>Mortality† (%)</th>
<th>CABG‡ (%)</th>
<th>PCI§ (%)</th>
<th>Cardiac event-free 30-year rate (%)</th>
<th>30–35-year survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suzuki15</td>
<td>150 Japanese patients</td>
<td>&gt;8 years</td>
<td>All sizes</td>
<td>Not reported</td>
<td>44.60</td>
<td>24.60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kato3</td>
<td>146 Japanese patients, single centre</td>
<td>Mean 13.6</td>
<td>All sizes</td>
<td>17.80</td>
<td>54.80</td>
<td>19.20</td>
<td>7.5 total, 46 GCA</td>
<td>3.4</td>
<td>4.8</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Samada11</td>
<td>48 Japanese patients, multicentre</td>
<td>Median 25.2</td>
<td>GCA† only</td>
<td>100</td>
<td>None</td>
<td>41.60</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suda6</td>
<td>76 Japanese patients, single centre</td>
<td>Median 19</td>
<td>GCA only</td>
<td>100</td>
<td>None</td>
<td>57.70</td>
<td>16</td>
<td>10.5</td>
<td>17.1</td>
<td>28.9</td>
<td></td>
<td>88</td>
</tr>
<tr>
<td>McNeel12</td>
<td>38 Canadian patients, multicentre using the Quebec KD registry</td>
<td>Median 9.26</td>
<td>GCA only</td>
<td>100</td>
<td>None</td>
<td>64.50</td>
<td>2.60</td>
<td>15.6</td>
<td>8.8</td>
<td>10.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holve 2013</td>
<td>110 American patients, multicentre using Kaiser Permanente Northern CA database</td>
<td>Mean 14.9</td>
<td>All sizes</td>
<td>Not reported</td>
<td>77.20</td>
<td>0.55</td>
<td>0.18</td>
<td>0.18</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsuda29</td>
<td>245 Japanese patients, multicentre</td>
<td>Median 20</td>
<td>GCA only</td>
<td>100</td>
<td>None</td>
<td>23</td>
<td>6</td>
<td>37</td>
<td>4</td>
<td>36</td>
<td></td>
<td>90</td>
</tr>
<tr>
<td>Lin27</td>
<td>196 Taiwanese patients, single-centre</td>
<td>Median 6.67</td>
<td>All sizes</td>
<td>13.80</td>
<td>68.60</td>
<td>11.70</td>
<td>7.1 total, 26 GCA</td>
<td>2.0</td>
<td></td>
<td></td>
<td></td>
<td>98 total, 69</td>
</tr>
</tbody>
</table>

ACC/AHA Guidelines, 2015

Recommendations

1. Before returning to competitive sports, athletes who initially present with an acute clinical syndrome consistent with myocarditis should undergo a resting echocardiogram, 24-hour Holter monitoring, and an exercise ECG no less than 3 to 6 months after the initial illness (Class I; Level of Evidence C).

2. It is reasonable that athletes resume training and competition if all of the following criteria are met (Class IIa; Level of Evidence C):
   a. Ventricular systolic function has returned to the normal range.
   b. Serum markers of myocardial injury, inflammation, and heart failure have normalized.
   c. Clinically relevant arrhythmias such as frequent or complex repetitive forms of ventricular or supraventricular ectopic activity are absent on Holter monitor and graded exercise ECGs.

   At present, it is unresolved whether resolution of myocarditis-related LGE should be required to permit return to competitive sports.

3. Athletes with probable or definite myocarditis should not participate in competitive sports while active inflammation is present. This recommendation is independent of age, gender, and LV function (Class III; Level of Evidence C).
Recommendations

1. Patients with 2 or more coronary aneurysms should continue antiplatelet therapy and possibly anticoagulant therapy. It is also reasonable for annual stress tests to be performed and activity to be guided by results, similar to adults with ASCAD (Class I; Level of Evidence C).

2. Patients with myocardial infarction or revascularization should follow the guidance for adults with ASCAD (Class I; Level of Evidence A).

3. Collision sports should be avoided in patients undergoing antiplatelet therapy (Class I; Level of Evidence C).

4. In the absence of exercise-induced ischemia or arrhythmias, it is reasonable for patients to participate in low- to moderate-intensity static and dynamic competitive sports. Patients with persistent small to medium-sized aneurysms in 2 or more coronary arteries should continue antiplatelet therapy and undergo ongoing surveillance (Class IIa; Level of Evidence C).

5. Patients with no coronary aneurysms during the convalescent phase and with no exercise-induced ischemia or arrhythmias may be considered for participation in all sports starting 8 weeks after the illness has resolved (Class IIIb; Level of Evidence C).

6. Patients with transient coronary aneurysms and with no exercise-induced ischemia or arrhythmias may be considered for participation in all sports 8 weeks after illness resolution. Risk reassessment is recommended at 3- to 5-year intervals or according to current guidelines (Class IIIb; Level of Evidence C).
The heart after MIS-C: Bottom line

**Acute Setting**

- MIS-C Patients are **sick**, and some degree of hemodynamic instability should be anticipated.
- Cardiovascular complications are the norm, most commonly:
  - Myocarditis
  - Coronary artery dilatation or aneurysm
  - Shock (compensated or decompensated)
- Treatment works.

**Long Term**

- Anticipate around 3 months of restriction from competitive sports.
  - Patients will likely be deconditioned when they return ➔ take it slow.
- With rare exceptions, cardiovascular complications resolve within a few months.
  - We still don’t know who will be a rare exception.
MIS-C Treatment and Pathology

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Disclosure

• No conflicts on interest to disclose
• No off-label products will be discussed
Case Presentation

- 4 y.o. black male had 4 days of fever, abdominal pain and watery non-bloody diarrhea
- Tmax was 105F and appeared to resolved after 2 days
- Not eating very much
- The PCP sent labs on the day PTA
  - ESR 103
  - CRP 27.3
  - RFP found AKI Cr 1.2
  - COVID PCR negative
- After labs resulted the PCP sent the patient to the ER
Case Presentation

- In the ED:
  - Vitals: Afebrile, HR 122, RR 38, BP 54/24, sat 100% on RA
  - Given 3, 20cc/kg NS boluses, BP up to 70’s/40’s, HR 122
  - Worsening abdominal pain, diffusely tender with a tense and hard abdomen
- Ceftriaxone and vancomycin given
- Chest x-ray showed borderline cardiomegaly with diffuse b/l reticular interstitial opacities
- KUB – normal
- Abd u/s – free fluid with gall bladder thickening

- Labs:
  - CBC: 37.4>8.6/25.1<236
  - BMP: 130/9.6/94/19/64/2.99<69
  - PT/INR 13.6/1.2
  - PTT 27
  - ALT/AST 24/50
  - CRP 39.92
  - Ferritin 614
  - Fibrinogen 591
  - D dimer 2334
  - Troponin 2.53
  - BNP 2104
Case Presentation

• ROS positive for conjunctival injection, fever, anorexia, malaise, diarrhea, abdominal pain, decreased urine output and rash
• PE positive for a firm and distended abdomen, erythematous, macular rash, conjunctival injection, gallop murmur and hepatomegaly
• Patient was admitted to the PICU for worsening blood pressure despite multiple fluid boluses, he was intubated and an epinephrine drip was started
Case Presentation - History

- Previously healthy
- No meds at home
- Immunizations UTD
- Lives with parents, paternal aunt and cousins
- Traveled to South Carolina in the month prior
- Multiple COVID exposures starting about 5 weeks prior to presentation from multiple family members
Case Presentation - Management

• Patient had blood and urine cultures sent and was started on broad spectrum antibiotics
• Only a partial ECHO was able to be done so patient was given IVIG and aspirin
• Full ECHO showed no cardiac involvement so aspirin was stopped and high dose steroids was started, all infectious workup was negative
• Improved rapidly after steroids
• His COVID PCR was intermittently positive and his IgG returned positive
• About 36 hours after steroids the patient was extubated and the epinephrine was stopped
• Later that day he was found unconscious with blood on the mattress and on his clothes
• CTA showed active arterial bleed in the proximal duodenem
Case Presentation

• EGD done, an ulcer was seen and clipped
• The steroids were stopped as it wasn’t clear if the bleed was from MIS-C or steroids
• After 2 days off steroids patient became hemodynamically unstable and had to be re-intubated and epinephrine restarted
  – Had some evidence of mild adrenal insufficiency but unable to account for severity of symptoms
• Anikinra was started and patient stabilized and was extubated and epinephrine was stopped the next day
• Kept on anikinra for 2 weeks
What are people using to treat MIS-C?

- IVIG and aspirin
- Steroids (low and high dose)
- Tociluzimab
- Anakinra
- Antibiotics
- Lovenox
What are people using to treat MIS-C?

• While many recommend using IVIG in all patients with MIS-C, this is based only on observational studies and the similarity between MIS-C and Kawasaki

• Three studies have shown that glucocorticoids and IVIG together are better than IVIG alone one study shows no difference\textsuperscript{1-4}

• Current American College of Rheumatology guidelines advocate for all patients to get IVIG based on a few cases of CA aneurysm seen during cardiology follow up\textsuperscript{5}

• However, one study that shows that the rates of CA aneurysm are the same regardless of which treatment is used\textsuperscript{4}
What data exists around possible causes for MIS-C?

• One study has found that children with MIS-C had more antibody dependent cellular phagocytosis than children with acute COVID, but is this pointing towards immune overreaction or is it a function of time?\(^4\)

• This same study found that pediatric patients with MIS-C had a greater proportion of IgG1 subclass spike proteins than IgG3 when compared with children with acute mild COVID.

• Another paper hints at a T cell clonal expansion driven by a type of superantigen, not dissimilar to the bacterial superantigen that drives toxic shock syndrome.\(^5\)
What data exists around possible causes for MIS-C?

• One study found that children with MIS-C have ongoing detectable levels of SARS-CoV-2 in their stool even when it is no longer detectable in NP secretions
• The authors suspect this persistent antigenemia might be at least partially responsible for why the vast majority of MIS-C patients have GI symptoms
• They found evidence of gut microbial translocation in children with MIS-C⁶
References


Questions?