Post-COVID Multisystem Inflammatory Syndrome in the Deployed Environment

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ABSTRACT Cases of multisystem inflammatory syndrome after current or previous SARS-CoV-2 infection have been extensively documented in children. Although there has been recent recognition of a similar adult post-COVID entity known as multisystem inflammatory syndrome in adults (MIS-A), these cases have rarely been reported. This report describes the case of a soldier in the deployed setting with a benign initial clinical presentation who rapidly developed life-threatening MIS-A.

BACKGROUND

Cases of multisystem inflammatory syndrome after current or previous SARS-CoV-2 infection have been extensively documented in children.[1,2] CDC reported 27 cases of multisystem inflammatory syndrome in adults (MIS-A) in direct reports through October 2020, as well as various case series and published case reports.[3,4] Current convention uses the CDC criteria which include:

1. a severe illness requiring hospitalization in a person aged ≥21 years;
2. a positive test result for current or previous SARS-CoV-2 infection (nucleic acid, antigen, or antibody) during admission or in the previous 12 weeks;
3. severe dysfunction of one or more extrapulmonary organ systems (e.g., hypotension or shock, cardiac dysfunction, arterial or venous thrombosis or thromboembolism, or acute liver injury);
4. laboratory evidence of severe inflammation (e.g., elevated CRP, ferritin, D-dimer, or interleukin-6); and
5. absence of severe respiratory illness (to exclude patients in which inflammation and organ dysfunction might be attributable simply to tissue hypoxia).

Although there have been other reported post-COVID inflammatory pathologies leading to significant morbidity and mortality,[3–6] for the purposes of this case report, we will use the CDC's definition. Thus far, there have been no reports of MIS-A within the military population, and given the seemingly benign presentation in a resource-limited setting coupled with the case's rapid progression, this report demonstrates the importance of considering MIS-A in military patients known to have recovered from COVID-19.

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HISTORY

In November 2020, a 28 year old African American male, U.S. Army Reservist on active duty orders presented to the physician at an outpatient clinic located in a role 1 facility in a deployed environment in Kuwait with 4 days of nausea, diarrhea, vomiting, and chills. Patient had no significant past medical or surgical history, was up to date on immunizations, and on no medications. At the time of presentation, the patient reported no dyspnea on exertion or other respiratory symptoms. He noted unformed loose feces without blood or purulence. He denied any subjective fever. Of note, 24 days earlier, the soldier previously developed anosmia and cough which led to a diagnosis of COVID-19 by a positive SAR-COV2 polymerase chain reaction test.

EXAMINATION AND CLINICAL FINDINGS

Presentation vitals were BP: 90/54 mmHg, HR: 144, RR: 28, T: 103.2 °F, HT: 67 in, WT: 182 lbs, O2: 97% in room air. Patient was alert and oriented x4, in discomfort, reporting nausea with diffuse epigastric pain unable to specific pinpoint tenderness. Patient's bowel sounds were normal, and no significant respiratory or cardiovascular findings other than tachycardia were noted on presentation.

After initial assessment, fluid resuscitation commenced initially with 2 L of lactated ringer's (LR) solution and ondansetron 8 mg IV for symptomatic nausea control.

Initial laboratory values ran locally (in conventional units) returned leukocytes 21.2, hemoglobin/hematocrit 16.2/50.0, platelets 155, and laboratory technician reported "lots of granulocytes" on peripheral blood smear, Na 136, K 3.5, CO2 23, Cl 95, Gluc 166, Creat 5.5, BUN unknown (multiple attempts to obtain value during initial evaluation was unsuccessful) Ca 9, ALT 38, and AST 64. Influenza and later respiratory viral panel were negative.

After a third liter of LR, the patient's blood pressure did not improve, staying at 90/66 mmHg. Because of the patient's failure to adequately respond to fluids and emerging concern for kidney injury, the clinical team urgently transferred the patient to the next echelon of care. Shortly after admission to the nearby role 3 facility, the intensive care team placed a central line and began a norepinenephrine drip to

support blood pressures, titrating to a mean arterial pressure of >65 mmHg. They continued fluid resuscitation and began empiric antibiotics. Initially, piperacillin/tazobactam and oral metronidazole were given because of the concern for possible infectious colitis.

Despite these interventions, the patient's clinical status continued to deteriorate. Echocardiogram at that time demonstrated preserved left ventricular ejection fraction, moderately dilated right ventricle, and inferior vena cava and computed tomography of the abdomen showed mild ascending/transverse colonic thickening.

Shortly after, the soldier became tachypneic with respiratory rate 44-50, O2 at 88%-92% on 8 L concentrating facemask. Vasopressin was added to maintain mean the arterial pressure of ∼60 mmHg. 27 hours after his initial presentation at role 1 clinic, the patient was intubated, and he was evacuated via Critical Care Air Transport Team (CCATT) to the role 4 facility, Landstuhl Regional Medical Center (LRMC), for further care.

After air transport to Germany, the soldier's critical care team initiated hydrocortisone and dosed intravenous immunoglobuin with further broadening of antibiotics, including meropenem, vancomycin, and doxycycline.

Computed tomography angiogram of the chest was performed on day 2 and demonstrated small bilateral pleural effusions, patchy ground glass opacities, bilateral interstitial, and alveolar infiltrates, but no evidence of pulmonary embolus or pneumothorax.

Infectious laboratories were negative for *Clostridium difficile, Rickettsia* labs, *Coxiella burnetii*, and *Francisella tularensis.* Aerobic and anaerobic blood cultures, as well as urine cultures, were unproductive. Although not explicitly noted in retrospective chart review, malaria was not noted by infectious disease in the blood smear, and Kuwait is considered a non-endemic country (only 18 noted cases involving Kuwaiti Nationals from 2013 to 2018, and all had recent history of travel to African countries).[7] Serology tests for viral hepatitis were negative. Influenza and respiratory viral polymerase chain reaction were all negative. The C reactive protein to be 4.2 mg/dL (ref 0-1.0) and improved during the course of patient's hospitalization. Fibrin D-dimer was 1.122 (ref 0-0.243), and erythrocyte sedimentation rate was 97 mm/hr (ref 0-15).

Eventually with continued supportive care along with adjunct therapies, the patient was extubated, afebrile, transitioned to oral hydration and nutrition (all on day 5 after presentation) and had significant improvement in symptoms. Although still currently rehabilitating at the time of submission, the patient is expected to return to full health.

DISCUSSION AND CONCLUSION

This case began with a soldier presenting to a small, resource limited clinic in theater with what appeared to be common gastroenteritis, which very quickly deteriorated. Within 27 hours of presentation, he was intubated and required norepinenephrine and vasopressin for blood pressure support. Shortly thereafter, CCATT evacuated the patient to an even higher level of care. During his deterioration, the patient remained a diagnostic dilemma.

This case demonstrates the possibility of MIS-A with previous SARS-CoV-2 infection. The patient's presenting creatinine of 5.5 was the only evidence of severe end organ damage, aside from his concerning blood pressures. In a deployed setting, it would be easy to not consider MIS-A and, thus, fail to act promptly, which could prove catastrophic in similar cases. This presentation highlights the importance of querying individuals for recent infection with COVID-19 in the setting of suspected sepsis. Consideration of this diagnosis should prompt emergent evacuation to a higher level of care.

The main limitation to this case is the fact that MIS-A is primarily a diagnosis of exclusion and requires extensive work-up to arrive at this conclusion. Only after multiple negative cultures, extensive advanced laboratory work up, and improvement with intravenous immunoglobulin and steroids was this diagnosis finally made.

Although the diagnosis was ultimately determined, one of the limitations of this case was the inability to obtain presenting advanced inflammatory biomarkers in a timely manner. This would not have changed initial management but had the elevated inflammatory markers been drawn in the deployed setting, it likely would have been an order of magnitude greater, further guiding the ultimate diagnosis using the CDC definition of MIS-A. Unlike in resource-rich settings, deployed clinicians must be able to consider a wide plethora of diagnostic possibilities in the absence of comprehensive diagnostic support. Thus, this case highlights the importance of clinician suspicion of MIS-A in a recovered COVID patient of African American ethnicity presenting with sepsis.

As additional data emerge about COVID-19, patient's race/ethnicity appears to be an independent risk factor for disease severity. For instance, while Black or African Americans are 1.4 times more likely to have COVID when compared to their White, Non-Hispanic counterparts,[8] they are 3.7 times more likely to be hospitalized, and end up with 2.8 times as many COVID-related deaths.[9]

In looking at current MIS-A data, we found about 12 Black/African American patients for every white patient in a review of current reports, which is a significant deviation from currently noted racial disparities in COVID data.[3–5] Although there are various theories as to the underlying physiology,[10] it is evident that patient's race/ethnicity plays a significant role as a risk factor for developing MIS-A.

The true prevalence of MIS-A is unknown at this time. Given the diagnostic definition created by the CDC, it is likely that adding MIS-A to the differential will increase the understanding of its true prevalence. Because prevalence is unknown, the astute clinician should consider this diagnosis as a possibility in patients with a recent history of COVID-19 infection, as in this case, where presentation consisted

of gastrointestinal complaints with hypotension and elevated creatinine. Future work should focus on estimating MIS-A prevalence and analyzing the relative importance of various MIS-A risk factors, in addition to establishing protocols to improve morbidity and mortality.

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I have obtained written permission from patient presented for write up and distribution of the details of his case.

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CONFLICT OF INTEREST STATEMENT

None declared.

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