Misa, Post COVID complication: case report & mini review

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Abstract---Multisystem inflammatory syndrome in adults (MIS-A) is an rare and underrecognised postinfectious manifestation that occurs 4–6 weeks after COVID-19 infection. Patients affected tend to be young or middle-aged, from ethnic minority backgrounds and previously healthy. The patient suffer from high fever and myalgia, and there is myriad of extrapulmonary symptoms and signs, including cardiac, gastrointestinal, neurological and dermatological involvement. Cardiovascular shock and markedly raised inflammatory markers are prominent features, while significant hypoxia is uncommon. Patients respond well to corticosteroid therapy, but failure of clinicians to recognise this recently identified phenomenon, which can mimic common conditions including sepsis, could delay diagnosis and treatment. Here we present a case of MIS-A in an adult men, with severe illness and positive test result for SARS-CoV-2 infection (PC, antigen, or antibody).There was severe extrapulmonary organ system dysfunction;There was markedly elevated acute inflammatory markers; .there was no any respiratory illness.
Introduction

Throughout the course of the COVID-19 pandemic, a hyperinflammation syndrome has been noted to affect patients in the 4–6 weeks postinfectious period.[1] With features similar to Kawasaki disease and toxic shock syndrome, patients display fever, shock, cardiac dysfunction, abdominal pain and grossly elevated inflammatory markers, without severe respiratory illness. Neurological symptoms including headache and meningeal signs have also been reported. Initially only reported in children, there are now isolated case reports in adults too. (MIS-A) is also adult-onset ‘paediatric multisystem inflammatory syndrome’ (PIMS).[2,3] Diagnosis can be delayed due to lack of awareness of this phenomenon by the clinician, as well as the unusual constellation of symptoms and signs acting as red herrings. Here, we report a case in an adult patient and reflect on the lessons learnt for timely diagnosis and commencing treatment.[4,5]

Case Presentation

A 23 year old previously healthy boy presented to Emergency department in Amrita hospital Kochi on November 2021 with a chief complaints of abdominal Pain. He reported 1 week of low grade fever, followed by mild cough. He was initially treated at a local hospital but was referred to Amrita for further management. He lived at home with family and had no recent travel or contact with sick patients. He had no habituations. He was not on any chronic medications and had no known allergies. On presentation, he was afebrile with hypotension (Blood pressure of 70/40mmhg) and saturation of 89% in room air. He appeared ill and tenderness over epigastric region. No signs of Guarding or rigidity. On Auscultation he had bilateral basal crepitations. Laboratory workup was notable for profound acute kidney injury, deranged LFT, elevated inflammatory markers and features of coagulopathy. Sars Cov-2 IgG from serum was positive. Blood and urine culture was negative. He was started on Meropenam, Teicoplanin. X-ray taken showed right sided pleural effusion. Poin of care Echocardiogram revealed severe LV dysfunction with global LV hypokinesia. Ultrasound showed Altered liver echotexture, minimal ascities, mild Gb wall edema. The patient was admitted to medical icu with diagnosis of MAS/Sepis with MODS and concern for possible MIS-C due to mucocutaneous, renal, GI and cardiac system involvement. In view of worsening respiratory distress and profound hypotension with impending cardiorespiratory arrest, he was electively intubated and put on mechanical ventilator.

He was started on ionotropics. As per nephrology advise he was started on continues renal replacement therapy with Cytosorb filter. Gastromedicine and rheumatology Opinion was taken and orders were carried out. He was pulsed with iv methypredinsolone. CT abdomen and chest was done which showed cardiomegaly with borderline dilatation of the main pulmonary artery. Right sided mild to moderate pleural effusion; patchy ground glass opacity seen in apicoposteriour segment of left upper lobe probably due to venous congestion:-

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liver shows patchy area of arterial enhancement with reactive gall bladder wall edema and mild to moderate ascites. Due to concern for inflammatory multi-system organ involvement similar to that seen in MIS-C, and risk of progression to more florid cardiac involvement, a risk-benefit discussion was held with the patient regarding treatment with intravenous immunoglobulin (IVIG), including potential risk of hypercoagulability. He was treated with IVIG 2 g/kg split equally between hospital days. Workup for other etiology including Dengue, Typhoid, Leptospirosis, Malaria, Hanta virus and Borrelia were negative. He had sudden cardiac arrest following which resuscitation was initiated as per ACLS protocol but ROSC could not be achieved. He succumbed to his illness.

**Heamatologic investigation**

The investigations report are as follows: CRP(57.6), Procalcitonin(1.08), RFT (Urea-114 mg/dL; Creatinine-2.39 mg/dL), (SGOT-3172.31 U/L, SGPT-3291.310 U/L). Cardiac biomarkers(CKMB-66.3 ng/mL; HsTropT-2 ng/mL; CK Total-1522 U/L), and elevated ferritin(8145 ng/mL) and coagulopathy (Fibrinogen-68 ng/mL; INR-3.53 sec; aPTT-42.9/32, D-dimer-19.82 Micro m/ml; DIC Score-6 (overt).

**Discussion**

Multisystem inflammatory syndrome (MIS) is temporally associated with COVID-19 has been reported in both adults and children, and is becoming increasingly recognised as a separate phenomenon to severe COVID-19 infection due to the recurrent lack of respiratory involvement. The syndrome is well described in children and has been defined by a number of organizations including the US and European Centres for Disease Control and Prevention (CDC), the World Health Organisation, and the UK’s Royal College of Paediatrics and Child Health (RCPCH).[6,7] According to Centers for Disease Control and Prevention (CDC)[9] The (CDC) has developed a working case definition for MIS-A which broadly includes: Age 21 years or older; Presence of a severe illness requiring hospitalization; Recent positive test result for SARS-CoV-2 infection (PC, antigen, or antibody); Severe extrapulmonary organ system dysfunction; Markedly elevated acute inflammatory markers; and/or Absence of severe respiratory illness (to exclude patients where tissue hypoxia causes organ system dysfunction) We reviewed a number of existing case reports of MIS-A and adult cases of PIMS, including a case series published by the US CDC in October 2020 of 16 cases, which we believe to be the largest cohort of reported MIS-A cases to date.
Our search yielded only two other case reports from the UK. Although the symptoms and signs are diverse, there are striking similarities between the majority of cases reported and those seen in our patient. For example, patients tend to be middle-aged, of black, Asian or minority ethnic origin (mirroring the demographics of children more commonly affected by MIS), and without extensive previous comorbidities. Symptoms appeared between 4 and 6 weeks after confirmed COVID-19 infection or a non-specific viral illness, after a period of initial improvement. Common symptoms include high fever, dyspnoea, lethargy, myalgia, abdominal pain, vomiting and diarrhoea, neck pain or sore throat, and a widespread rash. The rash is described mostly as a diffuse maculopapular or erythematous rash, affecting particularly the torso, upper limbs and palmar surfaces. Hypoxia was not a prominent feature, but many had significant cardiac dysfunction including shock requiring inotropic and/or vasopressor support, and arrhythmias including atrial fibrillation and atrioventricular block were also seen. Headache and neck stiffness seem to be commonly described neurological features, but most patients were not investigated any further than CT imaging of the head and/or neck and lumbar puncture.

Ahsan and Rani described a case of MIS-A with clinical bilateral facial nerve palsy for which an MRI brain and orbit was carried out (lumbar puncture was refused by the patient), which yielded no significant findings. It seems that while COVID-19 infection is known to be associated with a wide spectrum of neurological features including anosmia, ageusia, encephalopathy, encephalitis, Guillain-Barre syndrome and cerebrovascular events, these are not well described as part of MIS. Similar to our patient, many had negative COVID-19 PCR tests acutely, but subsequently tested positive for the virus by serology, suggesting recent infection. This is important to bear in mind, given that we know a significant proportion of COVID-19 infections are asymptomatic. The clinician should always ask about recent viral illnesses, possible COVID-19 contact, and if available test for COVID-19 serology routinely. A number of patients underwent extensive infectious and immunological work-up. Most patients also underwent CT imaging with findings of typical bilateral ground-glass shadowing in the lungs and non-specific findings in the abdomen and pelvis such as free fluid. Around half of the patients in the CDC case series had abnormal transthoracic echocardiogram findings including depressed left ventricular function. Some went on to have CT coronary angiograms which were unremarkable. Our patient did not receive any cardiac imaging, but on reflection an echocardiogram should have been arranged for completeness, given the anecdotal frequency of cardiac dysfunction as part of MIS-A. Finally, similar to many of the other patients detailed in case reports, corticosteroid therapy led to brisk improvement of symptoms, clinical stabilisation and normalisation of biochemical parameters.

The choice of steroid used included methylprednisolone, prednisolone and dexamethasone. All patients in the individual case reports we reviewed survived to discharge, as did 14 out of 16 patients in the CDC case series. The average length of stay in hospital was 10 days. The pathogenesis of MIS is not fully understood, but the delay to presentation after COVID-19 infection is presumed to be due to initiation by the adaptive immune response. Proposed mechanisms for extrapulmonary dysfunction include endothelial damage, dysregulated innate
immune system and subsequent cytokine storm. There are no existing guidelines for management of this condition, but what is clear from our review is that corticosteroids are an effective treatment, leading to often very rapid resolution of clinical and biochemical parameters. Other immune-modulating therapy administered, including intravenous immunoglobulin, anakinra (interleukin-1 receptor antagonist) and infliximab (tumour necrosis factor-alpha inhibitor), appear to be extrapolated from local management guidelines for other hyperinflammatory conditions such as Kawasaki disease and MIS in children.

COVID-19 remains a novel disease, and associated complications and overlap syndromes are likely to be under-recognised and under-reported. Definitions and classifications appear to be preliminary, non-specific and geographically different worldwide. As more clinical information is gathered, international efforts will be required to formulate more specific and globally recognised terminologies and diagnostic classifications. Furthermore, work is required to develop internationally accepted clinical guidelines for treatment strategies with the recognition of more cases and follow-up of medium-term and long-term outcomes.

References

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