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Multi System Inflammatory Syndrome Of Adults (Mis-A) As Delayed Presentation Of Sars Cov 2 Infection- A Case Report

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Abstract

Multisystem inflammatory syndrome in adults (MIS-A) is a rare but potentially fatal hyperinflammatory condition occurring weeks after SARS-CoV-2 infection, characterized by extrapulmonary organ dysfunction, elevated inflammatory markers, and minimal respiratory involvement. We report a 34-year-old woman with prior right anterior cruciate ligament surgery who presented with high-grade fever, vomiting, and polyarthralgia. Initial examination and infectious workup were unremarkable; however, she rapidly deteriorated with hypotension, altered sensorium, severe myalgia, and cool peripheries. Laboratory tests showed markedly elevated C-reactive protein, ferritin, D-dimer, creatine phosphokinase, NT-proBNP, and troponin I levels, along with progressive thrombocytopenia, coagulopathy, and acute kidney injury. SARS-CoV-2 IgG was strongly positive, with other infectious causes ruled out. Imaging revealed features of shock-related hypoperfusion. She was treated with airway protection, mechanical ventilation, inotropes, antibiotics, blood products, high-dose intravenous methylprednisolone, and intravenous immunoglobulin, along with continuous renal replacement therapy. Despite maximal supportive and immunomodulatory therapy, she progressed to refractory shock and died on day 5 of admission. This case meets CDC diagnostic criteria for MIS-A and underscores the importance of early recognition and prompt initiation of immunomodulatory treatment in adults with recent SARS-CoV-2 exposure presenting with unexplained systemic inflammation, as delayed diagnosis may result in poor outcomes.

Keywords: Multisystem inflammatory syndrome in adults, MIS-A, SARS-CoV-2, COVID-19, post-COVID complication, cytokine storm, intravenous immunoglobulin, case report

Introduction

Covid 19 is an infectious disease caused by SARS-COV-2. Hyper inflammation with multi organ damage has been noted in patients with post covid infection [1]. This triggers an aberrant host immune response and this response along with immune dysregulation causes accumulation of cytokines that results in tissue damage, capillary leak, intravascular thrombus formation and oxygen dysfunction leading to multi organ failure[4][5]. While children are most commonly affected by this multi organ inflammatory syndrome, similar cases of multi organ inflammatory syndrome has also been reported in adults [2] in United Kingdom, USA,Turkey and Germany. The diagnostic criteria for MIS-A have been established and include following five criteria 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 (antigen, antibody or nucleic acid)

3) severe dysfunction of one or more extra pulmonary organ system (hypotension or shock, cardiac dysfunction, thromboembolism, DIC, acute liver injury etc.,) 4) laboratory evidence of severe inflammation (e.g elevated CRP, Ferritin, D dimer etc.,) 5) absence of severe respiratory illness[10]. Once diagnosed, treatment includes steroids and IV immunoglobulins[6]. Here we have discussed a case that presented to our hospital

Case Report

A 34 years old female with past h/o right ACL tear surgery 2 years back now presented to ER with c/o fever for past 3 days associated with multiple episodes of vomiting and severe pain over both shoulder joint and both wrist joints.

PARAMETER	FINDINGS	INTERVENTION
Airway	Patent	
Breathing	B/l chest rise equal RR 20/min SPO2 99% on room air B/L air entry equal	
Circulation	All peripheral pulses felt Heart rate – 115/min Blood pressure – 100/60 mm hg	Wide bore cannula secured. IVF NS started at 100ml/hr
Disability	E4V5M6 B/l pupil reactive and equal GRBS – 144 mg/dl	
Exposure	Temp – 102.3 F Pain and tenderness over knee and shoulder joints	Inj.Paracetomol 1gm IV infusion given.

ECG taken shows normal sinus rhythm without any ischemic changes. Her initial blood workup and inflammatory markers were unremarkable. But in view of persisting fever spikes and arthralgia, patient was admitted and initially treated with antipyretics, analgesics and antibiotics. During the course of hospital stay, patient develops severe myalgia, palpitations and suddenly becomes tachypneic and mildly unresponsive withcool peripheries on examination she was found to be hypotensive, her GCS is low. Initially her Airway was stabilised and managed with crystalloids, inotropes and antibiotics were hiked in view of fever spikes and elevated infective markers. All inflammatory markers and other blood routine were repeated and monitored daily which is shown below.

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Parameters	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Normal range**
Hemoglobin	12.8	13		9.9	12-16g/dl
Total count	10,510	8010		13,900	4000-11000 cells/ul
Platelet	1.81 lakhs	1.05 lakhs	O.75	0.21	1.5-4.5 lakhs/ul
CRP	8.3	416			< 5 ng/L
Urea	33	78			15-45 mg/dl
Creatinine	0.6	4.5		3.2	0.6-1.3 mg/dl
Trop I	<1.50	1029	8312		<1.50 ng/dl
CPK	52	3461			25_135 IU/l
Prothrombin time	12	19.3			11-16 seconds
INR	0.8	1.55		2	0.8-1.2
Procalcitonin		>100			
NT pro BNP		>30000			<300pg/dl
aPTT			85		30-36 seconds
D dimer		3.5			<0.5
RA factor	Negative				
Fibrinogen			8.11		1.8-3.5
Ferritin		454			6.24 – 137 ng/dl

CPK- Creatinine phosphokinase, CRP- C reactive protein,RA -Rheumatoid arthritis, INR- international normalised ratio, aPTT- activated partial thromboplastin time

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Her serial blood investigation shows persistently elevated inflammatory markers with features of disseminated intravascular coagulation. In view of refractory shock, she was started on multiple inotropes support. ABG shows severe metabolic acidosis Infective workup done shows below

Dengue	Negative
Leptospira	Negative
Scrub typhus	Negative
Malaria	Negative
Chickengunya	Negative
Blood culture	Negative
Urine culture	Negative
SARS-COV-2 antibody	**Positive (34G3 AU/ml)**
CMV antibody	Negative
EBV antibodies	Negative

Initially her blood and urine cultures have no significant growth. Her C3,C4 levels were low and APLA workup turns to be negative. CT abdomen taken shows hyper enhancing adrenal glands on both sides, spleen shows loss of classical heterogeneity in arterial phase, mild diffuse wall thickening from caecum to sigmoid colon which all suggestive of acute shock and hypo perfusion. Her toxicology workup were unremarkable. She was continued on mechanical ventilatory support and inotropes. In view of worsening AKI and persisting acidosis, nephrology opinion was sought and patient initiated on continuous renal

replacement therapy .As MIS -A is considered patient was decided to start on steroid therapy and IVIG. Inj.methyl Prednisolone 1gm for 3 days and IVIG 70 GM and 140gm for 2 days given. ECHO taken shows no RWMA, LVEF 62%, good LV systolic function and diastolic function, no clots and effusion. Cardiology consultation taken in view of myocarditis. PRBC, platelet and FFP transfusion done in view of worsening coagulation profile. In spite of all these effective measures, on day 5 of hospital stay, patient went into cardiac arrest, resuscitative measures were initiated according to ACLA protocol. Despite all resuscitative measures, patient could not be revived and patient was succumbed to

death.

Discussion

Multi system inflammatory syndrome is a rare but late life threatening complication of SARS-COV-2 Infection. Though it's pathophysiology is unclear, it's said to be aberrant host immune response to infection leading to cytokine storm which in turn causes tissue damage, capillary leak and multi organ failure [4]. MIS-A is regarded as post infectious syndrome rather than acute infection as SARS COV 2 PCR is negative but antibodies against SARS COV 2 are typically positive.Most patients with MIS-A presented with fever (90%), hypotension(60%), cardiac dysfunction (54%) and other organ failures. Most of the patients need ICU hospitalization[8]. It can also present as AKI with rhandomyolysis worsening the condition of patient [3] . In some cases, there occurs disseminated intravascular coagulation leading to bleeding manifestations[7].

Case definitions for MIS-C vary between CDC and WHO[10]. The fundamental differences are the age of the patient, the length of the fever, and whether it requires a positive SARS- CoV-2 test, or exposure. To diagnose MIS-C, the CDC requires a history of hospitalization, age < 21 years, a positive laboratory

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test for current or recent SARS-CoV-2 infection, or exposure to SARS-CoV-2 within the past four weeks. However, MIS-C is diagnosed if the patient is less than 19 years, according to WHO . There is increasing evidence that COVID-19 pathogenesis involves an array of changes including mild, acute, chronic, multi-systemic inflammatory syndromes affecting every age group . Several reports of a similar syndrome in adults (MIS-A) more than 21 years of age after four weeks after initial infection withSARS-CoV-2 have been reported . Global attention has been drawn concurrently to reports of a similar syndrome in adults without severe respiratory illness who experience cardiovascular,gastrointestinal, dermatologic, and neurological symptoms. They either had polymerase chain reaction (PCR) results that showed SARS- CoV-2 infection or had a positive antibody test showing recent infection.Positive antibodies and negative PCR results suggest that MIS-A/MIS-C are post-infectious syndromes [9],[10]. In this case, patient fulfilled the diagnostic criteria as mentioned above. complement fractions were low and shows severe thrombocytopenia indicating the action via classical pathway linked to immune complex formation. Asystemic review published by shekhar kural et al, on March 2022 regarding the treatment used in MIS-A cases revealed that variety of anti inflammatory therapies were used including steroids, IVIG and biologics such as Tocilizumab and anakinra[6]. Concomitant antibiotic therapy was administered in 60% patients. The death were due to myocardial dysfunction and multi organ failure. Conclusion: Here we have discussed a case of 34 years female diagnosed as multi system inflammatory syndrome of adults with refractory shock and who was treated with IVIG and IV steroids, but succumbed to death despite effective measures. In conclusion, MIS-A is rare but life threatening delayed complication of SARS COV 2 infection which need early recognition and prompt treatment with steroids and IVIG which may sometimes favours positive outcomes

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