CASE REPORT

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COVID-19-Related Multisystem Inflammatory Syndrome in Adults: An Uncommon Case

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Abstract

Multisystem inflammatory syndrome in adults (MIS-A) is being recognised as a syndrome related to COVD-19 infection – more commonly in children, but occasionally in adults also.

A 28-year-old male with no co-morbidities presented with fever, abdominal pain, vomiting, chest and shoulder pains, and redness of eyes. He developed these symptoms 14 days post-COVID-19 vaccination. He was diagnosed with COVID-19 infection in September 2020. After excluding other causes for his clinical features, the diagnosis of MIS-A was made and IV immunoglobulin along with methylprednisolone was given. Patient responded to the therapy and remained symptom free on regular follow-up for 3 months.

We suggest that in a patient who presents with fever post-COVID-19 and/or post-immunisation with COVID-19 vaccination, the possibility of MIS-A should also be considered.

Key words: COVID-19, MIS-A, SARS-COV-2.

Introduction

COVID-19-related multisystem inflammatory syndrome (MIS) has been reported in children (MIS-C) and rarely in adults (MIS-A). Fever is generally the main finding of this syndrome and cardiovascular, gastrointestinal, haematological, and dermatological findings are prominent[1]. Involvement of lungs is rather uncommon in this entity. This is the only case of MIS-A at our hospital till date following the 1st and 2nd wave of COVID-19 infection. Our hospital is a designated COVID-19 (Level-3) hospital.

Centres for Disease Control and Prevention (CDC) gave the working case definition for MIS-A[2]. Here we report the case of a 28-year-old male who satisfied the case definition of MIS-A by the CDC (Centres for Disease Control), USA.

There is no set of guidelines available for the treatment of MIS-A and the options which have been tried are very limited. In many small studies including case reports, pulse therapy with intravenous (IV) corticosteroids are used with or without IV immunoglobulin (IVIG)[1]. Our patient responded to IV corticosteroid and IVIG treatment significantly.

Case report

A 28-year-old male patient was admitted to our hospital with the complaints of fever for 15 days, left upper abdominal pain for 15 days, and h/o redness over the chest and back with redness of eye 8 days back. He also complained of pain in chest over left side and left shoulder. The fever was of insidious onset, high-grade, 2 - 3 episodes per day which was relieved by taking paracetamol. During this period, he had occasional vomiting also.

There was no history of diarrhoea, shortness of breath, loss of consciousness, abnormal body movement, or bowel or bladder involvement. He had no co-morbidities like diabetes mellitus, hypertension, thyroid dysfunction. There was no history of any illicit drug use. Patient was diagnosed with mild COVID-19 (8 months before presentation), his 3 family members suffered from COVID-19 (3 months back) and he took 1st dose of a COVID-19 vaccine, 14 days before onset of symptoms.

On examination, the patient was conscious, alert, and oriented to time, place and person. His vitals included pulse rate of 108/min, blood pressure of 128/74 mm Hg, respiratory rate of 18/min, SpO2 of 97% on ambient air, and temperature of 102° F. Systemic examination was unremarkable.

On laboratory work-up as shown in Table I, it was found that the patient had significantly raised inflammatory markers like CRP, ESR, IL-6, D-dimer (mildly raised) before and at time of admission. ECG revealed T-wave inversion in leads II, III, aVF, V3, V4, V5 and V6 as shown in Fig. 1. The blood culture and urine culture showed no growth. Chest X-ray PA-view, HRCT thorax, CECT abdomen and 2-D echocardiography were within normal limits. Peripheral

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smear for malaria parasite, S. ANA and rheumatoid factor were negative. Urine (routine and microscopy), S. vitamin B-12, 25-OH Vitamin-D, S. amylase, S. lipase and thyroid profile were within normal limits. RT-PCR for COVID-19 was negative. Table I gives the details of other investigations.

This patient was diagnosed as a case of Multisystem Inflammatory Syndrome in Adults (MIS-A) according to CDC criteria[2]. He was managed with IV methylprednisolone (120 mg/day BD for 3 days), IVIG (2 gm/kg in 2 divided doses over 2 days), Inj. Ceftriaxone, tab. Ivabradine, tab. Apixaban, tab. Aspirin, multivitamin tablet, tab. Paracetamol and steroids (were tapered within 4 weeks). Patient's fever subsided within a day and his inflammatory makers decreased over the tab. aspirin, multivitamin tablet, tab. Paracetamol and next few days as shown in Table I. The ECG changes also reverted back to near-normal after 2 days as shown in Fig. 2. On day 10 of admission, the patient was discharged. On follow-up at 14 days, and 42 days post-discharge, the patient remained symptom-free, and his laboratory parameters were within limits as shown in Table I. Coronary angiography done on 10th August 2021 was within normal limits.

Table I: Serial investigations of the patient.

	19 May	25 May	27 May	04 Jun	08 Jun	09 Jun	10 Jun	11 Jun	13 Jun	24 Jun	27 Jun	29 Jun	20 July	05 Aug	10 Aug	Range	Units
Hb	14.9	14.6	12.8	13.6						14.6		14.3	15.2	14.1		13 - 17	g/dl
TLC	9800	7300	10300	8500						10100		9000	7900	5600		4000 - 11000	/mm^3
Platelets	283000	270000	313000	3250000						234000		165000	289000	238000		150-41000	/mm^3
ESR				22		60				22		17	5	8		0 - 15	mm/hr
CRP	21.18	64.35	21	25	102.5	96			12	2.58		24.21	1.01	1.72		< 5.0	mg/l
Ferritin			151.9		335	273			194	314			141.3			30 - 400	ng/ml
IL-6		4.58	30.4	26						2.5						< 7	pg/ml
D-Dimer	0.31	0.28	0.23		0.05	0.62			0.22	0.31			0.16			< 0.5	ug FEU/ml
Troponin T		14.04			110.5					13.68	18.64	18.64	19.09	22.44		< 14	pg/ml
Troponin I									0.32						0.03	< 0.02	ng/ml
S. LDH			245		267	447			264	211			199			120 - 246	U/L
Pro-Calcitonin						0.045				0.05			0.02			< 0.5	ng/ml
CPK-MB					21					2.7			11			0 - 16	U/L
NT-ProBNP				123						79			67			< 115	pg/ml
SGOP	33		20						21		24	21				< 50	U/L
SGPT	58	28	25						31	38		37	25	28.8		< 50	U/L
RET	WNL			WNL						WNL			WNL		WNL		
PT/INR			14/1.0														
Lipid profile													LDL = 147 triglyceride 292				
COVID-19	>400			22516						6546.2			3173.2				AU/ml
	SARSCoV-2 IgG antibody			anti-spike SARS CoV-2 IgG Ab						anti-spike SARS CoV-2 IgG Ab		anti-spike SARS CoV-2 IgG Ab				detects	
	< 12			< 50						< 50			< 50			range	
	CLIA			CMIA						CMIA			CMIA			method	
Mantoux			No induration														
Quantiferon Tb IGRA			Negative														
ECG	T wave inv		T wave inv		T wave inv		T wave inv		T wave inv	T wave inv		T wave inv	T wave inv		T wave inv		
			in aVF, II, III, V3, 4, 5, 6				in aVF, II, III, V3, 4, 5, 6		in aVF, III	in aVF, III		in aVF, III	in aVF, III		in aVF, III		
2-D ECHO		WNL		WNL			WNL				WNL				WNL		

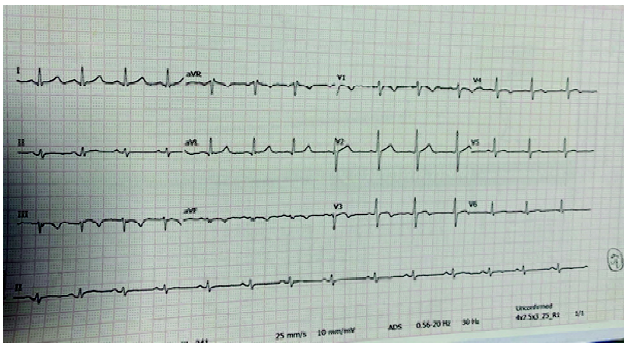

Fig. 1: *ECG on 09-06-2021.*

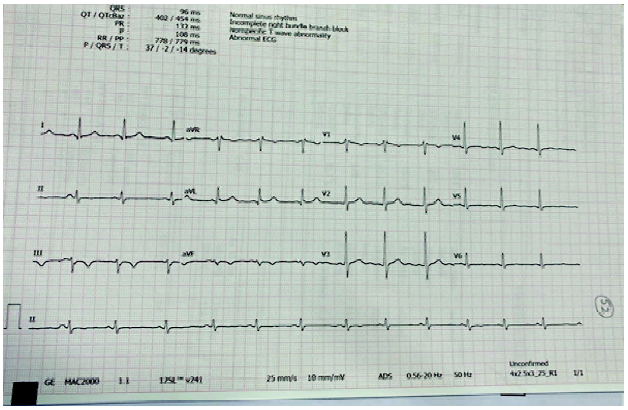

Fig. 2: *ECG on 11-06-2021.*

Discussion

The case definition for MIS-A as per CDC (Table II), includes a patient aged ≥ 21 years hospitalised for ≥ 24 hours, or with an illness resulting in death, who meets the clinical and laboratory criteria. The patient should not have a more likely alternative diagnosis for the illness[2]. In our patient, the clinical and laboratory criteria both were fulfilled including fever >38° C, myocarditis, rash, non-purulent conjunctivitis, abdominal pain, vomiting, elevated markers (like CRP, IL-6, ESR, procalcitonin) and antibodies against SARS-CoV-2 in high titres. The case series by Varadaraj *et al*[3] used morbidity and mortality weekly report[4] (MMWR) criteria for MIS-A but our patient satisfied the case definition of MIS-A as per CDC.

Our patient developed symptoms post-COVID-19 vaccination which could have been a triggering factor for the hyper-inflammation which is very similar to a case reported by Uwaydah *et al*[5]. They reported a 22-year-male who received inactivated SARS-CoV-2 vaccine, 6 weeks following a mild COVID-19 infection and developed MIS-A like symptoms. He responded well to steroids (IV dexamethasone 6 mg daily followed by oral steroids in tapering dose).

Table II: CDC case definition for MIS-A.

A patient aged ≥ 21 years hospitalised for ≥ 24 hours, or with an illness resulting in death, who meets the following clinical and laboratory criteria.

The patient should be not have a more likely alternative diagnosis for the illness (e.g., bacterial sepsis, exacerbation of a chronic medical condition).

I. Clinical criteria

Subjective fever or documented fever (≥ 38.0 C) for ≥ 24 hours prior to hospitalisation or within the first THREE days of hospitalisation* and at least THREE of the following clinical criteria occuring prior to hospitalisation or within the first THREE days of hospitalisation*. At least ONE must be a primary clinical criterion.

A. Primary clinical criteria

1. Severe cardiac illness includes myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new-onset right or left ventricular dysfunction (LVEF < 50%), 2nd/3rd degree A-V block, or ventricular tachycardia.
2. Rash AND non-purulent conjunctivitis

B. Secondary clinical criteria

1. New onset neurologic signs and symptoms includes encephatopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain Barrè syndrome)
2. Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy)
3. Abdominal pain, vomiting, or diarrhoea
4. Thrombacytopenia (Platelet count <150,000/microliter)

II. Laboratory evidence

The presence of laboratory evidence of inflammation AND SARS-CoV-2 infection.

A. Elevated levels of at least TWO of the following: C-reative protein, ferritin, IL-6, erythrocyte dedimentation rate, procalcitonin

B. A positive SARS-CoV-2 test during the current illness by RT-PCR, serology, or antigen detection

Note: **These criteria must be met by the end of hospital day 3, where the date of hospital admission is hospital day 0.*

Although the exact underlying immunopathology is not well understood, adaptive immunity may be the cause responsible for these features[6]. In a study by Morris *et al*, it was believed to be a post-infectious syndrome rather than an infection in acute stage of development which causes direct endothelial damage and associated thrombo-inflammation[4]. In our case, whether the patient had a re-exposure to COVID-19 virus when his family members developed symptoms or the immunisation with COVID-19 vaccine acted as a trigger, or both these events could have led to a hyper-immune response over a period of time.

There is no exact treatment guideline for MIS-A, but most of the reviews, case series and case reports have mentioned the use of IV corticosteroids with or without the use of IV immunoglobulin along with supportive measures[1,4-8]. The treatment with a combination of IV corticosteroids and IVIG had a better response than either of them when given alone[1,4-8]. The IV

immunoglobulin acts at multiple levels and has an anti-inflammatory role[9]. The dose used in various cases ranged from 1 - 2 gm/kg in divided dose/single dose[4-8]. In this case, we used it in a dose of 2 gm/kg in two divided doses over 2 days along with IV methylprednisolone which was switched to oral prednisolone tapering over a 4-week course. The patient response was satisfactory and over 3 months of follow-up as shown in Table I, the patient remained symptom free and his inflammatory markers were also within normal limits as shown in Table I.

We suggest that in a patient who presents with fever post-COVID-19 and/or post-immunisation with COVID-19 vaccination, the possibility of MIS-A should be considered after ruling out other causes.

Abbreviations

COVID-19, Coronavirus disease 2019; MIS-A, Multisystem Inflammatory Syndrome in Adults; IV, intravenous; MIS-C, Multisystem Inflammatory Syndrome in Children; CDC, Centers for Disease Control and Prevention; OPD, out-patient department; CRP, C-Reactive protein; ESR, erythrocyte sedimentation rate; ECG, electrocardiogram; HRCT, High resolution computerised tomography; CBC, complete blood count.

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