CASE REPORT

Multisystem inflammatory syndrome in an adult after Covid-19 vaccination (MIS-V): a case report and review of published literature

Namirah Iftikhar[1], Ashar Ekhlaq Ahmed[2], Muhammad Osama Rehman Khalid[3], Rameel Muhammad Aftab[4]

Abstract

The novel coronavirus SARS-CoV-2 pandemic began in Wuhan (China) in December 2019. Due to the severity of the illness, extent and speed of its spread, vaccines were developed rapidly, and concerns have remained about their safety profile. Although the vaccines have proven to be safe and effective in most cases, as the number of people getting vaccinated for SARS-COV-2 increased, several adverse reactions following the administration of vaccine were reported, one of them being Multisystem Inflammatory Syndrome secondary to vaccination (MIS-V). Here, we report the case of a patient with MIS-V as well as a summary of all other published cases of this syndrome to-date.

Keywords: Adverse events following immunisation, SARS-COV 2, Immunisation triggered inflammation, MIS-V, Immunisation related syndrome.

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Introduction

Emerging in late 2019, Covid-19 was declared a pandemic in March 2020 by the World Health Organisation (WHO). This led to a worldwide effort to stop the spread of the disease by developing effective vaccines. Due to the severity of Covid-19 and the extent and speed of its spread, vaccines were developed rapidly, though concerns remained about their safety profile. Although the vaccines have proven to be safe and effective in most cases, as the number of people getting vaccinated for SARS- COV-2 increased, several adverse reactions following the administration of vaccine were reported, one of them being Multisystem Inflammatory Syndrome secondary to vaccination (MIS-V). Here, we report the case of a patient with MIS-V as well as a summary of all other published cases of this syndrome to-date. It is important that clinicians have knowledge of this syndrome because of the endemic nature of Covid-19 infection as well as the ongoing need for vaccination boosters. With time more cases may emerge and, therefore, clinicians need to maintain a high index of suspicion when dealing with patients who present with inflammatory syndromes.

[1]Department of Internal Medicine, Ziauddin University Hospital, [2,3]Department of Medicine, Ziauddin University Hospital, [4]4th Year MBBS Student, Ziauddin University, Karachi, Pakistan.

Correspondence: Namirah Iftikhar. **Email:** namirah12364@gmail.com

ORCID ID: 0000-0002-4249-2205

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Case Report

A 67-year-old female patient was admitted to Ziauddin Hospital, Clifton, Karachi on 21st November 2021 with fever, dyspnoea, and drowsiness over the preceding four days. She had multiple areas of ecchymosis at insulin injection sites on her abdomen and had an erythematous non-itchy cutaneous rash covering most of her body. The patient did not report any allergies. She complained of bleeding from the gums and easy bruising along with a history of urticaria, palpitations, oedema, and pain on defecation.

She had a past medical history of type-2 diabetes mellitus, hypertension, and advanced chronic kidney disease requiring haemodialysis three times a week. She received a single dose of the CoronaVac-SinoVac (Covid vaccine) on July 26, 2021. Prior to this hospital admission, she had been hospitalised twice (at nearby hospitals) for brief periods. Subsequently, she was admitted one month prior with persistent diarrhoea in Dr Ziauddin hospital, Clifton, Karachi. A Computed Tomography (CT) scan of her abdomen revealed an area of probable colitis, however, on colonoscopy, this was not confirmed, and her diarrhoea spontaneously improved. Stool cultures were reported as normal. Two weeks later, she was readmitted with pleural and pericardial effusions. During that admission, she also required temporary cardiac pacing for junctional bradycardia before her arrhythmia settled. She was discharged with home oxygen and her pulse oximetry readings indicated low oxygen saturation levels over the preceding four days which coincided with the onset of dyspnoea.

She was admitted to the intensive care unit (ICU) with a temperature of 37°C. Her blood pressure was 107/60mmHg and pulse rate was 61 beats/minute. Oxygen saturations were 75% on room air. Physical examination revealed conjunctival pallor, extensive palpable purpura on both legs, normal heart sounds,

crepitations in the lungs bilaterally and reduced air entry in the middle and lower zones of the lungs. Her abdomen was distended due to ascites but was soft and non-tender. She had synovitis of multiple small joints in hands and feet, ankles, wrists, and knees, and bilateral lower limb weakness (Power grade 2/5) compared with upper limbs (Power grade 4/5). No other neurological deficit was identified.

Investigations: Her admission electrocardiography (ECG) showed a normal sinus rhythm and no evidence of ongoing cardiac ischaemia, and her haemoglobin was 8.7gm/dl. Serum creatinine was 2.96mg/dl (female 0.6- 1.1 mg / dl) with an estimated glomerular filtration rate of 17mL/min/1.73m (normal >60). The white cell count was 7.3 ×109 /L (4.1–11.0/L) with a neutrophil count of 8.2 ×109 /L (1.8–7.5). Lymphocyte and eosinophil counts were normal. The C-reactive protein (CRP) was elevated at 101mg/L (0–5mg/L), and troponin-I was 0.087 (up to 0.036ng/ml). D-dimer was raised at 3872mg/L (<500mg/L). The patient had a negative SARS-CoV-2 real-time reverse transcriptase-PCR test following a nasopharyngeal swab. Covid-19 serology was negative; however, her Covid-19 antibody S protein was positive (219.9). CPK was 523mcg/L (10-120mcg/L). HRCT (High-resolution CT chest) demonstrated patchy ground glass haziness in both lungs. There was mild interlobular septal thickening and moderate left-sided pleural effusion with underlying lung collapse. Cardiomegaly with extensive coronary artery calcifications and minimal pericardial effusion was also seen. There were signs of pulmonary hypertension. Her basic autoimmune workup, including antinuclear antibodies (ANA), extractable nuclear antigen testing (ENA), and double-stranded DNA (DsDNA), was normal. Coeliac workup was also normal (Anti-TTG IgA and IgG 2.3U/ml). Thyroid function tests revealed hyperthyroidism (TSH <0.015 FT3 1.67pg/ml and FT4 3.71ng/dl) (TSH 0.5 to 5.0 mIU/L, FT 32.3 – 4.1 pg/Ml, FT4 0.7 to 1.9 ng/dL). A thyroid scan was done which showed features consistent with thyroiditis. Electromyography and nerve conduction studies were performed because of her sudden onset lower limb weakness, and this revealed features consistent with myositis. IgG4 levels were checked and were observed to be normal (0.072g/L). CA-125 was checked which was only mildly elevated (318.6IU/ml). CT was also advised but was not done due to cost constraints and the unstable condition of the patient. Blood and urine cultures did not show growth of any organisms.

Differential Diagnosis: Various diagnoses were considered. These included lower respiratory tract infection and pulmonary oedema in view of decreased oxygen saturation, fever, and raised infective markers. Due to the presence of fever, Covid-19 infection was a possibility, however, the patient had multiple negative SARS-CoV-2 nasopharyngeal swabs. Primary autoimmune myositis was considered but the autoantibody tests including ANA and ENA profiles returned normal. Myositis-specific antibody tests could not be carried out as the cost was prohibitive. Also, autoimmune myositis alone could not explain the constellation of other symptoms. Septicaemia was ruled out due to normal bacterial cultures.

Due to the presence of inflammatory arthritis, cutaneous vasculitis, myositis, serositis, pneumonitis, thyroiditis, recent transient colitis (on CT scan but resolved by the time of colonoscopy), and probable recent myocarditis (transient dysrhythmia and elevated cardiac enzymes although no cardiac MRI was done) it was felt that multisystem inflammatory syndrome best explained her presentation as a unifying diagnosis. The timing of her vaccination for Covid-19 was also consistent with the diagnosis of MIS-V (multisystem inflammatory syndrome secondary to vaccination). Her presentation fit level-1 of diagnostic certainty as described by the Brighton Collaboration for case definition of multisystem inflammatory syndrome.

Treatment: The patient was initially treated with broad spectrum antibiotics (Levofloxacin 500mg 48-hourly and Injection Meropenem 500mg once daily). The dose was adjusted according to her Glomerular filtration rate (GFR) (17 mL/min/1.73m) and intravenous fluids; however, she did not show any improvement. Multiple blood cultures did not show growth of any organism, hence antibiotics were discontinued. After the clinical suspicion of MIS-V, steroid therapy was initiated with Prednisolone 40mg daily. Higher dose intravenous steroids were avoided due to her delicate fluid balance and poor diabetes control. Oral steroids led to gradual improvement in her symptoms. She required a prolonged hospital stay because of her slow recovery.

Outcome: After discharge from the hospital, the patient was lost to follow-up and it was later learnt, from her relatives, that following initial improvement, her condition deteriorated, and she passed away at home.

Discussion

Multisystem inflammatory syndrome (MIS) is a rare but fatal syndrome that was first identified in children (MIS-C) after being infected with Covid-19.[1] It usually manifests two to six weeks after severe SARS-CoV-2 infection.[2] Since June 2020, this syndrome has also been described in adults (MIS-A) after being infected with Covid-19. The

Centres for Disease Control and Prevention (CDC) have published several cases of multisystem inflammatory syndrome in adults.[3] MIS is a rare condition which can cause inflammation in any system of the body such as the heart, lungs, brain, GI system, and skin.[3] A total of 570 MIS-C patients who met the criteria of MIS-C, using the CDC MIS-C case report form, were reported to the CDC by 40 different health departments by July 29 2020.[4,5] MIS can present with different signs and symptoms, such as fever, rash , gastrointestinal symptoms, and myocardial injury.[5] At the beginning of June 2020, a similar condition was reported in adults as MIS-A.[6] The clinical course of MIS-C and MIS-A was predominantly reported to be the same. However, in patients with MIS-A evidence of prior Covid-19 infection through serological testing and lack of severe respiratory involvement differentiates it from MIS-C.[6] An explanation leading to the possibility of these syndromes is that of the dysregulated immune system post Covid-19; however, the mechanism is still unknown.[7]

The clinical presentation of patients presenting with MIS-C showed similarities with some already existing diseases such as Kawasaki disease (KD) and toxic shock syndrome.[8] Like Kawasaki disease there is no single diagnostic test to diagnose MIS-C; hence, it becomes important to identify the similarities and differences between KD and MIS-C. GI symptoms tend to predominate in patients with MIS-C, however, these symptoms are uncommon in patients with KD. It has also been noted that comorbidities such as obesity can be a predisposing factor for MIS-C but this connection has not been identified with KD (Kawasaki disease). Patients presenting with 24-hours of fever with high inflammatory markers can fit the definition of MIS-C as opposed to KD.[9,10,11]

With the increasing numbers of Covid-19 cases, several vaccines were developed worldwide. Data available regarding the safety and efficacy of these vaccines suggests that it is generally well tolerated and only mild to moderate side effects are noted.[12] Side effects that are generally noted include flu-like symptoms, arthralgia, and pain at the site of the injection.[13] However, several adverse reactions including a multisystem inflammatory syndrome (MIS-V) have been reported post Covid-19 vaccine administration which have generated an increased focus amongst clinicians and several cases have been reported.[14,15] MIS-V after Covid-19 vaccination is rare and remains of great clinical interest. The World Health Organisation has defined the adverse reactions post Covid-19 vaccine as any untoward medical occurrence which follows immunisation, which does not necessarily have a causal relationship with the usage of the vaccine.[16] The Brighton Collaboration network published a definition that can be used to classify patients who present with vaccine-induced multisystem inflammatory syndrome.[17]

One of the studies from NEJM reported that several patients developed hypersensitivity reactions after receiving Moderna vaccine. These reactions were termed as the "Covid-19 arm".[18] Similarly this patient's presentation was initially thought to be secondary to infectious aetiology; however, multi-system involvement, repeatedly normal blood and urine cultures, and lack of response to broad-spectrum antibiotics made the doctors reconsider the diagnosis. Her symptoms included relapsing fever, dyspnoea, recurrent pleural effusions, involvement of the GI system, inflammatory arthritis, thyroiditis, myositis, generalised rash, probable recent carditis, and altered mentation. Laboratory workup showed raised inflammatory markers. SARS-CoV-2 infection was excluded with Covid-19 PCR and antibody test which was suggestive of post vaccination status rather than infection. (She got vaccinated in July 2021 with Sino-pharm vaccine). As depicted by this case, MIS-V is the diagnosis of exclusion and needs a high index of clinical suspicion.

After a literature search, several cases that have already been published were identified (presented in Table 1,2 and 3). Twenty-five cases were reviewed ranging from age 18-73 years old, out of which 14 (56%) were males and 11(44%) were females. Eight patients (32%) were African American, five (2%) were Hispanic, one patient (0.04%) was Asian, one (0.04%) was Caucasian and eight (32%) patients were of unknown ethnicity. Ten (40%) patients were reported to have no prior comorbidities, while other patients had different conditions, such as asthma, hypertension, obesity, diabetes, hyperlipidaemia, and GERD. Out of 25, 19 (76%) patients had fever at the time of initial presentation; 17 (0.68%) patients had evidence of cardiac effects, including abnormalities in ECHO, raised cardiac enzymes, arrhythmias, cardiac discomfort, and cardiogenic shock. Out of 25, 18 (72%) patients had GI symptoms, and six (24%) had dermatologic manifestations, 13 (52%) had evidence of ground glass opacities and eight patients had pleural effusions on chest imaging. All patients had raised inflammatory markers, including CRP (84-580), D-dimers (275-8691) and ferritin ranging from 196 to >10,000. Out of 25, 12 (48%) patients had unknown respiratory Covid-19 infections/testing unknown. Twelve (48%) patients were given anticoagulation, two (0.08%) received Remdesivir and five (0.20%) patients were also given broad spectrum antibiotics. Eight (32%) patients were treated with IVIG, 17 (68%) patients with corticosteroids, and two (0.08%)

Table 1: Cases of multisystemic inflammatory syndrome in adults after COVID-19 vaccination

AGE	27	50	49	21	33	22	21	47
SEX	F	M	M	M	M	F	F	F
RACE	African American	African American	African American	African American	African American	African American	African American	African American
COMORBIDS	None	None	obesity, chronic right lower extremity pain	Obesity	Obesity, HTN, depression	None	Obesity	None
TYPES OF COVID-19 VACCINE	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
H/O COVID	No/ Testing unknown	No/ Testing unknown	Yes/ Testing unknown	No/ Testing unknown	Yes/PCR (+) 41 days earlier	No/ Testing unknown	Yes/PCR (+) 25 days earlier	Yes/ Testing unknown
SYMPTOMS / SIGNS	Rigors, profuse diarrhoea, diffuse rash x 5 days. Admitted with mixed shock (hypovolaemic, vasoplegic, cardiogenic) and acute renal failure	Poor oral intake, chest pressure, palpitations, diaphoresis x 3 days. Haemod-ynamicall unstable on admission	Malaise, bilateral tinnitus, chest pain, and vomiting x 4 days. Hypotensive and mildly hypoxaemic on admission	Fever, cough, nausea, vomiting, lymphadenopath y x 6 days	Fever, chest pain, abdominal pain, diarrhoea, dark urine x 4 days	Fever, chills, throat pain, odynophagia x 2 days	Fever, fatigue, throat and neck pain, nausea, vomiting x 1 day	Weakness, sore throat, shortness of breath, decreased exercise tolerance x 3 days
SARS-CoV2 TESTING TIME ADMISSION	PCR(-), Ab(+)	PCR(+), Ab(+)	PCR(-), Ab(+)	PCR (-) , Ab(+)	PCR(+), Ab(+)	PCR(+), Ab(+)	PCR(+), Ab(+)	PCR (+), Ab testing not performed
BP	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
HEART RATE	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
RR	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
BT	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
O2%	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
DAYS OF ONSET OF SYMPTOMS	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
FERRITIN	1082ng/Ml	1919ng/ml	>100,000ng/ml	4400ng/ml	375ng/ml	378ng/ml	351ng/ml	948ng/ml
TROPONIN I	0.43ng/ml	0.48ng/ml	2.5ng/ml	Not available	1.8ng/ml	Not available	Not available	Not available
TROPONIN T	Not available	Not available	Not available	0.65ng/ml	Not available	0.06ng/ml	0.04ng/ml	0.24ng/ml
0.4	37 IU/L	440 IU/L	>10,000 IU/L	279 IU/L	30 IU/L	119 IU/L	160 IU/L	45 IU/L
AST	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
ALC NADIR	420	2500	400	700	2070	360	260	1980
IL-6	Not available	Not available	Not available	7 pg/ml	74.3pg/ml	34.8 pg/ml	56.2 pg/ml	Not available
WBC	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
TLC	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available

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PLATELETS	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
CREATININE	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
LDH	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
D DIMERS	2818ng/ml	2310ng/ml	3790ng/ml	1760ng/ml	275ng/ml	1882ng/ml	713ng/ml	1365ng/ml
FIBRINOGEN	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
PROCALCITONIN	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
CRP	344mg/L	84mg/L	217mg/L	318mg/L	182mg/L	355mg/L	319mg/L	485mg/L
BNP	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
COMPLICATIONS	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available
TREATMENT	Norepinephrine, vasopressin, midodrine, heparin, corticosteroids	Remdesivir, corticosteroids	Vasopressors, tocilizumab x 1, heparin	ASA, corticosteroids, IVIG x 1	Anticoagulation	Phenylephrine, anticoagulation, corticosteroids	Dobutamine, heparin, ASA x1, corticosteroids x2	Heparin, convalescent plasma
IMAGING	**TTE:** mild to moderate global hypokinesis, left ventricular ejection fraction 45%, mildly dilated right ventricle, mild tricuspid regurgitation, pericardial effusion. **CT chest:** bilateral patchy ground-glass opacities, pleural effusion. **CT abdomen/pelvis:** abdominal free fluid	**EKG:** atrial fibrillation/flutter with rapid ventricular response, ST segment changes. **TTE:** ejection fraction 25%–30% with global hypokinesis. **CXR:** small pleural effusions	**EKG:** ST-T segment changes. **CT chest**: dependent ground glass opacities. **CT abdomen:** hepatic steatosis	**TTE:** severely decreased ejection fraction, mild mitral regurgitation, right ventricular dysfunction, coronary artery dilatation. **CT chest**: ground glass opacities and atelectasis	**CT chest:** atelectasis. **CT abdomen/pelvis:** normal. **TTE:** mitral and tricuspid regurgitation	**CT neck:** retropharyngeal and parapharyngeal oedema.. **EKG:** intermittent complete heart block with narrow junctional escape without haemodynamic compromise. **TTE:** ejection fraction 50%. **CXR:** dense bilateral lower lobe air-space disease	**CT neck:** bilateral supraclavicular and cervical lymphadenopathy with no discrete abscess or collection. **CT chest:** bilateral patchy ground-glass opacities, pleural effusion. **TTE:** mild to moderate diffuse left ventricular hypokinesis. Mild to moderate decreased left ventricular ejection fraction (40%). Small posterior pericardial effusion. Mild tricuspid and mitral valve regurgitation	**EKG:** first degree AV block and nonspecific T-wave abnormalities. **TTE:** borderline left ventricular ejection fraction (55%)
OUTCOME	Discharged after 13 days	Discharged after 17 days	Deceased	Discharged after 6 days	Discharged after 5 days	Discharged after 19 days	Discharged after 12 days	Discharged after 8 days

Table 2: Cases of multisystemic inflammatory syndrome in adults after COVID-19 vaccination

N	9	10	11	12	13	14	15	16	17	18
AGE	42	36	45	44	21	31	25	38	20	40
SEX	M	F	M	F	M	F	F	F	F	M
RACE	Asian	Hispanic	Hispanic	Hispanic	African	African american	Hispanic	Hispanic	Not available	Not available
COMORBIDS	obesity	None	None	GERD, mild obstructive sleep apnoea, depression	None	Obesity, HTN, diabetes mellitus type 2	None	None	Asthma	Depression, hyperlipi-daemia
TYPES OF COVID-19 VACCINE	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Inactivated SARS-CoV-2 vaccine	No description
H/O COVID	Yes/PCR (+) 37 days earlier	No/Not tested	No/Not tested	Yes/Not tested	No/Not tested	Yes/PCR (+) 14 days before admission	No/Not tested	Yes/PCR (+) 28 days earlier	No	No
SYMPTOMS / SIGNS	Fever, shortness of breath, cough, diarrhoea, poor appetite, dysuria x 5 days.	Fever, abdominal pain, vomiting, and diarrhoea x 7 days; arthralgias and diffuse rash x 2 days. On admission, nonexudative conjunctivitis, mucositis, edema of bilateral hands and feet, palmar erythema, diffuse maculopapular rash, and cervical lymphadenopathy. No/Not tested	Fever, sore throat, diarrhoea, lower extremity pain, and diffuse rash x 6 days. On admission, hypotensive and tachycardic with nonexudative conjunctivitis, periorbital oedema, mucositis, unot available ateral cervical lymphadenopathy, and diffuse exanthem	Chills, sore throat, cough, myalgias x 2 days (8 days before admission); followed by diarrhoea and back pain x 3 days; followed by pleuritic chest pain and diarrhoea. Admitted with profound cardiogenic shock.	Fever, headache, and abdominal pain x 6 days; transient palmar rash. Hypotensive on admission with nonexudative conjunctivitis, mucositis, cervical lymphadenopathy	Fever x 1 day, throbbing neck pain, nausea, vomiting.	Fever, weakness, and shortness of breath x 7 days; followed by sore throat, mild cough, vomiting, and diarrhoea. Hypotensive on admission with conjunctivitis, mucositis, cervical lymphadenopathy.	Fever, occipital headache, conjunctival injection, odynophagia, mucositis, glossitis shortness of breath, vomiting, polyarthralgia, and rash x 5 days	Fever, rash, diarrhoea, vomiting, cardiogenic shock, acute renal failure	Fever, malaise, diarrhea, neck pain, headache, lethargy

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SARS-CoV2 TESTING TIME ADMISSION	PCR (-), Ab testing not performed	PCR (+), Ab (+)	PCR (+), Ab testing not performed	PCR (+), Ab testing not performed	PCR(-), Ab(+)	PCR (-), Ab testing not performed	PCR(+), Ab(+)	PCR (+), Ab (+)	Not available	Not available
BP	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	73/56	136/88
HEART RATE	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	130	102
RR	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	20	20
BT	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	37.4°C	37.3°C
O2%	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	99	97
DAYS OF ONSET OF SYMPTOMS	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	15	48
FERRITIN	7529ng/ml	684ng/ml	21,196ng/ml	2564ng/ml	1249 ng/mL	793 ng/mL	798 ng/mL	196 ng/mL	533ng/mL	1079.7ng/mL
TROPONIN I	Not available	0.07ng/ml	8.1ng/ml	Not available	Not available	Not available	0.06 ng/mL	<0.03 ng/mL	Not available	Not available
TROPONIN T	0.60ng/ml	Not available	Not available	1810ng/L	3.3 ng/mL	Not available	Not available	Not available	Not available	Not available
0.4	66 IU/L	116 IU/L	133 IU/L	242 IU/L	330 IU/L	52 IU/L	25 IU/L	126 IU/L	28 IU/L	83 IU/L
AST	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	43	55
ALC NADIR	1740	900	700	670	390	2120	1150	120	not available	not available
IL-6	Not available	Not available	117pg/ml	53.3pg/ml	Not available	Not available	Not available	Not available	not available	not available
WBC	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	32300	11300
TLC	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	not available	not available
PLATELETS	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	155000	312000
CREATININE	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	2.64	1.12
LDH	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	251	156
D DIMERS	3519ng/ml	652ng/ml	2977ng/ml	8691ng/ml	4260 ng/mL	453 ng/mL	1918 ng/mL	1250 ng/mL	3.01FEU/mL	1.15FEU/mL
FIBRINOGEN	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	801	875
PROCALCITONIN	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	160.92	0.01
CRP	387mg/L	300mg/L	547mg/L	141mg/L	338 mg/L	580 mg/L	90 mg/L	217 mg/L	378mg/L	199.4mg/L
BNP	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	1498	672
COMPLICATIONS	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available	Not available

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TREATMENT	Vasopressors, anticoagulation, corticosteroids	ASA, IVIG x1, corticosteroids	Heparin, corticosteroids, IVIG x 2, Tocilizumab x 1	Norepinephrine, dobutamine, vasopressin, milrinone, IVIG x 5 days, ECMO to LVAD and RVAD.	ASA, corticosteroids, IVIG x 1	CPR	ASA, IVIG x 2, vasopressors	ASA, corticosteroids, IVIG x 2	Vasopressors × 3 d, IVIG 100 g, methylprednisolone 1 g/d for 3 days, heparin, broad spectrum antibiotics, remdesivir	Dexamethasone 6 mg/d for 10 days, ceftriaxone, azithromycin, enoxaparin
IMAGING	TEE: mildly dilated left ventricle, moderately dilated right ventricle, moderate biventricular hypokinesis, moderately decreased left ventricular ejection fraction (35%). CXR: bilateral lower lobe opacities/airspace disease.	TTE: moderate tricuspid regurgitation, pericardial effusion. CT chest: right pleural effusion. Ultrasound: gallbladder wall oedema.	EKG: ST elevations in anterolateral leads. TTE: ejection fraction 40% with global hypokinesis. CT head/neck: pre-septal edema. Slit lamp: uveitis.	EKG: submillimeter ST-segment elevation in leads I/aVL, low QRS voltage. TTE: severely depressed left ventricular function, trace pericardial effusion. CT chest: mild ground glass opacities bilateral lung fields. CT abdomen/pelvis: small amount of ascites, periportal oedema.	CT abdomen/pelvis: mesenteric adenopathy and ileitis. EKG: sinus tachycardia. CT chest: normal. TTE: normal. CT coronary angiogram: normal	Pathology: small-vessel cardiac vasculitis; new pulmonary thrombi in a background of otherwise reparative changes in the lungs. CT head/neck: bilateral enlarged parotid glands. CT chest: interval improvement of bibasilar ground-glass opacities with cervical and anterior mediastinal lymphadenopathy.	TTE: moderate to severely reduced right-sided ventricular dysfunction, flattened interventricular septum in systole consistent with right ventricular pressure overload. EKG: right axis deviation. CT chest: scattered patchy ground glass opacities and peripheral consolidation, small bilateral pleural effusions with adjacent atelectasis; mild enlargement of the main pulmonary artery without	TTE: trace pericardial effusion, elevated pulmonary artery pressure (46–51 mmHg), normal left ventricular ejection fraction, no coronary artery abnormalities. CT chest/abdomen/pelvis: no pulmonary emboli, right upper lobe perihilar ground-glass opacities, septal and bronchial wall thickening, bilateral small-to-moderate pleural effusions	TTE: normal LV, EF 45% 30–35%, the next day chest radiograph: subtle bibasilar ground glass opacities	TTE: normal LV; EF: 50–55%; CT angiogram: no pulmonary embolism, minimal ground glass opacities

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							pulmonary embolus. CT	abdomen/ pelvis: mild peripancreatic fat stranding, nonspecific bilateral perinephric fat stranding.Discharged after 5 days		
OUTCOME	Discharged after 9 days	Discharged after 7 days	Discharged after 9 days	Discharged to rehabilitation facility after 18 days; home 7 days later	Discharged after 8 days	Deceased at admission (ventricular fibrillation)		Discharged after 7 days	Survived	Survived

Table 3: Cases of multisystemic inflammatory syndrome in adults after COVID-19 vaccination.

AGE	18	22	44	67	52	58	73
SEX	M	M	F	M	M	M	M
RACE	Not available	Not available	Not available	Not available	Not available	Caucasian	Not available
COMORBIDS	Asthma	None	Asthma	Hypertension, diabetes mellitus	Not mentioned	obesity, GERD, chronic back pain	DM, atrial fibrillation, hypertension, hyperlipidaemia, seasonal allergies
TYPES OF COVID-19 VACCINE	No description	No description	BNT162b2	ChAdOx1 nCoV-19 vaccine	BNT162b2 mRNA	mRNA-1273	moderna covid vaccine
H/O COVID	No	COVID-19 (12 days before vaccination)	No	No	No	No	No
SYMPTOMS/SIGNS	Fever, abdominal pain, diarrhoea, vomiting, headache	Fever, sore throat, abdominal pain, headache, fatigue, conjunctival hemorrhage, generalized erythematous maculopapular rash	Fever, hypotension, Left arm pain with worse on limb movement	Fever, rash, diarrhoea, headache, chills, and dizziness	Fever conjunctivitus,vomiting,heache	headache, weakness, nausea, myalgia, chills, profuse sweat, fever and diarrhoea	weakness, poor apetite, fever, chills and headaches
SARS-CoV2 TESTING TIME ADMISSION	Not available	Not available	Not available	Not available	PCR(-)	PCR(-)	PCR(-)
BP	98/58	110/-	81/38	90/60	66/47	110/70	Not available
HEART RATE	96	140	100	106	110	100	Not available
RR	20	Not available	Not available	20	22	22	Not available

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BT	36.6℃	39℃	>38℃	38.9℃	38.2℃	35.5℃	Not available
02%	97	Not available	Not available	95	93	Not available	Not available
DAYS OF ONSET OF SYMPTOMS	18	few hours later	2	7	20	7 days	Not available
FERRITIN	3002ng/mL	4357ng/mL	normal	1948ng/mL	30165	4236	not available
TROPONIN I	Not available	Not available	Not available	Not available	Not available	Not available	Not available
TROPONIN T	Not available	Not available	Not available	Not available	13.4	135	Not available
0.4	58 IU/L	81 IU/L	Not available	87 IU/L	52IU/L	Not available	Not available
AST	59	53	Not available	15	32	Not available	116
ALC NADIR	Not available	Not available	Not available	Not available	1072	Not available	Not available
IL-6	Not available	Not available	Not available	Not available	Not available	Not available	Not available
WBC	7000	15000	17100	18790	11290	12400	35.16
TLC	Not available	Not available	Not available	Not available	Not available not available	Not available	0.034
PLATELETS	63000	122000	Not available	158000	Not available	Not available	Not available
CREATININE	1.12	1.15	1.93	1.07	Not available	1.22	Not available
LDH	291	Not available	Not available	228	Not available	Not available	Not available
D DIMERS	3.44FEU/mL	14FEU/mL	2.564FEU/mL	Not available	2.4ug/ml	Not available	Not available
FIBRINOGEN	639	639	Not available	Not available	Not available	780	Not available
PROCALCITONIN	4.41	9	Not available	4.42	0.13	Not available	Not available
CRP	185.5mg/L	249mg/L	539mg/L	247.28mg/L	110.15mg/l	331	15.9
BNP	106	> 8,000	Not available	4687	Not available	Not available	Not available
COMPLICATIONS	Not available	Not available	Not available	Not available	Not available	Not available	atrial fibrillation, rapid ventricular rate, worsening hyponatraemia, decrease mental status and acute kidney injury, erythematous nonpruritic rash on arms and chest.
TREATMENT	IVIG 100 g, methylprednisolone 1 g/d for 3 days, anakinra 100 mg/d for 3 days, broad-spectrum antibiotics, aspirin	Dexamethasone 6 mg daily	Methylprednisolone 1 g/day for 3 days.Enoxaparin Aapixaban 5 mg two times per day for 6 months	Methyprednisolone 1 mg/kg/day for 5 days, and tapering as a half dose	oral prednisolone 20mg OD,colchicine0.6mg BD enoxaparin 40mg OD	doxycycline, trimethoprim/sulfa methoxazole	levoflaxacin, cefepime, metronidazole, hypertonic saine, fluid restriction, oral histamines, furosemide.

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IMAGING	TTE: normal LV size EF 40–45%, right ventricle mildly dilated with normal systolic function; chest radiograph: right pleural effusion; CT abdomen and pelvis: hepatomegaly, splenomegaly, small ascites; pericholecystic fluid; retroperitoneal adenopathy	Chest CT: Negative for pulmonary embolism, bilateral moderate pleural effusion, basal atelectasis. TTE: severe tricuspid regurgitation, pulmonary hypertension, RAE, RVH, EF 45%, thin pericardial effusion	Enoxaparin Aapixaban 5 mg two times per day for 6 months	PET-CT: reactive lymph node (Lt. cervical chain, Lt. Supraclavicular regions, both axillae, mediastinum, portocaval, pericaval, Lt. paraaortic, bilateral external iliac chains, inguinal regions), splenic hyperplasia No other focal inflammatory lesions were observed	(CT) imaging of the chest and abdomen revealed enlarged lymph nodes with soft tissue infiltrations in the left axilla and mesentery	chest X-ray and chest CT angiogram, abdominal CT: nonspecific bilateral fascial thickening, mesenteric fat, standing and lymph node enlargement, mild splenomegaly, dilated small bowel loops. ECG showed normal sinus rhthym with ST segment elevation. Echocardiogram showed elevated right ventricular systolic pressure, enlarged RV chamber size and hypokenisis, ejection fraction of 45%. cholangiopancreatography ruled out any billiary obstruction.	chest -ray clear, CT chest/abdomen/pelvis: showed nonspecific ground glass opacities in the lung and 18mm lesion on left hepatic lobe consist haemangioma.
OUTCOME	Survived	Survived	Survived	Survived	Survived	Survived	discharged after 18 days	

Table 4: Rheumatic inflammatory diseases post COVID-19 vaccination

Serial	Rheumatological syndrome	Gender, Age	Past COVID-19	Vaccine (days*)	Case description	Auto-antibodies	Treatment	Follow-up, weeks	Patient's status
1	**Skin vasculitis**	F, 64	No	MRNA-1273 (2)	Palpable purpura of the trunk and upper and lower limbs	None	GCs	N/A	N/A
2		F, 25	No	BNT162b2 (6)	Palpable purpura of the upper and lower limbs, erythematous facial rash	ANA	GCs, H1RAs	2	Remission (drug free)
3		M, 53	No	BNT162b2 (7)	Palpable purpura of the upper and lower limbs	None	GCS, H1RAs	12	Remission (drug free)
4		F, 31	No	BNT162b2 (7)	Urticarial vasculitis of the lower limbs, erythematous facial rash	None	GCs	6	Remission (drug free)
5		F, 43	No	AZD1222 (8)	Urticarial vasculitis of the upper and lower limbs	None	GCs	4	Remission

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6		F, 67	No	BNT162b2 (10)	Urticarial vasculitis of the lower limbs, fever	None	GCs	8	Remission
7		F, 68	No	AZD1222 (10)	Livedo reticularis of the upper and lower limbs	ANA	GCs	4	Active
8		F, 25	No	MRNA-1273 (10)	Palpable purpura of the upper and lower limbs	None	GCs	3	Remission (drug free)
9		F, 77	No	BNT162b2 (10)	Palpable purpura of the lower limbs, puffy hands	ANA	None	1	Remission (drug free)
10		F, 47	No	BNT162b2 (15)	Palpable purpura of the lower limbs	RF	GCs	8	Remission
11		F, 29	Yes	BNT162b2 (18)	Palpable purpura of the lower limbs	None	GCs	2	Remission (drug free)
12		M, 38	Yes	BNT162b2 (21)	Urticarial vasculitis of the lower limbs, fever	None	GCs, H1RAs	4	Remission (drug free)
13	**Undifferentiated CTD**	F, 61	No	BNT162b2 (3)	Fever, chest pain, fatigue, arthralgia, myalgia. Laboratory and imaging studies demonstrated inflammatory pleuro-pericardial effusion with no evidence of infection or cancer. Lack of response to GCs/NSAIDs/colchicine treatment; good response to anakinra	ANA, anti-SSA	GCs, NSAIDs, colchicine, anakinra	4	Improved
14		M, 50	No	AZD1222 (3)	Scarring alopecia, arthralgia of large joints, myalgia	ANA	GCs	8	Improved
15		M, 45	No	BNT162b2 (5)	Chest pain, fatigue, arthralgia, myalgia. Imaging demonstrated pericardial effusion with no evidence of infection or cancer	ANA	NSAIDs	N/A	N/A
16		M, 32	Yes	BNT162b2 (5)	RP with non-specific NVC abnormalities, polyarthritis of large joints, proximal myalgia with normal CPK values, sudden-onset dysphagia	ANA, anti-Jo-1	GCs, MTX	4	Active
17	**Sjögren's syndrome**	F, 44	No	AZD1222 (4)	Xerostomia, xerophthalmia, dry cough, dyspnoea, RP with non-specific NVC abnormalities. HRTC showed bilateral basal GGO opacities	ANA, anti-SSA	GCs	12	Improved
18		F, 62	No	AZD1222 (15)	RP with non-specific NVC abnormalities, xerostomia, xerophthalmia	FR, ANA, anti-SSA	HCQ	N/A	N/A

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19	**Very early systemic sclerosis**	F, 42	No	BNT162b2 (20)	RP with puffy fingers and NVC evidence of early scleroderma pattern, arthralgia, myalgia, fatigue	ANA, anti-centromere	GCs, HCQ, Felodipine	12	Improved
20	**Overlap CTD (scleromyositis)**	F, 37	No	BNT162b2 (4)	Sudden-onset muscle pain/weakness with markedly increased CPK levels, RP with NVC evidence of early scleroderma pattern	ANA, anti-Pm/Scl-75, anti-Ku, anti-RNA polymerase III, anti-fibrillarin	GCs, IVIG	1	Active
21	**Atypical acrosyndrome**	F, 41	Yes	MRNA-1273 (2)	Acrocyanosis with puffy fingers and non-specific NVC abnormalities, arthralgia, myalgia	ANA	NSAIDs, aminaphtone	4	Active
22		F, 37	No	AZD1222 (28)	RP with puffy fingers and non-specific NVC abnormalities	None	NSAIDs, Felodipine	12	Remission (drug free)
23	**Iperinflammatory syndrome**	M, 16	No	BNT162b2 (2)	Pharyngodynia, intermittent erythematous skin rash, arthralgia, flexor tenosynovitis of the fingers, fever. Laboratory tests showed marked increase in inflammatory markers and neutrophil count, liver injury, and hyperferritinaemia.. PET/CT scan revealed accumulation of 18-FDG in axillar and inguinal lymphnodes, bone marrow, and spleen (enlarged)	None	GCs, NSAIDs	3	Active
24	**Giant cell arteritis**	M 78	No	AZD1222 (1)	Temporoparietal headache, jaw claudication, fatigue. TAB showed findings consistent with inflammation of the vessel wall and the presence of giant cells. PET/CT scan showed	None	GCs	3	Active

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					18F-FDG accumulation in proximal aorta				
25		F, 82	No	MRNA-1273 (8)	Tenderness and swelling of the right temporal artery followed by sudden-onset visual loss	None	GCs	6	Remission
26		F, 67	No	AZD1222 (14)	Jaw claudication, fatigue. Temporal artery US showed the typical "halo" sign	None	GCs	6	Remission
27	**Takayasu's arteritis**	F, 31	No	BNT162b2 (1)	Carotidynia, fatigue, night sweating. Doppler US of neck vessels showed diffuse thickening of right CCA; FDG PET-CT scan confirmed accumulation of 18-F FDG in right CCA and both subclavian arteries	None	GCs	8	Remission
28		M, 39	No	AZD1222 (12)	Fever, fatigue, erythematous rash of the trunk. PET/CT scan showed 18-F-FDG accumulation in ascending aorta and aortic arch	None	GCs	12	Remission
29	**Small-vessel vasculitis**	M, 73	No	BNT162b2 (5)	Axonal sensorimotor polyneuropathy, moderate proteinuria, microscopic hematuria, RP with non-specific NVC abnormalities, nodular lesions, and consolidation on HRTC	RF	GCs	4	Active
30	**Cryoglobulinemic vasculitis**	F, 60	No	AZD1222 (10)	Lower limb petechiae, fever, fatigue. Laboratory test showed complement consumption and acute kidney injury with moderate proteinuria	ANA, aPL, cryoglobulins	GCs	8	Remission

patients received Tocilizumab. Eight (32%) patients needed vasopressor support, 10 (40%) required ICU care, three (0.12%) required mechanical ventilation and one required mechanical circulatory support. Two out of 25 patients died, while the rest survived.[18,19]

Moreover, the development of autoimmunity post Covid-19 vaccine has fascinated researchers due to the molecular mimicry of the specific human protein and the components of the vaccine.[19] Usually adverse reactions of the vaccine are mild and restricted to the injection site but amongst systemic adverse effects, arthralgias are the most common symptom noted as mentioned above. Few cases of rheumatic inflammatory diseases post vaccination have been reported.[19] Until now, 12 (40%) patients with skin vasculitis, four (13.3%) with undifferentiated connective tissue diseases (CTD), two (6.7%) with Sjogren's syndrome (SjS), one (3.3%) with very early systemic sclerosis (SSc), one (3.3%) with overlap CTD (scleromyositis), two (6.7%) with atypical acrosyndrome,[10] one (3.3%) with hyper-inflammatory syndrome, three (10%) with giant cell arteritis (GCA), two (6.7%) with Takayasu's arteritis (TAK), one (3.3%) with small vessel vasculitis, and one (3.3%) with cryoglobulinaemic vasculitis have been reported.[19] All patients were followed up to four weeks and it was noted that 70% of the patients had remission, whereas 23.3% of the patients had ongoing disease. 10% of the patients were lost to follow-up. Steroids, DMARDS, NSAIDS, and IVIG, Histamine receptor 1 antagonist or vasoactive drugs were used to treat majority of the patients. The data has been compiled in Table 4.

With time and the increasing number of such cases being reported, the management for MIS-V has become a little clearer. Steroids, IVIG and other immunomodulatory agents can be used to treat MIS-V as for MIS-C/A.[19-24]

We hope that this series will help guide clinical assessment, management and a better understanding of the relationship between the risks of inflammatory disease as a consequence of vaccination which still remains controversial. Further attention should be paid to classify the patients who are at an increased risk of developing these manifestations.

Conclusion

This case underscores the importance of recognizing and understanding Multi-System Inflammatory Syndrome secondary to vaccination (MIS-V) as a rare but severe complication post-COVID-19 vaccination. The patient's complex presentation and unfortunate outcome highlight the challenges in managing such cases, emphasizing the need for continued vigilance, research, and collaboration among healthcare professionals. As vaccination efforts persist, awareness of potential adverse reactions, including rare syndromes like MIS-V, remains critical for informed decision-making and patient care.

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NI: Writing.
AEA: Writing and editing.
MORK, MRA: Editing.