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Original Research

Multisystem inflammatory syndrome associated with SARS-COV-2 infection in an older adult: Case presentation

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Abstract

Multisystem inflammatory syndrome (MIS) post-SARS-COV-2 infection has been described in children. Few case reports of MIS in adults are available, the majority described in young previously healthy persons. Here we report the case of MIS that meets the Center for Disease Control definition of MIS in adults in an elderly patient with known type 2 diabetes with a recent history of COVID-19. As the number of COVID-19 cases continues to rise, we believe that more and more cases of adult MIS will be reported. Thus, investigations aiming to characterize the full spectrum of clinical manifestations, to clarify the pathogenetic mechanisms leading to adult MIS as well as long-term consequences are needed.

Keywords: COVID-19, SARS-COV-2, multisystem inflammatory syndrome, adult, elderly, type 2 diabetes.

Background and aims

Multisystem inflammatory syndrome (MIS) post-SARS-COV-2 infection has been described in children [1–3]. Usually, it occurs after viral clearance, within weeks post infection and includes shock, cardiac dysfunction, and increased inflammatory markers [1].

Several similar reports of MIS cases following SARS-COV-2 infection have been also recently described in adults [4–7], and Center for Disease Control (CDC) has developed case definitions for adult MIS that include 1) severe illness; 2) SARS-CoV-2 infection during hospitalization or within the previous 12 weeks before the current episode identified either by polymerase chain reaction (PCR), by antigen rapid testing or antibody identification; 3) severe dysfunction of ≥1 extrapulmonary organ or system (including shock, arterial hypotension, cardiac dysfunction, thrombosis, thromboembolism, or acute liver injury); 4) increased levels of inflammatory biomarkers (ferritin, C-reactive protein [CRP], interleukin-6 or D-dimer); 5) no severe respiratory illness [4]. Despite this proposed definition, no clear picture of the epidemiology of MIS in adults is available, the pathogenetic mechanism is not currently known and neither are the long-term effects of this syndrome [4].

Case presentation

A 69-year-old woman was admitted on the 5th of March 2021 to the diabetes department through the emergency room (ER) for worsening dyspnea and fatigue in the past week and syncope occurring in her family physician's office.

The patient was known with insulin-treated type 2 diabetes mellitus (T2DM), pulmonary silicosis stage 2/3, arterial hypertension (treated with angiotensin-receptor blockers, alpha-blockers, and beta-blockers), cholelithiasis, chronic venous insufficiency CEAP V, umbilical hernia, and urinary incontinence. The patient had a history of moderate SARS-COV-2 infection needing hospitalization diagnosed by RT-PCR test on 28.01.2021, 4 weeks prior to the current presentation, and was discharged from the hospital 2 weeks prior to presentation in the ER on prednisone therapy with gradually reduced doses. At presentation, the prednisone dose was 20 mg/day.

At ER presentation on 4th of March 2021, physical exam was normal, blood pressure (BP) was 144/74 mmHg, heart rate (HR) 84 bpm. There was no fever, no motor weakness, and no sensory loss. ECG was normal and chest X-ray showed accentuation of bilateral interstitial markings; abdominal ultrasonography reported a fatty liver only. Laboratory investigations showed hyperglycemic hyperosmolar state with blood glucose on presentation – 893 mg/dl, K=7.29 mmol/l, Na=119 mmol/l (corrected for hyperglycemia 138 mmol/l), arterial pH=7.348, pO_2=110.1 mmHg; SaO_2=99%, pCO2=25.2%, calculated plasma osmolarity=336 mOsm/kg, cholestasis, hyperferritinemia (579 ng/ml [reference range 10–120 ng/ml]) (Table 1). SARS-CoV-2 rapid antigen test was negative. Urinary tests were normal except for glycosuria. Initial evolution under insulin therapy, rehydration, and salbutamol were favorable and the patient was transferred on the same day to the diabetes department for further therapy of hyperglycemia.

On presentation in the diabetes department patient was conscious, with dried skin and mucosa. Pulmonary auscultation revealed bronchovesicular sounds on the posterior chest. The abdomen was soft with an umbilical hernia, approximately 8 cm diameter with slight palpatory tenderness and no signs of ischemia, with normal bowel sounds. BP was 101/50 mmHg, heart rate 72 bpm, SaO2=97%. The rest of the systemic examination was unremarkable. Laboratory investigations showed a glycaemia of 447 mg/dl, hyperkalemia (6.54 mmol/l), hyponatremia, cholestasis, and hepatic cytolysis, leukocytosis (12.04*10^9/l) with neutrophilia (10.10*10^9/l), high CRP (2.75 mg/dl), negative urine culture – Table 1. It was decided to continue insulin therapy, rehydration, therapy with loop diuretics, salbutamol, anticoagulant therapy, prednisone, and empiric large spectrum antibiotic therapy, although no cause for bacterial infection could be established.

Liver tests brought out a hepatocytolysis syndrome, normal bilirubin but high alkaline phosphatase (FA), and gamma-glutamyl transferase (GGT). The peak (Table 1) occurred on days 4 and 5 when pyridoxine hydrochloride, DL-aspartic acid, ursodeoxycholic, acid and arginine were added with favorable outcomes. Possible viral and autoimmune etiology was investigated with negative outcomes (HCV antibodies, HBS antibodies; ANA, anti-SM, AMA, anti-LKM, anti-MPO antibodies). An abdomen ultrasound examination was performed and showed the presence of gall bladder stones, two simple liver cysts, and umbilical hernia with no signs of complications.

On day 5 of hospitalization, due to persistent hypotension despite rehydration and stalled hypertension therapy, lab tests showed slightly elevated troponin I (12.9 pg/ml), with a growing tendency reaching maximal value the next day (18.7 pg/ml). A cardiac examination and echocardiography were performed on day 10 revealing an ejection fraction >50%, minor mitral insufficiency, diastolic dysfunction stage 1, no signs of pulmonary hypertension, and no pericardial effusion. Thyroid function was normal with FT4, TSH within normal range.

Considering the patient was still on prednisone therapy we decided to postpone the dose reduction and continue hepatic supportive therapy mentioned above as well as anticoagulant therapy, with favorable evolution. At discharge (day 12), all laboratory investigations were normal except for persistent hepatocytolisis, cholestasis, and inflammation which still persisted. D-dimers are not routinely measured and were not assessed.

Discussion

Although SARS-CoV-2 infection-related MIS has been well described in children, few case

Table 1: Vital signs and laboratory investigations.

Markers	04.03.2021	05.03.2021	08.03.2021	09.03.2021	10.03.2021	11.03.2021	15.03.2021	Reference range
Vital signs								
Temperature, °C		36.4	36.3	36.5	36.4	36.5	36.3	<37.0
Heart rate, beats per minute	84	72	93	90	94	69	70	60–100
Systolic/diastolic blood pressure, mmHg	144/74	101/50	96/66	105/66	103/72	115/67	155/82	≤130/80
Oxygen saturation, %	98	97	93	97	99	97	96	≥95
Hematologic								
White blood cells, per 10^9/l	13.44	12.04	9.19		9.69	6.4	7.25	4–10
Neutrophils, per 10^9/l	11.43	10.1	7.61		7.03	4.49	4.22	1.8–7.4
Lymphocytes, per 10^9/l	1.32	1.1	0.98		1.93	1.49	2.5	1.1–3.5
Hemoglobin, g/dl	12.3	10.3	11.0		11.1	8.9	9.4	12.0–15.5
Hematocrit, %	35.8	30.3	33.1		32.7	26.0	29.0	37.0–47.0
Platelet count, per 10^9/l	345	306	243		256	185	220	150–400
Chemistry								
Sodium, mmol/l	119	131	131	125	138	143	138	136–146
Potassium, mmol/l	7.29	6.54	4.92	4.43	4.57	4.26	3.51	3.5–5.1
Chloride, mmol/l	93	103	98	103	95	100	105	101–109
Glucose, mg/dl	893	447	296	188	240	180	111	

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Urea, mg/dl	134	101.21	57.72				29.86	17–43
Creatinine, mg/dl	1.67	1.16	1,12			0.74	0.72	0.51–0.95
Aspartate aminotransferase, U/l	27	34	128	85	117	69	41	<35
Alanine aminotransferase, U/l	53	52	173	145	163	116	76	<35
Alkaline phosphatase, U/l	202	125		260	373	283	245	30–120
GGT, U/l	463	398		889	1148	869	757	<38
Total bilirubin, mg/dl	0.77	0.78		0.70		0.6	0.69	0.3–1.2
Creatine kinase, U/l	105			57				<142
CK-MB, U/l	29			15				<24
LDH	299							<247
Inflammation								
C-reactive protein, mg/dl		2.75	12.51		12.11	8.42	3.9	<0.5
Ferritin, ng/ml	579						746	10–120
Fibrinogen					534.8		528.8	200–400
Troponin, pg/ml				12.9	18.7	10.8		<11.6
Procalcitonin, ng/ml						0.07		<0.05

reports of MIS in adults are available, the majority described in young previously healthy persons. Clinical presentation varied and included neurological involvement [8, 9], cardiogenic and vasoplegic shock [5], gastrointestinal symptoms, or dermatologic manifestations [4]. Paraclinical changes of these cases included elevated inflammatory markers, such as D-dimers, ferritin and CRP, increased levels of B-type natriuretic peptide (BNP), and troponin, as well as anemia, lymphopenia, and hypoalbuminemia in some cases [10, 11]. Despite various clinical presentation the common ground was represented by the history of SARS-COV-2 infection and markedly increased inflammatory markers.

Although our case presented initially as an acute hyperglycemic complication in a patient with known T2DM, it meets the CDC definition of MIS in adults, with a recent history of COVID-19, lack of any respiratory infection, markedly elevated inflammatory markers (CRP and ferritin) and dysfunction of two extrapulmonary organs or systems (arterial hypotension and acute liver injury). Regarding cardiac involvement suggested by the persistent low blood pressure, we could not perform NT-pro-BNP and no structural or functional changes related to myocardium could be identified on ultrasonography. However, the increase of troponin levels is in line with previous adult MIS cases reported in the literature [12]. Unlike other cases reported in the literature, our patient had a mild form of MIS, with no shock, probably due to undergoing corticoid therapy. Also, the age of our patient is unusual, as many MIS cases are reported in young adults [4], with only one case reported in the elderly [11]. This may also explain the mild clinical presentation.

The mechanism involved in the adult MIS is unknown. However, in children it was described as a late-onset cytokine storm due to aberrant immune response, genetic variation of mechanisms involved in immune complexes clearance or delayed interferon response [10, 11, 13]. Aberrant immune response results in antibodies against SARS-COV-2 triggering systemic inflammation and mediating organ damage post-SARS-CoV-2 infection [10]. Also, it is hypothesized that SARS-COV-2 infection may trigger an autoimmune/auto-inflammatory response [13].

Conclusions

In conclusion, here we present a case of adult MIS post-COVID-19 in an old adult. As the number of COVID-19 cases continues to rise, we believe that more and more cases of adult MIS will be reported. Thus, investigations aiming to characterize the full spectrum of clinical manifestations, to clarify the pathogenetic mechanisms leading to adult MIS as well as long-term consequences are needed.

Conflict of interest

The authors declare no conflict of interest.

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