



Case Report

An unusual presentation of recurrent COVID-19 associated systemic capillary leak syndrome in a patient with multi-system inflammatory syndrome in adults (MIS-A) due to prior COVID-19 infection: Case report and literature review

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ABSTRACT

Introduction: and importance: Systemic capillary leak syndrome (SCLS) and multisystem inflammatory syndrome in adults (MIS-A) are very rare multifactorial etiology disorders associated with COVID-19 infection. Both conditions are thought to be manifested by the inflammatory state induced by COVID-19 infection. Recurrent COVID-19-associated concomitant/successive manifestations of both disorders have not been reported yet.

Case presentation: We report a 38-year-old Asian gentleman who presented initially with fever, cough, shortness of breath, body aches, dizziness, and epigastric pain due to COVID-19 infection. A few days before this presentation, the same patient developed multisystem inflammatory syndrome in adults (MIS-A). Later, based on clinical and laboratory investigations, he was diagnosed with new-onset systemic capillary leak syndrome (SCLS). Despite resuscitative measures, the patient passed away.

Clinical discussion: The increased risk of inflammatory complications associated with COVID-19 infection is an emerging concern. Our case report signifies the importance of COVID-19 awareness in less educated and underserved areas with fewer information resources. Rare and fatal manifestations should also be advertised and discussed with the general masses with equal emphasis.

Conclusion: This case signifies the importance of understanding the pathophysiology of new-onset systemic capillary leak syndrome in a patient with recurrent COVID-19 infection and utilizing clinical knowledge and decision-making to manage such rare and complex disorders.

1. Introduction

Systemic capillary leak syndrome (SCLS) is a very rare disorder of multifactorial etiology which manifests initially as a prodrome of non-specific symptoms, ultimately leading to a cluster of fatal symptoms like hypotension, edema, hemoconcentration, and shock [1]. Most cases of SCLS are idiopathic, but identifiable triggers like viral infections, long traveling, and vigorous physical activity have been identified [2]. A case reported by Ebdrup et al. linked influenza virus infection with new-onset SCLS [3]. Increased vascular permeability due to endothelial damage from inflammatory substances is the underlying pathophysiology of SCLS [4]. The Coronavirus disease 2019 (COVID-19) can lead to a generalized inflammatory state in the body, manifesting as a broad spectrum of symptoms [5]. SCLS has been rarely reported in patients

with COVID-19 disease [1,2]. We report the first case of new-onset systemic capillary leak syndrome in a patient with recurrent COVID-19 infection who had underlying multi-system inflammatory syndrome in adults (MIS-A) due to prior covid-19 illness. Our case is unique from other previously published cases in that the patient developed SCLS right after developing MIS-A due to a second COVID-19 infection. This case report has been reported in line with the SCARE Criteria [6].

2. Case Presentation

A 38-year-old gentleman initially presented with fever, cough, shortness of breath, body aches, dizziness, and epigastric pain for one day. This patient was admitted to the same hospital twice before for a

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COVID-19 infection and its complications. At his first-ever visit in November 2021, he presented with fever, cough, and severe shortness of breath. He was diagnosed with severe COVID-19 infection based on clinical and radiographic features on high resolution computed tomography (HRCT) of the chest (Fig. 1). A reverse transcription-polymerase chain reaction (RT-PCR) test was also positive for COVID-19 infection. At first, he was administered oxygen via a simple oxygen mask and was transferred to the isolation floor. He could not maintain his oxygen saturation and was shifted on oxygen therapy via a non-breathable (NRB) mask. Despite all measures, his respiratory status continued to deteriorate. He was transferred to the COVID critical care unit of the hospital, where he received mechanical ventilation and other medical interventions. His respiratory status improved gradually, and he was discharged after 22 days after a series of double negative RT-PCR tests for COVID-19 infection.

In the first week of January 2022, the same patient presented in the emergency department with fever, an altered level of consciousness, abdominal pain, diarrhea, and a maculopapular rash on the chest and abdomen. There was no cough or shortness of breath. His pulse rate was 120 bpm, blood pressure was 110/70 mmHg, a fever of 39.5°C, and oxygen saturation was 96%. On systemic examination, the patient's Glasgow coma scale (GCS) level was 12/15 (E3V4M5). A

Blanching and non-pruritic maculopapular was observed on the chest and abdomen. The patient was treated with isotonic fluids, empiric antibiotics, i.e., ceftriaxone and vancomycin, and paracetamol. A venous blood sample, urine sample, and COVID-19 nasopharyngeal swab were taken for routine laboratory investigations. All the results of the investigations are given in Table 1. The RT-PCR test came out negative twice. The patient was hospitalized but did not show any improvement with ongoing medications. Computed tomography (CT) of the chest, abdomen, and pelvis was done, not showing any significant findings. All the blood cultures were negative for any infection. The patient's condition was getting deteriorated. The maculopapular rash spread to both upper and lower limbs but spared hands and feet. Based on the clinical and radiological investigations, a diagnosis of Post-COVID multisystem inflammatory syndrome in adults (MIS-A) was made. The patient was initiated on intravenous dexamethasone therapy, which was then changed to oral form once the patient's condition became stable. The



Fig. 1. High-resolution computed tomography (HRCT) chest showed multifocal, multi-lobar ground-glass opacities in central and peripheral locations, more pronounced in middle and lower lobes, with septal thickening, giving a classical crazy paving appearance.

Table 1

Laboratory investigations of the patient at the time of admission (2nd visit) and discharge against the diagnosis of multisystem inflammatory syndrome in adults (MIS-A).

Laboratory Investigation	At Hospital Admission (Day 0)	Day 3	At Discharge (13th day)	Normal Reference Range
Hemoglobin	15.2 g/dL	16.5 g/dL	17.4 g/dL	13.6–17.7 g/dL
WBCs Total count	21672/ μ L	18436/ μ L	6780/ μ L	4500–11000/ μ L
Neutrophils (%)	80%	76%	48%	40–60%
Lymphocytes (%)	12%	16%	28%	20–40%
Platelets (10^3 / μ L)	111	143	267	150–450
D-Dimer	1173 ng/mL	863 ng/mL	156 ng/mL	100–250 ng/mL
LDH	944 U/L	632 U/L	212 U/L	140–280 U/L
Serum ferritin	550 ng/mL	414 ng/mL	189 ng/mL	20–336 ng/mL
CRP	156.3 mg/L	86.5 mg/L	6.4 mg/L	\leq 10 mg/L
Serum Creatinine	2.1 md/dL	1.8 md/dL	0.8 md/dL	0.7–1.3 md/dL

WBC= White blood cells; LDH = Lactate dehydrogenase; CRP= C- reactive protein.

inflammatory markers gradually reduced with the treatment, and the maculopapular rash disappeared. The antibiotics were stopped after five days. The patient was stable on the 12th day of admission, and all the laboratory investigations were in the normal range. He was discharged on the 13th day after proper counseling.

Three days after the patient was discharged, he returned to the emergency department with complaints of fever, cough, shortness of breath, body aches, dizziness, and epigastric pain for one day. On presentation to the hospital, the blood pressure was 80/40 mmHg, pulse rate was 136 bpm, respiratory rate was 28/min, and oxygen saturation was 88% on room air. On examination, the patient had coarse crackles in bilateral lower lung fields. Massive bilateral edema was also observed on both lower limbs. Due to the high clinical suspicion, a nasopharyngeal swab was collected for COVID-19 RT-PCR, which was positive, confirming recurrent COVID-19 infection. The patient was administered 5 L of crystalloid along with broad-spectrum antibiotics. Echocardiography



Fig. 2. Transthoracic echocardiography (apical two-chamber left ventricle view) showing large pericardial effusion (Arrows).

was done, which showed pericardial effusion (Fig. 2). All other parameters were normal. A venous sample was drawn for laboratory investigations. All the results are given in Table 2. Based on clinical and laboratory investigations, a diagnosis of systemic capillary leak syndrome (SCLS) was made. The patient's condition kept deteriorating, and he went into a hypotensive shock requiring steroids, vasopressors, intubation, and mechanical ventilation. Despite ongoing resuscitative measures, the patient's condition worsened, and he developed cardiac arrest. Cardiopulmonary resuscitation was unsuccessful, and he passed away.

3. Discussion

The increased risk of inflammatory complications associated with COVID-19 infection is an emerging concern. A few but notable cases of both multisystem inflammatory syndrome in adults (MIS-A) and systemic capillary leak syndrome (SCLS) have been reported distinctively in the existing literature. Our case reported a patient who developed both conditions due to recurrent COVID-19 infection. To our knowledge, this is the first case report in which the patient developed new-onset SCLS due to recurrent COVID-19 infection right after the development of MIS-A due to prior COVID-19 infection.

The underlying pathophysiology for developing both complications is unclear, but the cytokine

Storm and raised inflammatory markers are presumed to be the cause of these manifestations [7].

COVID-19 virus, upon entry into the human body, binds the angiotensin-converting enzyme 2.

(ACE-2) receptor, which is expressed on pulmonary type 2 pneumocytes, cardiac myocytes, and vascular endothelial cells. This explains their role in COVID-19 associated endothelial cell damage [8]. Existing literature supports these kinds of inflammatory complications associated with COVID-19 infection. For example, a case study by Knox et al. reported a similar presentation of new-onset SCLS [2]. Various other cases have been reported showing the association of MIS-A with COVID-19 [9, 10].

Our case report signifies the importance of COVID-19 awareness in less educated and underserved areas with fewer information resources. Rare and fatal manifestations should also be advertised and discussed with the general masses with equal emphasis. In addition, physicians should be made aware and trained to go out of the preset diagnostic protocols for COVID-19 and keep the rare vascular/inflammatory manifestations in differential diagnosis while assessing such patients. Finally, we suggest that further studies should be done to understand this association of COVID-19 infection and atypical symptoms, along with a better insight into underlying pathophysiology.

4. Conclusion

The COVID-19 associated rare manifestations may be multifactorial secondary to the inflammatory state, vascular injury, or autoimmunity. Therefore, understanding the pathophysiology of new-onset systemic capillary leak syndrome in a patient with recurrent COVID-19 infection and utilizing clinical knowledge and decision making is vital in managing such rare and complex disorders.

Ethical approval

Nishtar Medical University and Hospital, Multan0000-NMU-0068.

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Table 2

Laboratory investigations of the patient at the time of presentation to the emergency department (3rd visit) against the diagnosis of systemic capillary leak syndrome (SCLS).

Laboratory Investigation	At Hospital Admission	Normal Reference Range
Hemoglobin	18.7 g/dL	13.6–17.7 g/dL
WBCs Total count	5400/ μ L	4500–11000/ μ L
Hematocrit (%)	56%	40–52%
Albumin	1.2 g/dL	3.4–5.4 g/dL
Serum Creatinine	1.8 mg/dL	0.7–1.2 mg/dL
Erythrocyte Sedimentation rate	28 mm/h	0–20 mm/h
CRP	14.5 mg/L	\leq 10 mg/L

WBC= White blood cells; CRP= C- reactive protein.

Author contribution

SY conceived and designed the study. SY and HM were responsible for data collection, acquisition and analysis and/or interpretation the data. SY and HM performed the literature review and wrote the initial manuscript. HM critically revised the manuscript. All authors have approved the final manuscript.

Registration of research studies

- 1 Name of the registry: NA.
- 2 Unique Identifying number or registration ID: NA.
- 3 Hyperlink to your specific registration (must be publicly accessible and will be checked): NA.

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Consent for publication

Written informed consent was obtained from the patient for publication of this case report and

Any accompanying images. Written informed consent was also taken from the patient's next of

Kin, his son in this case. A copy of the written consents is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

Not applicable.

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Declaration of competing interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104309>.

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