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Systemic Capillary Leak Syndrome Secondary to Coronavirus Disease 2019



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Systemic capillary leak syndrome is a rare disorder characterized by dysfunctional inflammatory response, endothelial dysfunction, and extravasation of fluid from the vascular space to the interstitial space leading to shock, hemoconcentration, hypoalbuminemia, and subsequent organ failure. The condition may be idiopathic or secondary to an underlying cause, which can include viral infections. Here we describe a patient with acute coronavirus disease 2019 (COVID-19) infection who presented with hemoconcentration, shock, and hypoalbuminemia. The patient subsequently developed rhabdomyolysis and compartment syndrome of all four extremities, requiring fasciotomies. This is the first reported case of systemic capillary leak syndrome associated with COVID-19 infection. This case adds to the evolving spectrum of inflammatory effects associated with this viral infection. CHEST 2020; 158(6):e267-e268

KEY WORDS: capillary leak; COVID-19; shock; systemic capillary leak syndrome

Systemic capillary leak syndrome (SCLS) is a rare disorder characterized by severe hypotension, hemoconcentration, and hypoalbuminemia due to extravasation of plasma and proteins into the interstitial space as a result of endothelial dysfunction.^{1,2} SCLS may be idiopathic or secondary to an underlying cause. Viral infections have been reported to be a cause for secondary capillary leak syndrome.³ We report a case of SCLS in a patient who presented to our institution with coronavirus disease 2019 (COVID-19) pneumonia and developed profound shock.

Case Report

A 63-year-old man with a medical history of systemic hypertension presented to our facility with symptoms of fevers, chills, nonproductive cough, and epigastric pain for 3 days. Laboratory examination revealed a lactic acidosis of 4.9 mmol/L, serum creatinine of 2.34 mg/dL,

hemoglobin of 21.6 g/dL, hematocrit of 65.6%, serum protein of 6.4 g/dL, albumin of 3.5 g/dL, and normal liver enzymes. Testing for severe acute respiratory syndrome coronavirus 2 was positive. Despite volume crystalloid resuscitation, and broad-spectrum antibiotics, his condition rapidly deteriorated and required initiation of vasopressors, intubation, and mechanical ventilation. CT scan of the chest and abdomen showed scant peripheral ground-glass infiltrates but was unrevealing for a cause for his abdominal pain or source of septic shock. On echocardiogram, bilateral ventricular function was normal; there was a pericardial effusion without signs of tamponade.

Over the next few hours, despite ongoing resuscitation, vasopressor requirement increased, lactic acid rose to >20 mmol/L, and serum protein and albumin dropped to <3.0 g/dL and <1.5 g/dL, respectively. His

ABBREVIATIONS: COVID-19 = coronavirus disease 2019; SCLS = systemic capillary leak syndrome

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DOI: <https://doi.org/10.1016/j.chest.2020.06.049>

vasopressor requirements were norepinephrine at 1 µg/kg/min, vasopressin 0.03 units/min, and epinephrine 0.15 µg/kg/min.

He developed tense anasarca, contractures of extremities, and rising creatine kinase at over 20,000 U/L. Measured intracompartmental pressures in all compartments of his extremities revealed elevated pressures that ranged from 50 to 79 mm Hg and were all within 30 mm Hg of the diastolic BP, consistent with compartment syndrome. The surgical team then performed fasciotomies of both arms and both lower legs. Up to this point, he had received 15 L balanced crystalloid and had been initiated on continuous renal replacement therapy. However, despite maximal supportive care, the patient's condition continued to decline. The family decided to withdraw care approximately 24 hours after admission.

Discussion

Idiopathic capillary leak syndrome was first described by Clarkson et al¹ in 1960. The syndrome is characterized by episodic hypotension, edema, hemoconcentration, and hypoalbuminemia due to extravasation of fluid and proteins from the intracellular space into the interstitial space. The exact cause of the hyperpermeability is not clear, though it is believed to be the result of a cytokine-mediated response leading to apoptosis of the endothelium.^{1,2} Patients with idiopathic SCLS often report a preceding trigger, which is often reported as a flu-like syndrome, before developing an episode with acute presentation of hypotension. The acute phase of SCLS is referred to as the “acute leak phase,” during which patients present with hypotension and may have hemoconcentration due to loss of intravascular volume. This phase may last up to 3 days. A recovery phase may follow with return of fluid into the vascular space with subsequent diuresis.⁴ Hemoconcentration is a potential diagnostic clue for SCLS and may help to differentiate the condition from other causes of shock.⁵ In a series of nearly 30 patients at the Mayo Clinic, rhabdomyolysis occurred in 36% of cases and compartment syndrome in 20%.⁵ A drop in albumin by more than 2 g/dL was associated with a higher likelihood of developing rhabdomyolysis in that case series. The case we described had similar features, with an initial hematocrit of 64%, a drop in albumin of more than 2 g/dL, and subsequent rhabdomyolysis that required fasciotomy of

all extremities. Secondary SCLS is a diagnosis of exclusion. In our case, other causes of shock were not apparent based on advanced imaging. Despite having areas of ground-glass change on the chest CT, the patient was not reporting dyspnea and was on room air up until his shock-state precipitously worsened a few hours after admission.

Secondary SCLS has been associated with underlying causes such as hematological malignancies, medical treatments such as therapeutic growth factors or chemotherapies, and viral infections.⁶ Considering how the condition can mimic other common causes of shock in the ICU, possibly the condition is underrecognized. The spectrum of disease associated with the newly described COVID-19 virus continues to evolve. The virus has been associated with overproduction of pro-inflammatory cytokines that may lead to multiorgan failure, referred to as a cytokine storm.⁷ It also has been associated with development of multisystem inflammatory syndrome in children, with features of vasculitis.⁸ To our knowledge, there have been no reports of SCLS secondary to COVID-19 infection. This case adds to our evolving understanding of the varied presentations of the inflammatory response associated with COVID-19 infection.

Acknowledgments

Financial/nonfinancial disclosures: None declared.

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