Annals of Case Reports
Sullivan AR, et al. Ann Case Rep: 8: 1155
www.doi.org/10.29011/2574-7754.101155
www.gavinpublishers.com

Case Report

Management of Systemic Capillary Leak Syndrome, a Rare and Potentially Fatal Disease: A Case Study

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Citation: Sullivan AR, Ignatz CM, Agarwal P, Herman JB, Platt AB, et al. (2023) Management of Systemic Capillary Leak Syndrome, a Rare and Potentially Fatal Disease: A Case Study. Ann Case Report 08: 1155. DOI: 10.29011/2574-7754.101155

Received Date 31 January 2023; **Accepted Date:** 03 February 2023; **Published Date:** 07 February2023

Abstract

We present a case of an elderly Caucasian woman with past medical history significant for diabetes mellitus and morbid obesity who developed abdominal pain, vomiting, and lightheadedness one day prior to hospital presentation. On admission, the patient was hemodynamically unstable with blood pressure 60/39 mmHg and heart rate 126 bpm. She was afebrile and ill appearing with abdominal distention and tenderness and newly edematous lower extremities bilaterally. She was COVID 19 positive on admission and diagnosed with diabetic ketoacidosis, for which insulin infusion and volume resuscitation was initiated. Additional abnormal laboratory investigations included severely elevated hematocrit and hypoproteinemia. The patient was diagnosed with COVID-19 induced SLCS on hospital day two and received high dose Intravenous Immunoglobulin (IVIG) (1 mg/kg) for a total of 66 gm with rapid de-escalation of vasopressor support within 4 hours. Unfortunately, the patient developed bilateral anterior tibial compartment syndrome on hospital day 3 which required bilateral fasciotomies. She was discharged to a physical rehabilitation facility following a prolonged hospitalization.

Keywords: Clarkson Disease; Idiopathic Systemic Capillary Leak Syndrome; Shock; Hypoalbuminemia; Systemic Capillary Leak Syndrome; Hemoconcentration.

Introduction

Systemic Capillary Leak Syndrome (SCLS), also known as Clarkson disease, was first recognized in 1960 as a case of cyclical episodes of hypovolemic shock and anasarca in a young woman [1]. This rare disease has been reported less than 300 times since it was first identified in 1960 and is characterized by hemoconcentration, hypoalbuminemia, and hypotension [2]. Clinical presentation is a consequence of endothelial barrier dysfunction, resulting in extravasation of proteins and plasma into the interstitium [2,3]. Upper respiratory tract infections, especially viral infections, have been reported to precipitate acute SCLS attacks [2-5]. We report a case of COVID-19 infection precipitating the development diabetic ketoacidosis and SCLS in a woman, whose hospital course was complicated by bilateral lower extremity compartment syndrome requiring fasciotomies.

Case Details

A 68-year-old Caucasian woman with a medical history significant for obesity and diabetes mellitus was hospitalized with a chief complaint of vomiting and lightheadedness. Home

medications at presentation included sitagliptin-metformin 100-1,000 mg daily and dapagliflozin 10 mg daily. The patient was hemodynamically unstable upon admission, with blood pressure 60/39 mmHg, pulse 126 bpm. She was afebrile and maintained an oxygen saturation of 97% on room air. Clinical exam revealed an ill appearing woman in acute distress with abdominal distension and tenderness, edematous lower extremities bilaterally, which were cool to touch, and diminished breath sounds bilaterally. Chest radiograph and computed tomography of the abdomen and pelvis were unremarkable for acute pathology.

On admission, the patient was noted to have a several serum testing abnormalities including elevated beta-hydroxybutyrate, hyperglycemia, hypoalbuminemia, lactic acidosis and elevated hematocrit (Table 1). She tested positive for COVID-19 on admission, however, did not present with symptoms of acute respiratory infection or radiographic infiltrates. The patient received a total of 7.5 L of crystalloid fluid and 500 mL of colloid fluid without improvement of shock state and ultimately required epinephrine, norepinephrine, phenylephrine and vasopressin infusions and stress dose steroids to maintain a MAP above 65 mmHg. She suffered a witnessed cardiac arrest on the day of admission with return of spontaneous circulation following multiple rounds of advanced cardiac life support cardiopulmonary resuscitation.

Test	Reference Range	Day of Admission
Venous pH	7.35-7.45 pH	6.973
Venous pCO_2	32.0-45.0 mmHg	<15.4
Venous pO_2	83.0-108.0 mmHg	34.7
Serum glucose	70-99 mg/dL	381
Serum creatinine	0.60-1.30 mg/dL	1.56
Serum CO2	21.0-31.0 mmol/L	11.1
Serum albumin	3.5-5.7 g/dL	1.7
Serum total protein	6.4-8.9 g/dL	<3.0
Serum lipase	11-82 IU/L	31
Serum lactic acid	0.6-1.4 mmol/L	23.0
White blood cell	4.8-10.8 10E3/uL	15.9
Hemoglobin	12.0-16.0 g/dL	25.0
Hematocrit	35.0-47.0%	74.1
Platelet	130-400 10E3/uL	425

Table 1: Laboratory Results.

The patient was diagnosed with SCLS on hospital day 2 due to profound, refractory shock, hypoalbuminemia, elevated hematocrit, and diffuse anasarca. Serum immunoelectrophoresis subsequently confirmed presence of IgG kappa monoclonal gammopathy. The patient received high dose IVIG (1 mg/kg) for a total of 66 gm with subsequent reduction of vasopressor requirements to only norepinephrine infusion within 4 hours. Unfortunately, the patient's course was complicated by the development of bilateral lower extremity compartment syndrome, which required bilateral fasciotomies on hospital day 3. With these therapies, the patient demonstrated rapid resolution of refractory shock and successful avoidance of lower extremity amputation. The patient was discharged to an outpatient rehabilitation center on hospital day 18 for generalized deconditioning.

Discussion

SLCS was first reported in 1960 as cyclical episodes of hypovolemic shock of unknown etiology in a young woman. Since first described, there have been a small number of published cases characterized by shock, hemoconcentration, hypoproteinemia (predominately IgG kappa monoclonal gammopathy) [5,6]. These cases are frequently precipitated by viral infections with associated prodromal fatigue, myalgias, fevers, vomiting, abdominal pain, and diarrhea followed by rapid development of shock [2,7]. Since identification of COVID-19, there have been few published cases of COVID-19 associated SLCS [3,8]. For those patients diagnosed with SLCS who have cyclical disease, the reported frequency of acute SCLS attacks has varied significantly in literature [7,9]. This case illustrates how early recognition is crucial. Several lessons can be learned.

First, timely diagnosis and management is challenging. The main characteristics include hypotension, hypoproteinemia, and hemoconcentration. The majority of adult SLCS cases are associated with monoclonal gammopathy, particularly IgG kappa, and to a lesser extent *IgG* lambda [3,4,7]. The role by which monoclonal gammopathy, regarding acute SLCS attack, is unknown. Hemoconcentration has resulted in misdiagnosis of polycythemia vera but is a key diagnostic clue in the setting of acute episodes [3].

Second, in the setting of acute SLCS attack, the crux of management is intravascular volume resuscitation to maintain perfusion of organs and mitigate metabolic acidosis [2]. Significant volume resuscitation is associated with an increased risk of compartment syndrome, especially in the anterior tibial compartments [6]. Compartment pressures should be carefully evaluated, potentially with serial intracompartmental pressure monitoring when needed. We recommend surgical evaluation for fasciotomies and muscle debridement as early as clinically

indicated, as there has been one case of SCLS reported cardiac arrest due to acute hyperkalemia following muscle reperfusion [7].

Lastly, syndromes associated with monoclonal gammopathy of unknown significance and autoimmune etiology have been increasingly treated with IVIG. Based upon observational data, there is speculation regarding use of IVIG in both acute SLCS attacks and as prophylactic therapy [2,4,7]. At this time, the role of IVIG in SLCS is unknown and will require further study. In conclusion, this rare case of SCLS demonstrates the importance of early diagnosis and serial examinations to reverse shock and treat associated complications.

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