Case Report

Systemic capillary leak syndrome requiring fasciotomy for limb compartment syndrome: A case report and literature review

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Background: Limb compartment syndrome (LCS), a rare but serious complication of systemic capillary leak syndrome (SCLS)-related systemic edema, warrants prompt decompressive fasciotomy. We report a case of SCLS complicated by LCS of four extremities requiring emergent fasciotomies; furthermore, we reviewed existing published reports on SCLS with LCS.

Case Presentation: A 36-year-old man was diagnosed with SCLS based on profound vascular permeability with no other underlying conditions. Within a few hours of admission, LCS was noted in the patient's lower legs and thighs and he was treated using decompressive fasciotomy. Additional forearm fasciotomy was subsequently carried out. After fluid management, vasopressor support, mechanical ventilation, and renal replacement therapy, the patient was discharged without any neuromuscular deficits caused by LCS. Literature review suggested that lower legs are prone to LCS in patients with SCLS.

Conclusion: Limb compartment syndrome is a serious complication that clinicians must be aware of and requires prompt decompressive fasciotomy.

Key words: Compartment syndrome, edema, fasciotomy, hypovolemic shock, systemic capillary leak syndrome

INTRODUCTION

SYSTEMIC CAPILLARY LEAK syndrome (SCLS) is a rare disease characterized by recurrent hypovolemia, systemic edema, hypoalbuminemia, hypotension, and hemoconcentration due to life-threatening attacks on capillary hyperpermeability.[1] Due to significant fluid and protein shifts to extravascular spaces, initial treatment of SCLS requires remarkable fluid resuscitation to maintain hemodynamic stability. Profound systemic edema could cause limb compartment syndrome (LCS), a rare but serious complication warranting decompressive fasciotomies.[2,3]

Herein, we report a case of SCLS complicated by LCS of four limbs that required emergent fasciotomies. We reviewed existing studies on SCLS with compartment syndrome as there were only sporadic cases previously reported. In addition to raising awareness of this rare disease as a differential diagnosis of significant hypovolemic shock, our aim was to emphasize the importance of appropriate management of compartment syndrome because delayed intervention could induce neuromuscular sequalae and impact the patient's functional prognosis.

CASE PRESENTATION

A 36-year-old man presented to our hospital emergency department with dizziness and vomiting. He had experienced mild flu-like symptoms including nasal discharge and sputum production the day prior. Initial physical examination revealed the following: mild disorientation; Glasgow coma scale score, 14 (E4V4M6); body temperature, 36.3°C; blood pressure, 71/41 mmHg; pulse rate, 113 b.p.m.; respiratory rate, 20 breaths/min; and oxygen saturation, 93% with 4 L/min oxygen. He had no fever, rash, or skin bruising. Initial arterial blood gas analysis showed metabolic acidosis (Table 1). Laboratory results showed an increased

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hematocrit level of 71% and hemoglobin level of 23 g/dl (Table 1). Laboratory results did not indicate cytopenia and imaging studies did not indicate any notifiable infections, malignancy, or trauma; indications of splenomegaly, lymphadenopathy, or intracorporeal fluid accumulation were absent.

He was admitted to the intensive care unit and required resuscitative treatment for hypovolemic shock. He received 6 L crystalloid fluid during the first 4 h, vasopressor support, and antibiotics including meropenem and vancomycin for suspected bacterial infection. Although aggressive resuscitation was performed, he remained hypotensive and continued to require fluids. Eight hours after admission, mechanical ventilation and continuous renal replacement therapy (CRRT) were initiated to support respiratory failure and metabolic acidosis with oliguria, respectively. An increase in hematocrit and decrease in total protein and albumin levels indicated significant capillary permeability. Because of the profound hypotensive shock, which required a large quantity of fluid, and progressive systemic edema, we considered a diagnosis of capillary leak syndrome. Given the absence of medication or underlying condition that might induce capillary leak syndrome, and laboratory and imaging findings suggestive of differential diagnoses such as hemophagocytic lymphohistiocytosis or multicentric Castleman disease, the patient was diagnosed with idiopathic SCLS. Plasma electrophoresis confirmed the presence of monoclonal immunoglobulin (kappa).

Table 1. Laboratory results on admission of a 36-year-old man with systemic capillary leak syndrome complicated by limb compartment syndrome

Variable	Reference range	Results
Arterial blood gas analysis (10 L/min oxygen)		
pH	7.35–7.45	7.330
$PaCO_2$ (mmHg)	35.0–45.0	26.9
PaO_2 (mmHg)	–	194.0
HCO_3^- (mmol/L)	22.0–28.0	13.8
Lactate (mmol/L)	0.4–2.2	3.8
Complete blood cell count		
White blood cells (/μL)	3,300–8,600	18,000
Red blood cells ($\times 10^4$/μL)	405–585	818
Hemoglobin (g/dl)	13.7–16.8	22.9
Hematocrit (%)	40.7–50.1	71.2
Platelets ($\times 10^4$/μL)	13.0–35.0	28.2
Blood biochemistry		
Total protein (g/dl)	6.6–8.1	5.9
Albumin (g/dl)	4.1–5.1	3.5
Urea nitrogen (mg/dl)	8.0–20.0	18.1
Creatinine (mg/dl)	0.65–1.07	2.07
Total bilirubin (mg/dl)	0.40–1.50	0.27
Aspartate aminotransferase (U/L)	13–30	29
Alanine aminotransferase (U/L)	10–42	19
Lactate dehydrogenase (U/L)	124–222	535
Creatine kinase (U/L)	59–248	118
Glucose (mg/dl)	73–109	223
C-reactive protein (mg/dl)	0.00–0.14	0.92
Blood coagulation		
Prothrombin time (%)	75.0–120.0	39.7
Activated partial thrombin time (s)	24.0–39.0	38.7
Fibrin/fibrinogen degradation products (μg/ml)	<5.0	<5.0
Fibrinogen (mg/dl)	200–400	410
D-dimer (μg/ml)	0.0–1.0	1.5

Within 1 h of admission and during the subsequent 6 h, he experienced pain with increased muscular tension in the lower extremities. After intubation, compartment syndrome was suspected in the lower limbs as the muscular tension worsened. The compartment pressure of the lower legs and thighs was 40–100 mmHg under a diastolic pressure of 70 mmHg. Physical examination findings, clinical course, and increased compartment pressures were consistent with compartment syndrome of the lower limbs. We performed decompressive fasciotomies on the lower legs and thighs. Over several subsequent hours both forearms developed compartment syndrome, also requiring fasciotomies. Vacuum-assisted dressings were placed on all extremities.

In addition to supportive treatments including fluid management, vasopressor support, mechanical ventilation, and CRRT, intravenous immunoglobulin and steroid therapy were administered for acute phase treatment. Theophylline and β-adrenergic agonist (salbutamol) were added for maintenance therapy.

By admission day 3, his hemodynamic state had gradually recovered, and he required small quantities of fluids and vasopressors. Continuous renal replacement therapy was discontinued on day 3, and the patient was extubated on day 5. The first closure surgery for fasciotomy wounds on the left forearm, right thigh, and left leg were carried out on day 4, and the remaining wounds were closed on day 7. His clinical course was good until he experienced another attack of hypotensive shock after the last closure surgery. Seven hours after the second closure surgery, he showed a drop in blood pressure (75/48 mmHg) and sinus tachycardia of 135 b.p.m.; he required fluid resuscitation and vasopressor support. During this transient hypotension and tachycardia, changes in hematocrit and albumin levels were minimal. As there was no pain and swelling of the extremities and creatine kinase levels did not increase, there were no

indications of a compartment syndrome relapse. The patient showed no signs of infection and achieved negative blood culture results without requiring antibiotics. His clinical course indicated the possibility of a second attack of mild capillary leak syndrome, which occurred when the initial attack seemed to have resolved. He was discharged from the intensive care unit on day 11 and from the hospital on day 18 without any neuromuscular deficits caused by compartment syndrome (Fig. 1).

DISCUSSION

LIMB COMPARTMENT SYNDROME is known to occur after limb trauma; however, it might not be easily recognizable when caused by nontraumatic diseases. Recognizing SCLS as a nontraumatic condition that causes LCS and understanding its clinical time course could increase LCS awareness among clinicians and help them perform fasciotomies in a timely manner.

Systemic capillary leak syndrome episodes have an infectious trigger, especially mediated by viruses[1]; however, the overall pathophysiology of SCLS remains unclear. Although our patient experienced mild flu-like symptoms, no viral etiologies were identified, and the event did not occur during the influenza season or COVID-19 pandemic. The clinical diagnosis of SCLS often requires the exclusion of other conditions such as sepsis, angioedema, anaphylactic shock, hemophagocytic lymphohistiocytosis, or multicentric Castleman disease.[1] Although it is difficult to distinguish other differential diagnoses from the first impression, the current patient's clinical course, including profound vascular permeability with the absence of other underlying conditions, was more likely to fit the clinical picture of SCLS. Hemoconcentration and monoclonal gammopathy could be diagnostic clues for differentiating SCLS from other conditions.[4]

Patients with SCLS typically develop prodromal symptoms, such as weakness, malaise, myalgias, or abdominal pain, followed by a leakage phase represented by hypotensive shock and edema. This phase, which lasts for 1–3 days,[1] is the critical period where patients are prone to hypoperfusion-related multiorgan dysfunction and LCS as severe complications[2–10]; patients require the administration of fluids (in massive quantities), vasopressors for resuscitation, and additional treatments for complications. The leakage phase is followed by the postleakage phase, in which vascular permeability starts to be restored with fluid recruitment into the intravascular circulation.[1] Our patient experienced a typical course of SCLS, where the leakage phase lasted for approximately 3 days, with kidney dysfunction warranting CRRT and LCS requiring decompressive fasciotomies. Specific treatments for SCLS, including intravenous immunoglobulin, steroids, β-adrenergic agonists, and theophylline, have been reported for acute treatment and recurrence prevention. Although medical treatments for

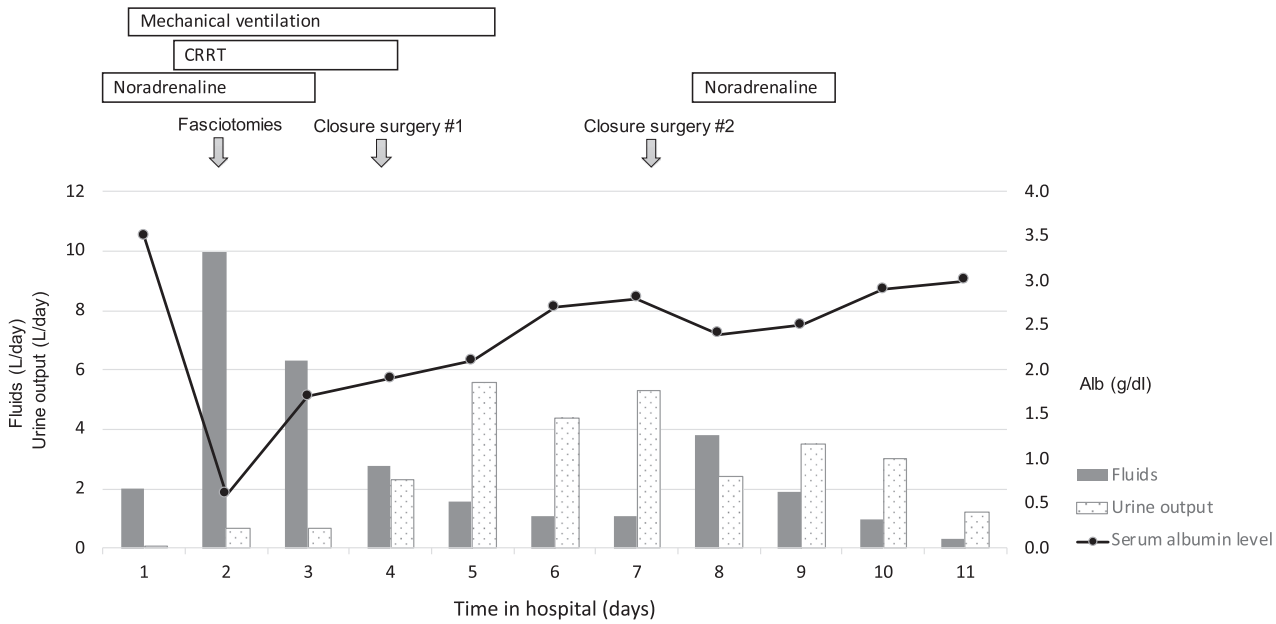

Fig. 1. Clinical course of a 36-year-old man with systemic capillary leak syndrome complicated by limb compartment syndrome during his stay in the intensive care unit. Alb, albumin; CRRT, continuous renal replacement therapy.

Table 2. Clinical review of reported cases of systemic capillary leak syndrome with limb compartment syndrome (LCS) in the last 22 years

Authors	Age (years)	Sex	Chief complaint	Location of LCS requiring fasciotomies or decompressive procedures				Complications associated with LCS	Outcome
				Forearms	Thighs	Lower legs	Other		
Kyeremanteng *et al.*[2]	57	M	Bilateral lower leg pain and swelling	+	+	+	–	Bilateral median and ulnar nerve neuropathies	Survived
Saugel *et al.*[3]	41	M	Bilateral leg pain	–	+	+	–	–	Survived
Matsumura *et al.*[5]	26	F	Nausea, malaise	–	–	+	–	Bilateral foot drop	Survived
Sanghavi *et al.*[6]	48	M	Bilateral leg pain and swelling	–	–	+	–	Wound infection with *Bacillus cereus*; deep peroneal neuropathy	Survived
Brown *et al.*[7]	32	M	Pain in all four extremities	+	–	+	–	–	Survived
Lamou *et al.*[8]	54	M	Dizziness, weight gain, syncope	+	+	+	Abdomen	Lower limb weakness upon dorsal flexion; requirement for hand rehabilitation in the left upper limb	Survived
Perry *et al.*[4]	54	M	Left lower leg pain	–	+	+	–	–	Death
Simon *et al.*[9]	57	M	Fatigue, flu-like symptoms, bilateral lower leg pain and swelling	+	+	+	–	Left median and ulnar nerve deficits requiring hand rehabilitation	Survived
Miyata *et al.*[10]	40	M	Nausea, malaise	–	–	+	Brain	Right hemiparesis	Survived
Present case	36	M	Dizziness, vomiting	+	+	+	–	None	Survived

Abbreviations: +, present; –, not present; F, female; M, male.

SCLS are based on reported cases and their effectiveness remains unproven, intravenous immunoglobulin is a promising therapy.[11]

PubMed and Google Scholar searches using the keywords "systemic capillary leak syndrome" and "compartment syndrome" identified nine reported cases of adult SCLS complicated by LCS, published in English since 2000 (Table 2). Eight of these patients were men (average age, 45 years). Most patients presented with lower leg pain and swelling as the chief complaint, indicating that the diagnosis of LCS was made prior to or during the recognition of SCLS. Thus, LCS could be the primary presentation of SCLS patients seeking medical care. However, some patients present with nonspecific complaints and later develop LCS, as in our case. Although most patients survived, notable complications associated with compartment syndrome were neuropathies. Thus, lower legs are prone to LCS in patients with SCLS, and early recognition as well as timely decompressive fasciotomies are mandatory to avoid neuromuscular complications.

Limb compartment syndrome is a serious complication that clinicians must be aware of and requires prompt decompressive fasciotomy. Careful examination of the extremities is essential, as symptoms in the early phase, including pain or paresthesia, could be difficult to assess when the patient is under intensive care.

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DISCLOSURE

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Animal studies: N/A.

Conflict of Interest statement: None.

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