

Systemic leak capillary syndrome with myocardial involvement and cardiogenic shock: a case report

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Background

Systemic capillary leak syndrome (SCLS) is a potentially fatal disorder characterized by relapses of hypovolemic shock episodes.

Case Summary

We present a case of a 58-year-old man who presented to the Emergency Department with a history of recurrent episodes of syncope in the last hours. A few days before medical contact the patient complained of sore throat, fever, and flu-like symptoms. He was initially admitted with a diagnosis of suspected myopericarditis. Forty-eight hours later, the haemodynamic status suddenly deteriorated to a mixed cardiogenic and shock; an endomyocardial biopsy showed localized inflammatory infiltrates and areas of necrosis of cardiomyocytes with positive viral search for parvovirus B19 (PVB19), therefore the patient was treated with methylprednisolone pulses. Based on the concurrent presence of the typical triad of hypotension, hypoalbuminaemia, and haemoconcentration we suspected systemic leak capillary syndrome potentially triggered by the PVB19 infection with acute myocarditis. The clinical conditions further deteriorated with rhabdomyolysis and acute kidney injury: we started continuous veno-venous haemofiltration adding a cytokines adsorber. In the following hours, we observed a significant clinical improvement. The patient was discharged 1 month later and 5 months after discharge he experienced a new attack of SCLS, this time without myocardial involvement and with prompt symptoms resolution.

Conclusion

Systemic capillary leak syndrome is a potentially fatal disorder: early recognition of this entity and prompt initiation of supportive therapy are warranted, therefore, it is paramount that an emergency physician thinks of SCLS in patients with signs of cardiogenic shock and the classical triad of hypotension, hypoalbuminaemia, and haemoconcentration.

Keywords

Capillary leak syndrome • Cardiogenic shock • Acute myocarditis • Renal replacement therapy • Parvovirus B19 • Case report

ESC Curriculum 6.5 Cardiomyopathy • 6.4 Acute heart failure • 7.1 Haemodynamic instability

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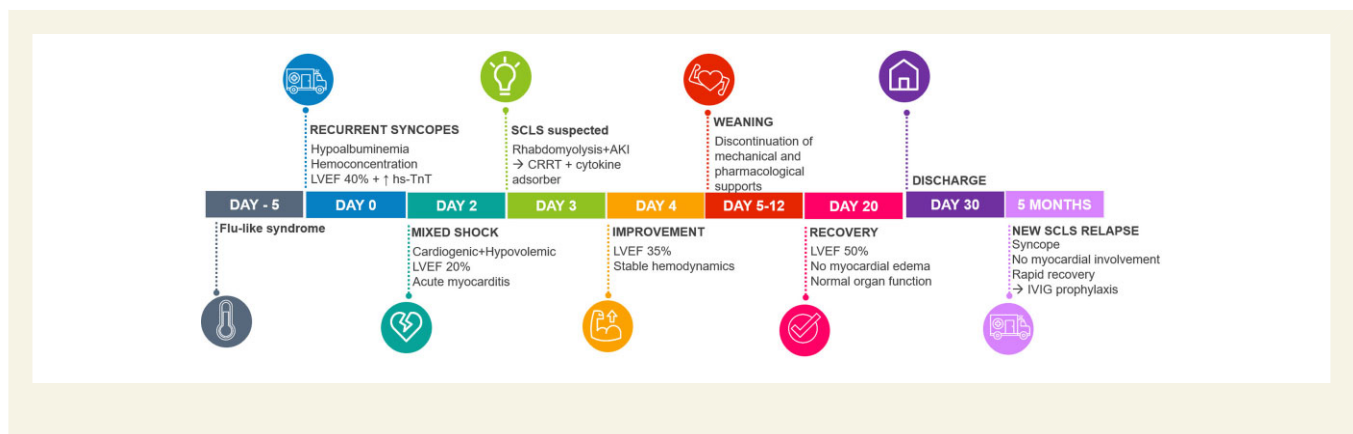
Learning points

- Systemic capillary leak syndrome is a potentially fatal disorder characterized by acute and severe recurrent attacks associated with a rapid fall in blood pressure.
- The sudden capillary leak causes severe hypotension, a decrease in serum albumin level (hypoalbuminaemia) and a parallel increase in the level of haematocrit (haemoconcentration).
- Myocardial involvement with acute ventricular dysfunction may occur, and it is mainly due to interstitial oedema.
- Based on the possible role of circulating permeability factors SCLS pathophysiology, treatments targeting cytokines might be effective strategies in acute phases.

Introduction

Systemic capillary leak syndrome (SCLS) is a potentially fatal disorder characterized by relapses of hypovolemic shock episodes.^{1–5} Myocardial involvement in SCLS has been rarely reported, and it is likely due to interstitial oedema.^{6,7} In this report, we describe the first case of SCLS attack triggered by Parvovirus-B19 infection with myocardial involvement, leading to acute heart dysfunction and life-threatening cardiogenic shock.

Timeline



Case presentation

A 58-year-old male patient presented to our Emergency Department (ED) complaining of recurrent episodes of syncope in the previous hours. Few days before ED admission the patient complained of sore throat, fever, and flu-like symptoms. One year before admission, he had already experienced a syncope during a febrile episode, associated with haemoconcentration (haemoglobin value 18.7 g/dL) and oedema of lower extremities. Moreover, his past medical history included a previous hospital admission (3 years before) for suspected myopericarditis, not confirmed by cardiac magnetic resonance imaging (CMRI). He had no personal nor family history of immune diseases. He was not taking any regular medication at the time of admission.

On arrival, he was normotensive (blood pressure 115/70 mmHg), with normal heart rate (80 beats per minute) and normal oxygen saturation of 98%. Physical examination was negative, without any sign of peripheral or pulmonary congestion. Electrocardiogram showed

sinus rhythm without conduction disorders and with normal ventricular repolarization. Transthoracic echocardiogram revealed decreased left ventricular (LV) ejection fraction (LVEF) of 40% with normal LV volume, mild concentric remodelling (basal interventricular septum and inferolateral wall of 11 mm), and a diffuse mild pericardial effusion. Chest X-ray was negative. Initial laboratory tests showed moderate leukocytosis (16.170×10^9 L), polyglobulia (haematocrit 57%), decreased serum albumin concentration (2.85 g L, normal range 4.02–4.76 g L), mildly increased C-reactive protein (CRP—2.0 mg dL, normal range 0.0–0.5), elevated high sensitivity troponin T (hs-TnT 400 ng/L, normal values 0–14 ng L), and

NT-pro-B natriuretic peptide (NT-proBNP 14 343 ng/L, normal value 0–155 ng L). Based on the evidence of decreased LV function with mild pericardial effusion, raised troponin, NT-pro-BNP, and CRP values, and a recent history of flu-like symptoms, he was then hospitalized for suspected myopericarditis.

Within 48 h from admission, the clinical status deteriorated, with rapid development of hypotension (systolic blood pressure of 60–70 mmHg), pulmonary oedema, and signs of hypoperfusion (cold extremities, oliguria, and raise of blood lactates to 4 mmol/L). Repeated echocardiography showed LVEF of 20%, increased LV wall thickness (basal interventricular septum of 14 mm, basal inferolateral wall of 12 mm), and a restrictive transmitral filling pattern, without increase of the pericardial effusion (see [Supplementary material online, Videos S1A and S1B](#)). The patient was then admitted to ICU with a diagnosis of cardiogenic shock. Once in ICU, mechanical ventilation was started and high dosage of vasoactive drugs (epinephrine and norepinephrine) was necessary to maintain a mean arterial pressure of >60 mmHg. Due to the acute ventricular

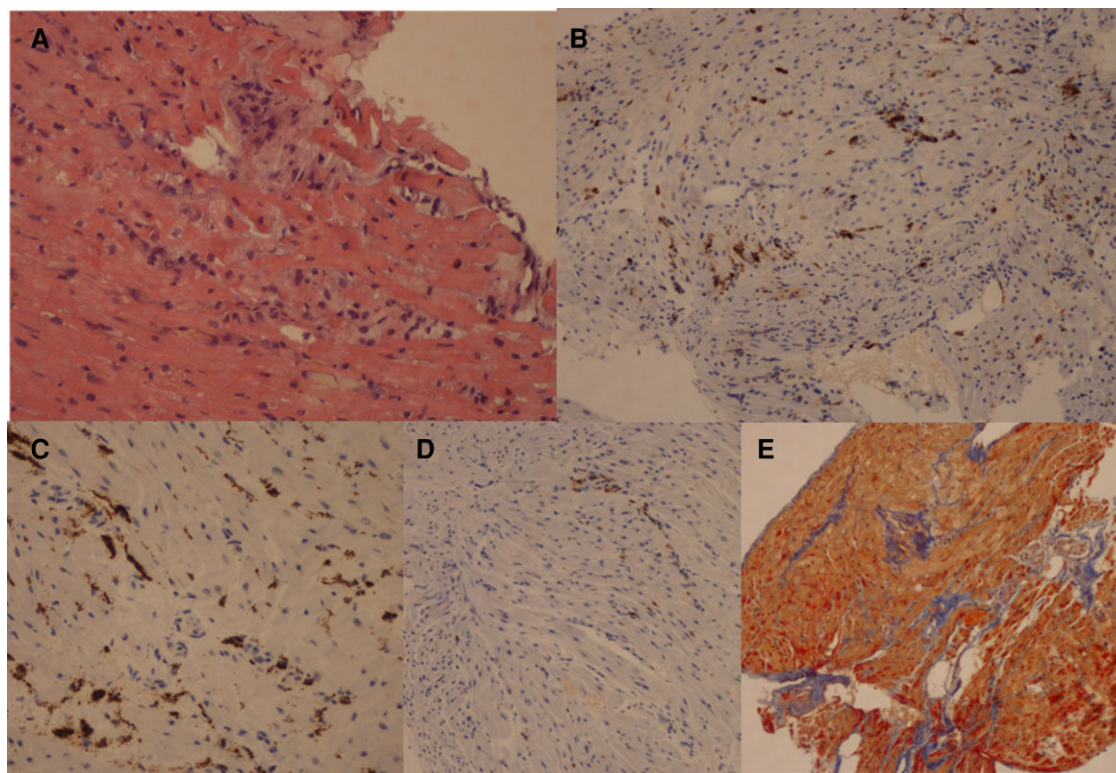


Figure 1 Myocardial histology confirming the diagnosis of acute myocarditis. (A) Haematoxylin and eosin section of the endomyocardial biopsy showing lymphoid infiltrates with cardiomyocytes necrosis supporting the diagnosis of active myocarditis based on Dallas criteria. (B) Staining for CD45 confirmed the infiltration of inflammatory cells, (C) composed mainly of macrophages (CD68 positive), and (D) few lymphocytes (CD3+); whereas in (E) focal areas of fibrosis can be seen (Masson's trichrome staining).

dysfunction with further raise of hs-TnT to 3066 ng L, a coronary angiography and an endomyocardial biopsy were performed. The former showed normal coronary vessels, while the biopsy was diagnostic for active myocarditis, with evidence of localized inflammatory infiltrates and areas of myocardial necrosis (Figure 1). The polymerase chain reaction assay on the histological sample was positive for parvovirus B19 (PVB19).

Moreover, blood cultures were obtained (based on haemodynamic instability and elevation of CRP, despite the absence of fever or other clear signs of sepsis) and were negative.

Despite initial resuscitation, the haemodynamic status remained severely impaired. Therefore, mechanical support with intra-aortic balloon pump (IABP) was started and a pulmonary artery catheter was inserted to better monitor the haemodynamic status and treatment responsiveness. Right heart catheterization showed ongoing mixed hypovolemic-cardiogenic shock: right atrium pressure was 10 mmHg, pulmonary artery pressure 25/14 mmHg, capillary wedge pressure 12 mmHg, cardiac index 1.77 L min m²; both pulmonary (PVR-I) and systemic (SVR-I) vascular resistance index were high: PVR-I 3.4 WU/m², SVR-I 41.8 WU/m².

Because of the refractory shock and the histopathological diagnosis of acute myocarditis, we administered high doses of i.v. methylprednisolone (i.e. 1 g on the first day followed by 500 mg od for the next 2 days).^{8,9}

Based on the concomitant presence of the typical triad of hypotension, hypoalbuminaemia, and haemoconcentration, the diagnosis of SCLS triggered by PVB19 infection was suspected.

Despite circulatory support, shock persisted and the patient developed rhabdomyolysis (creatinine kinase 9297 U/L, normal range 0–200 U/L) and acute kidney injury, which was treated with continuous renal replacement therapy (CRRT). Based on previously reported data about a possible role of soluble factors on vascular hyperpermeability in SCLS,^{1–3} we added a cytokine adsorber haemofilter to CRRT treatment.

Twenty-four hours after starting CRRT, the patient significantly improved: LVEF raised to 35% and he was progressively weaned from IABP on Day 7 and from inotropes and vasopressors on Day 11. Haemofiltration was stopped after 72 h. Ventilatory weaning was postponed due to ventilatory-associated pneumonia, and was finally accomplished on Day 12.

A CMRI performed 20 days after admission showed improvement of biventricular performance (LVEF 50%) and complete resolution of myocardial oedema (Figure 2). Late gadolinium enhancement images showed intramyocardial mild, widespread enhancement (non-ischaemic pattern). Pre-discharge echocardiography confirmed restored LVEF of 52% and reduced LV wall thickness (basal interventricular septum and inferolateral wall of 12 and 11 mm, respectively; [Supplementary material online, Videos S2A and S2B](#)).

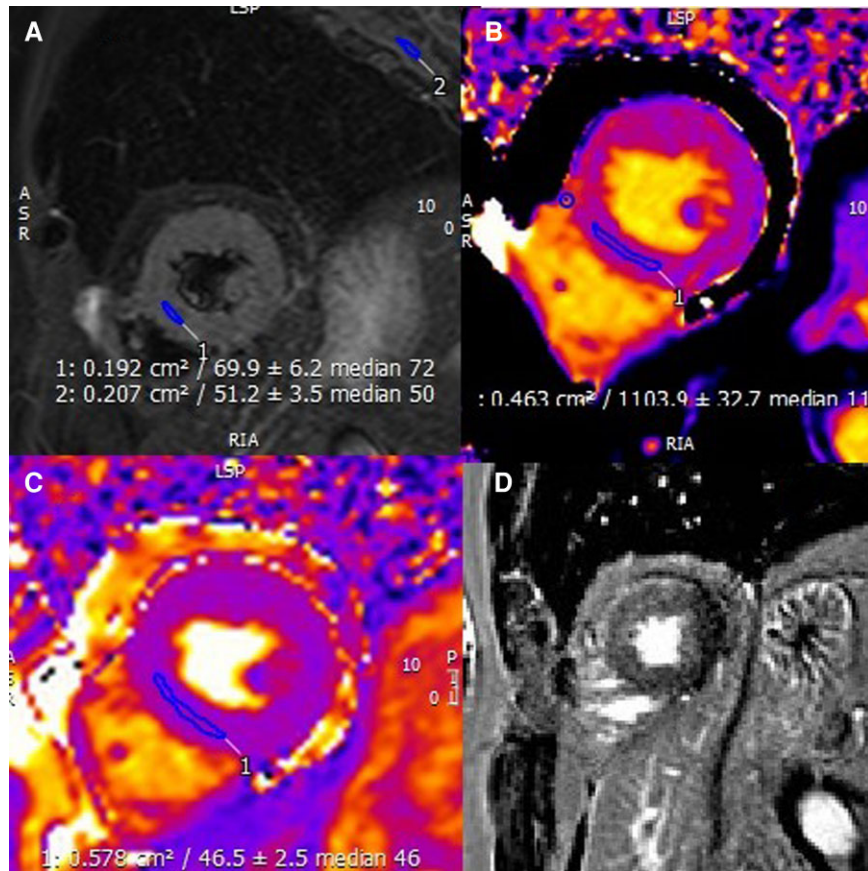


Figure 2 Cardiac magnetic resonance imaging performed 20 days after admission showed improvement of biventricular performance (LVEF 50%, right ventricular ejection fraction 55%). Negative T2-STIR images (A) and normal value of T1–T2 tissue mapping (mid-ventricular pre-contrast T1 maps: 1093 ms (B); mid-ventricular post-contrast T1 maps: 301 ms; mid-ventricular T2 maps: 46 ms (C); extracellular volume: 28.4%) confirmed complete resolution of myocardial oedema. Late gadolinium enhancement images (D) showed intramyocardial mild, widespread enhancement (non-ischaemic pattern).

Tests for autoimmune diseases were all negative. Further investigations on polyglobulia excluded JAK 2 mutation. Eventually, infection and organ failure resolved, and the patient was discharged 30 days after admission. At discharge, restoration of normal haematocrit values and renal function was confirmed (Hb 10.4 g/dL, HcT 32.2%, creatinine 0.95 mg/dL). Total serum proteins and albumin values took several weeks to return to the normal range.

Five months later, the patient experienced a new ISCLS flare during a flu-like syndrome: he presented to the ED complaining of hypotension and syncope, accompanied by haemoconcentration (Hb 16.4 g/dL, HcT 49%). Viral search on nasal swab revealed rhinovirus infection. In that occasion, the patient was prudentially admitted to ICU, but he remained haemodynamically stable and myocardial dysfunction did not occur. A prophylactic regimen of intravenous immunoglobulin (IVIg) 1 g/kg administered monthly was started, without any new syncopal episode for the next year. At now, 3 years after the index hospitalization, the patient is in good clinical condition and he has not experienced any new SCLS flare.

Discussion

This case illustrates several typical aspects of SCLS, which usually develops with the following phases: (i) prodromal phase, characterized by flu-like syndrome; (ii) acute (extravasation) phase, characterized by the classical triad of hypotension, haemoconcentration, and hypoalbuminaemia, and (iii) recovery phase, which carries the risks associated with the return of leaked fluids into the vascular bed (e.g. acute pulmonary oedema).^{1–5}

Knowledge about the pathophysiological mechanisms underlying acute SCLS flares is still very limited. Circulating permeability factors, increased during acute SCLS flares, can cause endothelial hyperpermeability.¹

Inflammatory—infectious syndromes, psychological stress, and hormonal changes are possible triggers of acute SCLS flares.² In our case, PVB19 acute infection was likely to be the trigger of the SCLS flare.

Myocardial involvement in SCLS, based on echocardiographic finding of severe LV systolic dysfunction, has been sporadically reported in the past years.^{6,7} A recent description of a series of 10 SCLS life-threatening attacks (during which echocardiography assessment was

systematically performed) showed that myocardial involvement always occurs during acute SCLS attacks, causing systolic and/or diastolic LV impairment.⁷ Myocardial involvement is usually due to acute oedema, which mimics myocardial hypertrophy due to other causes (such as arterial hypertension), but typically resolves within 2–3 days (thus it can be correctly defined as pseudohypertrophy). In our case, endomyocardial biopsies showed a mild inflammatory infiltrate and myocytes necrosis suggestive of acute lymphocytic myocarditis (a possible manifestation of PVB19 infection), which may explain the severity of the myocardial dysfunction.

The management of the acute phase is a very difficult task, and requires early ICU admission for prompt initiation of supportive therapies and fluid resuscitation.^{10,11}

Fluids do not restore the intravascular volume, while they may worsen oedema exacerbating tissue hypoperfusion and facilitating compartment syndrome.^{10,11} Therefore, clinicians should be alert to the futility of any attempt to restore intravascular volume and should tolerate a 'permissive hypotension'.¹⁰

Vasoactive amines are recommended in case of early signs of hypoperfusion, but a careful use of low doses should be recommended.¹¹

Administration of IVIG has been suggested based on limited studies of a few patients.¹² However, the efficacy of this treatment in the acute setting has not been established, while IVIG are considered a treatment of choice for long-term prophylaxis.¹²

Apart from the initial resuscitation with vasoconstrictors, inotropes, and IABP, we wonder whether the turning point in the severely unstable clinical picture was represented by the use of a cytokine adsorber: this observation suggests that treatments targeting cytokines might be attractive potential strategies during SCLS flares.

In conclusion, early recognition of this potentially fatal disorder and prompt initiation of supportive therapy are warranted. Therefore, it is of paramount importance that an emergency physician thinks of ISCLS in patients with shock and the classical triad of hypotension, hypoalbuminaemia, and haemoconcentration.

Lead author biography



Laura Garatti is a current young cardiologist at the ASST Grande Ospedale Metropolitano Niguarda in Milan, Italy. She has completed her cardiology fellowship at the University of Milano Bicocca in 2021.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case series including images and associated text has been obtained from all three patients in line with COPE guidance.

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