

Case report

Idiopathic Systemic Capillary Leak Syndrome Treated Successfully with High-Dose Intravenous Immunoglobulins

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Abstract

Idiopathic systemic capillary leak syndrome (ISCLS) is characterized by a triad of hypotension, hemoconcentration and hypoalbuminemia due to a shift of intravascular fluid and albumin to the extravascular area. We describe a hypovolemic patient with hemoconcentration and hypoalbuminemia who was successfully treated with high-dose intravenous immunoglobulins (IVIG). The purpose of this case report is to discuss the clinical management of idiopathic systemic capillary leak syndrome on the background of relevant literature review.

Keywords: systemic capillary leak, hypoalbuminemia, intravenous immunoglobulins

Introduction

Systemic capillary leak syndrome (SCLS) was first reported by Clarkson *et al.* 55 years ago [1]. This syndrome is a rare condition characterized by unexplained episodic capillary hyperpermeability and by chronic recurrent episodes of a triad of hypotension, hypoalbuminemia and hemoconcentration associated with paraproteinemia. Rare

complications of SCLS are renal damage and rhabdomyolysis, ascribable to increased compartment pressure and ischemic myonecrosis, which were seen in our patient [2]. We report the case of a 57-year-old woman with chronic SCLS treated with high-dose intravenous immunoglobulins (IVIG) after she failed to respond to other treatments. The patient was successfully treated with IVIG.

Case Report

A 57-year-old woman came to our hospital presenting with episodes of resting dyspnea, abdominal pain, vomiting, diarrhea, oliguria and anasarca, which had started a week ago. When admitted to the Emergency Department the patient showed hemodynamic instability, and hence she was referred to the intensive care unit.

Systolic blood pressure was 90/60 mmHg, heart rate: 130 beats/min. Her breath and cardiac sounds were normal. The laboratory finding showed hemoglobin: 17.9 g/dL, hematocrit: 51%, leukocytes: 22.500/mm², platelets: 346000/mm², blood urea nitrogen creatinine (BUN/Cr): 33/0.8 mg/dL, total protein/albumin: 5.3/3.2 g/dL, C-reactive protein (CRP): 1.03 mg/L creatinine phosphokinase: 3011 U/L, CK MB: 77.62 ng/ml, troponine: 1.86 ng/ml

Table 1. Laboratory findings of the patient

Peripheral blood		Biochemistry
White blood cell count:	22.500 K/uL	Total protein: 5.3 g/dl
Hemoglobin	17.9 gr/dl	Albumin: 3.2 g/dl
Hematocrit	51.7 %	Blood urea nitrogen: 33 mg/dl
MCV	87.3 fL	Creatinine: 0.8 mg/dl
Platelet	346 K/uL	Glucose: 111 mg/dl
ESR	4 mm/h	Sodium: 128 mmol/L
Serology		Potassium: 4.09 mmol/L
Antinuclear antibody	negative	Calcium: 8.4 mg/dl
C-reactive protein	1.03 mg/dL	Phosphorus: 3 mg/dl
Endocrinology		AST: 448 U/L
Cortisol:	17.8 µg/dL	ALT: 186 U/L
Free T3:	4.82 pg/mL	LDH: 1139 U/L
Free T4:	1.28 ng/dL	ALP: 48 U/L
TSH:	0.513 uIU/mL	Creatine phosphokinase: 3011 U/L
		CK-MB: 77.62 ng/ml
		Troponin: 1.86 ng/ml

(Laboratory findings of the patient are shown in table 1). Common causes of generalized edema accompanied by hypoproteinemia, such as nephrotic syndrome, liver dysfunction, congestive heart failure and gastrointestinal protein-losing enteropathy, were excluded. We had to exclude acute myocardial infarction (echocardiography was normal and acute ischemic findings were not observed on electrocardiography), rhabdomyolysis, hypothyroidism, adrenal insufficiency, exercise, trauma, using alcohol and drugs were excluded.

Leukocytosis and erythrocytosis of the patient was connected to hemoconcentration since there was no evidence of infection evaluated with physical examination, imaging and laboratory tests. It turned out that she had SCLS 10 years prior to this admission and was being followed up. We considered SCLS exacerbations. Central venous pressure was 4 cm H₂O, and aggressive fluid support in the form of 2 liters of i.v. fluids (normal saline) were given over the next 6 hours and saline treatment was continued. Intravenous methylprednisolone 1 mg/kg daily was started after the intravenous fluid substitution. We also used theophylline, terbutaline, salbutamol, diuretics and calcium antagonists. She did not respond to the treatment because of an increase in cardiac enzymes and CK levels, failure to provide adequate diuresis and continuation of muscle pain. Based on literature reports, intravenous immunoglobulin (IVIg) 0.5 g/kg was administered for 4 days. After this therapy her blood pressure and CVP returned to normal levels the next day. During the follow-up elevated CK levels up to 20160 U/L decreased after IVIg 193 U/L, and cardiac enzymes returned to normal.

Discussion

SCLS is a disorder which presents with recurrent episodes of hypovolemic shock, due to leakage of plasma to the extravascular compartment reflected by concomitant hemoconcentration, hypoalbuminemia and edema. It is a rare, but life-threatening disorder characterized by unexplained episodic capillary hyperpermeability due to a shift of fluid and proteins from the intravascular to the extravascular space [2].

Actually, the pathogenic mechanisms of SCLS and the cause of the episodes of capillary leakage remain unclear. According to one proposed theory, the origin of the increased susceptibility to vascular hyperpermeability is thought to lie in serum factors, not in the vasculature itself, as endothelial cadherin internalization and disruption of interendothelial junctions with subsequent increased permeability were inducible in human microvascular endothelial cells by exposure to sera from SCLS patients [3]. A study demonstrated that serum taken from patients with SCLS mediated extensive apoptosis and contraction of endothelial cells in vitro [4]. Also, endogenous interleukin-2 (IL) may contribute to the pathogenesis of this syndrome [4]. In most cases of IL-2-induced capillary leak syndrome, however, attacks developed during the IL-2

therapy [5]. Other than IL-2 several factors mediating the increased vascular permeability have been proposed, primarily cytokines, such as interleukins 6, 8, and 12, interferons gamma and alpha, tumor necrosis factor alpha, vascular endothelial growth factor, and C-X-C motif chemokine 10 and chemokine (C-C motif) ligand 2 [6-8]. Standard treatment of SCLS is not yet established. Multiple regimens, based on possible pathological mechanisms, have been tried with various degrees of success, including theophylline, terbutaline, salbutamol, steroids, diuretics, calcium antagonists, and plasmapheresis [9]. In addition to the treatment of the acute phase, several prophylactic therapies have been tried. Recurrence is a notable feature of SCLS, so its prevention is important. Terbutaline and theophylline therapy have been reported to be apparently effective against SCLS recurrence. Although morbidity and mortality rates associated with SCLS are high, the prognosis seems to have improved recently. However, the most successful therapeutic measure during an attack to date is the application of intravenous immunoglobulin [8,10]. Firstly, according to the article which was published by Vigneau and Lambert IVIg were effective against acute-phase of SCLS [11, 12]. IVIg prevent it from mediating tissue damage by scavenging its active components and diverting complement attack from cellular targets.

Based on these promising results, we repeatedly administered IVIg (0.5 g/kg over 4 days) to our patient. We achieved a milder clinical presentation of acute attacks and dramatically reduced the frequency of recurrence. In conclusion, awareness of SCLS is most important for improving the outcome because early diagnosis and immediate fluid replacement therapy are essential.

Conflict of interest statement. None declared.

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