Systemic Capillary Leak Syndrome Complicated by Rhabdomyolysis: Case Report

Rabdomiyoliz ile Seyreden Sistemik Kapiller Kaçış Sendromu Olgusu

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Geliş Tarihi/*Received:* 02.06.2010
Kabul Tarihi/*Accepted:* 14.12.2010

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ABSTRACT Systemic capillary leak syndrome (SCLS) is an idiopathic, rare condition, characterized by recurrent episodes of various manifestations, such as generalized edema, hypotension, hypovolemic shock, hemoconcentration and hypoproteinemia with monoclonal gammopathy. Here, we describe a 45 year-old woman who was admitted to our coronary intensive care unit due to hypotension, massive edema and hemoconcentration. Clinical and laboratory findings were all consistent with SCLS complicated by rhabdomyolysis. High dose steroid, inotropic drugs, intravenous fluids and human albumin were administrated as first-line therapy. The patient then was put on prophylactic therapy with theophylline and terbutaline. During follow-up of 2 years recurrence was not observed.

Key Words: Capillary leak syndrome; rhabdomyolysis; edema

ÖZET Sistemik kapiller kaçış sendromu (SCLS), jeneralize ödem, hipotansiyon, hipovolemik şok, hemokonsantrasyon ve monoklonal gamopati ile birlikte hipoproteinemi gibi çeşitli bulguların tekrarlayan atakları ile karakterize idyopatik, nadir bir durumdur. Koroner yoğun bakım ünitemize hipotansiyon, yaygın ödem, ve hemokonsantrasyon nedeniyle kabul edilen 45 yaşında bir kadın olgu sunmaktayız. Klinik ve laboratuvar bulguları rabdomiyolizle seyreden SCLS ile uyumlu idi. Başlangıç tedavisi olarak yüksek doz steroid, inotropik ajanlar, intravenöz sıvılar, human albumin kullandık. Hastamıza daha sonra profilaktik tedavi amacıyla teofilin ve terbutalin verdik. İzleyen 2 yıl içinde nüks gözlenmedi.

Anahtar Kelimeler: Kapiller kaçak sendromu; rabdomiyoliz; ödem

Turkiye Klinikleri J Cardiovasc Sci 2012;24(3):306-9

Systemic capillary leak syndrome (SCLS) is a rare disorder that was first described by Clarkson and colleagues in 1960.[1] The disease is characterized by recurrent-reversible episodes of generalized edema, with hemoconcentration and hypoalbuminemia, associated with monoclonal gammopathy.[1-3] Rhabdomyolysis may occur secondary to SCLS and can cause acute renal damage.[4,5]

A sudden and reversible increase in capillary permeability results in a rapid shift of plasma from the intravascular to the extravascular space and this is responsible for the clinical and laboratory manifestations of SCLS. Although etiology and pathogenesis of this syndrome is still unknown, it is suggested that monoclonal gammopathy can play a direct role in capillary hyperper-

meability.[6,7] In addition to acute form, chronic form of this syndrome has also been described.[8]

Here we describe an acute type of SCLS complicated by rhabdomyolysis and treated effectively with positive inotropic agents, human albumin and high dose steroids.

CASE REPORT

A 45 year-old woman presented to our hospital complaining of nausea, light-headedness and generalized muscle ache. She had no chronic disease, nor smoking nor use of any illicit drugs. Two years ago, the patient had been admitted to another hospital due to hypotension and hypoalbuminemia and lower tract urinary infection. Unfortunately these signs remained unexplained.

During initial examination there was diffuse edema at her pretibial and sacral regions as well as her face. The systolic blood pressure was 55 mmHg and pulse rate was 148 beats/min. The lungs were clear. Despite severe hypotension, the patient was alert and oriented and neurologic examination was normal. The first blood tests revealed the following values: haemoglobin 202 g/L, hematocrit 0.54, albumin- globulin and C3-C4 levels were decreased. Blood urea nitrogen was increased mild but glomerular filtration rate was normal (Table 1). ECG showed sinus tachycardia with normal axis. The patient had been admitted to the intensive care unit. The patient received 9.3 L fluid (0.9% NaCl and Ringer's lactate) and human albumin (20%, 400 mL) for the first three days. Second day after the fluid replacement we have begun dopamine (8 μ/kg/min)-dobutamine (4 μ/kg/min) and 1 g/day methyl prednisolone because of overt hypotension. On the third day of hospitalization, central venous pressure (CVP) began to increase and pulmonary edema developed. High dose diuretic therapy was administered until CVP returned to normal level (N: 1-8 cm H_2O).

From the second to the fifth day, creatine kinase increased gradually and peaked on the third day (Figure 1). There was no change in renal function during this period. On the fifth hospital day, haemoglobin level returned to normal level and albumin level rose to 33 g/L.

TABLE 1: The initial laboratory data.

Laboratory studies	Normal range	Patient's value
WBC, X 109 /L	3.8-10.8	22
Hemoglobin, g/L	120-156	202
Hematocrit, proportion of 1.0	0,35-0,46	0,54
Creatinine, plasma, μmol/L	50-110	79.5
BUN, mmol/L	2.5-10.7	12.5
GFR,mL/min/1.73 m^2	90-140	101.8
Albumin, g/L	35-55	26
Globulin, g/L	20-35	20
Total protein, g/L	55-80	46
Creatine kinase, U/L	40-150 (female)	260
Na, mmol/L	135-146	130
K, mmol/L	3.5-5.3	4
C3, g/L.	0.86-1.84	0.54
C4, g/L	0.20-0.58	0.09
IgG, g/L	6.14-12.95	4.67
IgM, g/L	0.63-3.34	0.70

Detailed laboratory exams revealed that serum cortisol, thyroid function tests, protein electrophoresis, viral studies, blood cultures, C_1-esterase level, toxicology screen and anti-joy antibody concentration were normal. Immunoelectrophoresis showed an IgG monoclonal protein spike (13 g/L), while bone marrow findings were normal. Echocardiography revealed minimal pericardial effusion. Abdominal USG, CT scan of entire abdominal and chest and thyroid USG failed to detect any abnormalities. Electromyographies that were performed on the tenth hospital day and three months later disclosed normal records.

After 2 weeks, the patient was dismissed from the hospital on a regimen of terbutaline, 5 mg four times daily, and theophylline, 400 mg twice daily. Three months later, she had a less severe episode that required a 4-day hospital stay. The peak hematocrit value was 0.46.6 and her blood pressure was 75/45 mm Hg. The theophylline level was subtherapeutic at 37.19 mol/L (target level, 55.5 to 111 mol/L). After the patient was educated properly about the disease and taking medicine, no attacks has been observed during our follow-up for the last 2 years. Written informed consent was obtained from the patient for publication of this case report.

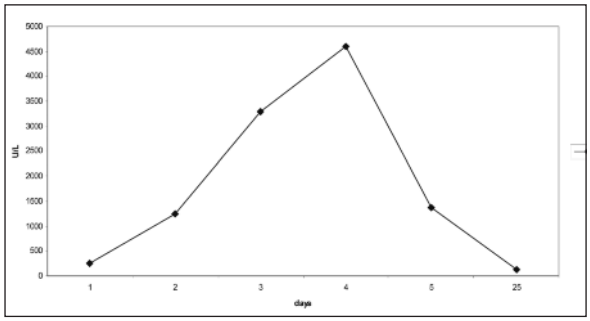

FIGURE 1: The course of creatine kinase.

DISCUSSION

We described a 45 year-old woman who was hospitalized because of generalized edema, hypotension, hypoproteinemia. She was diagnosed as SCLS due to the characteristic clinical presentations and laboratory findings.

As Atkinson et al.[3] demonstrated; during acute attacks of SCLS, plasma-albumin and other molecules mostly smaller than 200 kda, are rapidly transferred from intravascular compartment to the extravascular area and cause hemoconcentration; leukocytosis, increase in IgM concentration, decrease in albumin, IgG, C3, C4 concentrations and acute hypovolemia that is responsible for the unexplained hypotension. All of these occur in the initial capillary leak phase and continue for 1 to 4 days. Our patients' findings were consistent with these and first phase of this attack ended on the third hospital day.

The etiology of SCLS is unknown, although a possible role of viral infection has been proposed.[2,9] It has been hypothesized that IgG paraprotein, interleukin-2, leukotriene E4- B4, CD8 cells could be responsible for endothelial damage[3,10-12] A possible role of complement system also has been investigated.[6]

The recovery phase is recruitment of fluids that initially passed to extravascular compartment by spontaneous restoration of capillary integrity. This may cause severe acute intravascular fluid overload that depend on severity and duration of the initial leak phase as well as fluids given to correct the hypovolemia. As a result, pulmonary edema[9] may develop and may be fatal. In our patient pulmonary edema developed on the third hospital day. The recruitment of the initially extravasated fluids and macromolecules and our intravascular overloading may be responsible of this pulmonary edema. The two serious complications of SCLS are rhabdomyolysis and acute renal failure. Rhabdomyolysis may be due to increased compartment pressure and ischemic myonecrosis.[3-5,11] The diagnosis of rhabdomyolysis can be confirmed by assessing creatine kinase (CK). Creatine kinase levels 5 times higher than normal suggests rhabdomyolysis.[13,14] In our patient rhabdomyolysis was seen and treated rapidly to prevent acute tubular necrosis secondary to myoglobin toxicity. From the second to the fifth day, creatine kinase increased gradually and peaked on the third day.

Although multiple regimens have been tried in SCLS including theophylline, terbutaline, salbutamol, steroids, diuretics, calcium antagonists, plasmapheresis and gingko biloba extracts no curative treatment is available for this disease. During acute attacks hemodynamic monitorisations can be made by measurement of CVP and pulmonary artery catheterisation. The basic of the treatment is replacement of fluids (crystaloids, colloids) and inotropic agents as necessary. The most successful and populer prophylactic therapy is to use terbutaline and theophylline together that are proposed as first line prophylactic therapy by Droder at al.,[15] and reports confirm this conceivable therapy that decreased the number and severity of SCLS attacks.[15,16] Lee et al. used Pentastarch, that has a higher molecular weight than albumin, during initial capillary leak phase in order to elevate blood pressure in two patients and had a dramatic response.[17] Our patient received, human albumin, dopamine-dobutamine, adequate fluid and 1 gram/day methyl prednisolone. After 2 weeks, the patient was dismissed from the hospital on a regimen of terbutaline, 5 mg four times daily, and theophylline, 400 mg twice daily.

We report a case of a SCLS complicated by rhabdomyolysis. Acute tubular necrosis and rhabdomyolysis are the serious complications of this disease. A therapeutic regimen with terbutaline and theophylline seems to be effective for reducing and impeding attacks. Therefore, all physicians must be aware of this disease to prevent at least recurrence and perhaps death.

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