

Idiopathic Systemic Capillary Leak Syndrome: A Case Report

Bulent Yardimci,^{1,*} and Rumeysa Kazancioglu²

¹Department of Internal Medicine, Istanbul Florence Nightingale Hospital, Istanbul, Turkey

²Department of Nephrology, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey

*Corresponding Author: Bulent Yardimci, Department of Internal Medicine, Istanbul Florence Nightingale Hospital, Istanbul, Turkey. Tel: +90-2123756565, Fax: +90-2122244982, E-mail: bulentyardimci@yahoo.com

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Abstract

Introduction: Idiopathic systemic capillary leak syndrome (ISCLS) is rarely seen, and presents with recurrent episodes of hypotension, shock, hemoconcentration, and hypoproteinemia. The main pathology is the dysfunction of the vascular endothelium, and it is characterized by an increase of capillary permeability that is accompanied by the loss of intravascular fluid and protein.

Case Presentation: We present a 58-year-old female who presented with peripheral edema, leg pain, and syncope at the emergency department. Interestingly demyelinating neuropathy, which is a rare finding, ensued on day 4. She is still being treated using intravenous immunoglobulin therapy.

Conclusions: The early signs and symptoms of ISCLS may be subtle; therefore the diagnosis can easily be missed and prompt treatment of the syndrome may be postponed. Thus, the clinician must consider ISCLS in differential diagnosis in cases of hypotension, hemoconcentration, and hypoalbuminemia.

Keywords: Capillary Leak Syndrome, Clarkson Disease, Systemic Capillary Leak Syndrome, Edema, Shock, Multiple Organ Failure

1. Introduction

Idiopathic systemic capillary leak syndrome (ISCLS) or Clarkson's Disease is a rare and systemic disease, which affects the entire vascular system (1). The triad of hypotension, hemoconcentration, and hypoalbuminemia is highly suggestive of the diagnosis (1-3). It may be difficult to differentiate ISCLS from sepsis, toxic shock syndrome, anaphylaxis, and drug reactions, especially during the acute phase (3). An early diagnosis may prevent overtreatment and may lead to an effective therapy.

2. Case Presentation

A 58-year-old female presented with syncope at the Istanbul American hospital emergency department on September 21, 2012. Her symptoms, which were present for the past two days, included fatigue, diarrhea, swollen legs, and leg pain. The patient was conscious, sweaty, anxious, and pale. Her arterial blood pressure (ABP) was 80/40 mmHg, pulse rate was 118/minute with a regular rhythm, and her body temperature was 37.2 C. Heart sounds did not reveal any abnormality, the respiratory rate was slightly higher (28/minute), and pulmonary auscultation was normal. She complained of muscular pain during palpation of the leg muscles. She had bilateral lower limb edema. The laboratory analysis revealed high hemoglobin and hematocrit levels. A thorax computed tomography (CT) scan did not reveal any abnormalities, and echocardiography revealed a hyperkinetic heart but there was no wall distress.

Two hours after her admission, the patient's general condition deteriorated. Hypotension was augmented and anuria ensued. She was followed up at the ICU with intensive hydration. Enoxaparine sodium 40 mg sc BID and oral acetylsalicylic acid tablet 300 mg were started. Abdominal ultrasonography showed two gallstones of 2 cm in diameter and a left kidney stone of 1.5 cm in diameter. Urinalysis showed 20 - 30 leucocytes in every microscopic area. Intravenous Levofloxacin 500 mg/day was thus added to the treatment. Her urine culture showed 100.000 CFU *Escherichia Coli*, but a hemoculture and throat culture were negative. The initial laboratory tests are presented in Table 1. Protein electrophoresis showed only alpha-2 increase. On the second day, her blood pressure and pulse stabilized, and intravenous isotonic sodium therapy was continued. On day four, neuropathy in the limbs developed and electromyographic evaluation of lower extremities showed a bilateral axonal injury of the fibular nerve. Intravenous methyl-prednisolone, tramadol hydrochloride tablets, and alpha-lipoic-acid tablets were commenced. With intensive hydration therapy, antibiotic treatment, and neuropathy treatment, the general condition of the patient stabilized and she was able to walk 10 days after the onset of the symptoms. She was discharged on the 15th day with Alpha-lipoic acid tab 2 × 600 mg, terbutaline tab 5 mg/day, Teophylline tab 400 mg/day, and Tramadol hydrochlorur tab 150 mg/day. She is still being treated with IV Immunoglobulin therapy in the 27th month.

Table 1. The Laboratory Results of the Patient

Serum	Patient's Initial Result	Normal Range
Hemoglobin	18.3, gr/dL	11.7 - 16
Hematocrit	54.3, %	35 - 47
White Blood Cell	11850, mm ³	4100 - 11000
Blood Urea Nitrogen	47.3, mg/dL	8 - 23
Creatinine	2.6, mg/dL	0.6 - 1.1
Creatinine Kinase	630, U/L	< 170
Albumin	3.3, mg/dL	3.5 - 5.5

3. Discussion

Idiopathic systemic capillary leak syndrome (ISCLS) is a rare disorder which was first described by Clarkson in 1960 (1). In the past 54 years, around 150 cases have been diagnosed (2). The main symptoms of ISCLS are hypotension or shock, hemoconcentration, and hypoalbuminemia due to a sudden shift of fluid and macromolecules from the intravascular space to the interstitial space (2, 3).

The patient in our case showed signs of shock, acute renal failure, hemoconcentration and hypoalbuminemia without proteinuria, and edema during presentation. These findings are suggestive of ISCLS. It is necessary to exclude anaphylaxis, sepsis, septic shock, toxic shock syndrome, hereditary angioedema, and drug reactions for an ISCLS diagnosis (4, 5). She had a prodromal period of two days, which presented with weakness, leg pain, and diarrhea. Her medical history was lacking any signs or symptoms of a disease. A monoclonal gammopathy is reported in the majority of ISCLS patients and supports the diagnosis. Nevertheless, we did not find monoclonal gammopathy in our case. This may be the weak point of diagnosis in our case, but it is not an absolute diagnostic criterion (6, 7). Moreover, rhabdomyolysis, demyelinating neuropathy, and absence of paraproteinemia are distinctive characteristics of our case. Despite bilateral leg edema neither abdominal compartment syndrome nor an extremity compartment syndrome occurred. The presentation of this case is in accordance with Kapoor et al. (8), who reported fatigue, pre-syncope, and generalized or localized pain in 88, 76, and 76% of the patients, respectively. Again, according to Kapoor et al., acute renal failure, rhabdomyolysis, and compartment syndrome were present in 57, 36, and 20% the patients, respectively. Interestingly, our case showed all these three complications together (8).

A urinary infection may be a precipitant factor, but our case did not have any urinary symptoms or high fever. She also got worse in two hours in the emergency department. This clinical condition led to a confusion concerning diagnosis and treatment. After a series of investigations, the probability of ISCLS was sought. Intravenous immunoglobulin (IVIG) therapy was started three months later. The treatment during the acute phase consisted of rapid fluid infusion, intravenous

vasopressors, and measures to maintain proper blood oxygenation. For prevention of possible future episodes, various methods of treatment have been tried. We prefer Terbutaline and Theophylline at first. These agents are bronchodilators and mainly used for Asthma Bronchiale. They are used for ISCLS as off-label agents, because they increase intracellular cyclic adenosine-monophosphate (cAMP) content and the subsequent rise of cAMP inhibits capillary leakage (5). IVIG therapy is the other choice for ISCLS treatment. IVIG therapy might be effective in acute attacks (9), and it is also used to prevent future attacks (3). IVIG therapy was started 4 months after the presentation. She had a new attack after 11 months with hypotension, edema, and hemoconcentration, and she was hospitalized. After 10 days she was discharged with IVIG therapy. Our patient is still in remission and we haven't seen any new attacks.

3.1. Conclusion

ISCLS is a rare and potentially fatal syndrome. Prodromal symptoms may be missed by the clinician, because the clinical picture is usually similar to a viral infection. Nevertheless, the main clinical presentation may be severe, and it may cause a missed diagnosis and therefore an inappropriate treatment. Furthermore, the presence of hypotension, hemoconcentration, and hypoalbuminemia should add ISCLS to a differential diagnosis.

References

- Govig BA, Javaheri S. The systemic capillary leak syndrome. *Ann Intern Med.* 2010;**153**(11):764. doi: 10.7326/0003-4819-153-11-201012070-00014. [PubMed: 21135305]
- Duron L, Delestre F, Amoura Z, Arnaud L. [Idiopathic and secondary capillary leak syndromes: A systematic review of the literature]. *Rev Med Interne.* 2015;**36**(6):386-94. doi: 10.1016/j.revmed.2014.11.005. [PubMed: 25600329]
- Gousseff M, Arnaud L, Lambert M, Hot A, Hamidou M, Duhaut P, et al. The systemic capillary leak syndrome: a case series of 28 patients from a European registry. *Ann Intern Med.* 2011;**154**(7):464-71. doi: 10.7326/0003-4819-154-7-201104050-00004. [PubMed: 21464348]
- Dams K, Meersseman W, Verbeken E, Knockaert DC. A 59-year-old man with shock, polycythemia, and an underlying paraproteinemia. *Chest.* 2007;**132**(4):1393-6. doi: 10.1378/chest.07-0456. [PubMed: 17934127]

5. Rabbolini DJ, Ange N, Walters GD, Pidcock M, Randall KL. Systemic capillary leak syndrome: recognition prevents morbidity and mortality. *Intern Med J.* 2013;**43**(10):1145-7. doi: 10.1111/imj.12271. [PubMed: 24134172]
6. Xie Z, Chan E, Yin Y, Ghosh CC, Wisch L, Nelson C, et al. Inflammatory Markers of the Systemic Capillary Leak Syndrome (Clarkson Disease). *J Clin Cell Immunol.* 2014;**5**:1000213. doi: 10.4172/2155-9899.1000213. [PubMed: 25405070]
7. Druey KM, Greipp PR. Narrative review: the systemic capillary leak syndrome. *Ann Intern Med.* 2010;**153**(2):90-8. doi: 10.7326/0003-4819-153-2-201007200-00005. [PubMed: 20643990]
8. Kapoor P, Greipp PT, Schaefer EW, Mandrekar SJ, Kamal AH, Gonzalez-Paz NC, et al. Idiopathic systemic capillary leak syndrome (Clarkson's disease): the Mayo clinic experience. *Mayo Clin Proc.* 2010;**85**(10):905-12. doi: 10.4065/mcp.2010.0159. [PubMed: 20634497]
9. Zipponi M, Eugster R, Birrenbach T. High-dose intravenous immunoglobulins: a promising therapeutic approach for idiopathic systemic capillary leak syndrome. *BMJ Case Rep.* 2011;**2011** doi: 10.1136/bcr.12.2010.3599. [PubMed: 22696704]