ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

CASO CLÍNICO

Idiopathic Systemic Capillary Leak Syndrome: Report of a Pediatric Case

Síndrome de Extravasamento Capilar Sistémico Idiopático: Relato de um Caso Pediátrico

João VASCO✉[1], Francisca ALBUQUERQUE[2], Francisca COSTA[3], Ana DIAS CURADO[4], Carlos ESCOBAR[3]
Acta Med Port (In Press) ▪ https://doi.org/10.20344/amp.21531

ABSTRACT

The idiopathic systemic capillary leak syndrome is characterized by recurrent episodes of hypovolemia, with an unknown cause, presenting as a distributive and hypovolemic shock, due to fluid loss to the extravascular space. We describe a case of a previously healthy seven-year-old boy, who started with prodromal symptoms (abdominal pain, fatigue, nausea), followed by a fluid extravasation phase, with hemoconcentration, hypoproteinemia, and muscular edema in the abdominal wall and lower limbs, accompanied by pain – compartment syndrome. After a couple of days, spontaneous and fast recovery was noted, with clinical and analytic improvement. The inflammatory markers were always normal, and the blood cultures were negative. In this case, it is possible to distinguish the three idiopathic systemic capillary leak syndromes phases, as described in the literature. Although rare, this syndrome can be fatal, and the differential diagnosis with other causes of shock represents a challenge.
Keywords: Capillary Leak Syndrome; Child; Shock

RESUMO

A síndrome de extravasamento capilar sistémico idiopático é caracterizada por episódios recorrentes de hipovolemia, apresentando-se como um choque distributivo e hipovolémico, pela perda de líquido para o espaço extravascular, sendo a sua fisiopatologia desconhecida. Descrevemos o caso de um rapaz de sete anos, previamente saudável, que iniciou um quadro clínico de sintomatologia inespecífica, com evolução para uma fase de extravasamento de líquidos, com hemoconcentração, hipoproteinemia e edema intermuscular abdominal, progredindo para os membros inferiores, com queixas álgicas – síndrome compartimental. Posteriormente, evoluiu favoravelmente com recuperação espontânea após recrutamento do líquido extravascular, com melhoria clínica e analítica. Os parâmetros inflamatórios permaneceram negativos e não foi isolado nenhum microrganismo. Perante esta evolução característica, com as três fases descritas na literatura, admitimos uma síndrome de extravasamento capilar sistémico que, apesar de rara, pode ser fatal, fazendo diagnóstico diferencial com outras causas de choque, com tratamento urgente, demonstrando a importância do diagnóstico precoce.
Palavras-chave: Choque; Criança; Síndrome de Vazamento Capilar

INTRODUCTION

Idiopathic systemic capillary leak syndrome (ISCLS) was first described in 1960 by Clarkson *et al*.[1] Characterized by recurrent episodes of increased vascular permeability, with loss of protein rich fluid to the extravascular space, it can result in a distributive and hypovolemic shock, mimicking serious conditions, such as septic shock or anaphylaxis.[2-5] Idiopathic systemic capillary leak syndrome is a rare disorder, with around 500 adult cases reported in the literature, and is even less common in children, with around 30 cases described.[2]

The etiology and pathophysiology are unknown, although several theories of pathogenesis have been proposed.[4] In adults it has been associated with monoclonal gammopathy,[2-5] but this correlation is not present in the pediatric population.[2-4] Another distinctive factor is that in children, almost every episode is triggered by an acute infection.[2,3] Intense physical exercise may also trigger attacks.[6]

The syndrome progresses in three distinct phases, starting with a prodromal phase consisting of symptoms like fatigue, nausea/vomiting, abdominal pain, edema and myalgias. After one to four days the second phase takes place, presenting as a hypovolemic shock, with hypotension, hypoalbuminemia, and hemoconcentration due to fluid extravasation.[2-4] In this phase, acute kidney injury, compartment syndrome of the extremities, and cerebral edema can occur.[2-5] The last stage is the recovery phase, with fluids recruited back to the vascular bed, and normalization of blood tests and clinical condition.[2-4] Therapy is mostly supportive in the various stages, according to needs. In patients with ISCLS already diagnosed, prophylactic immunoglobulin seems to reduce the number of acute episodes and improve morbidity and mortality.[2,4]

Here we present the case of a seven-year-old with an acute episode of ISCLS, describing the clinical manifestations and evolution, and addressing this rare condition and the importance of an early diagnosis.

1. Serviço de Pediatria. Hospital do Divino Espírito Santo. Ponta Delgada. Portugal.
2. Serviço de Pediatria. Unidade Local de Saúde do Alentejo Central. Évora. Portugal.
3. Unidade de Cuidados Intensivos e Especiais Pediátricos. Unidade Local de Saúde Amadora/Sintra. Amadora. Portugal.
4. Unidade de Infeciologia e Imunodeficiências. Serviço de Pediatria. Hospital de Santa Maria. Unidade Local de Saúde de Santa Maria. Lisboa. Portugal.
✉ **Autor correspondente:** João Vasco. jgoncalvesvasco@gmail.com
Recebido/*Received*: 18/03/2024 - **Aceite/*Accepted*:** 08/07/2024 - **Publicado *Online*/*Published Online*:** 23/08/2024
Copyright © Ordem dos Médicos 2024

ARTIGO ACEITE PARA PUBLICAÇÃO DISPONÍVEL EM WWW.ACTAMEDICAPORTUGUESA.COM

CASE REPORT

A seven-year-old boy, previously healthy, presented with a three-day history of fatigue, arthralgias, muscle soreness, abdominal pain, dysuria and periorbital edema. A week before he had a self-limited viral infection and sustained physical exercise. After the first observation in the emergency room, he started vomiting and abdominal pain intensified. Lab results showed hemoconcentration (Hb 18.1 g/dL; Htc 54.7%) due to fluid loss. Fluid therapy was initiated, with a first bolus, but persistent tachycardia and oliguria were noted. Analytic reevaluation revealed an abnormal renal function (serum creatinine 1.09 mg/dL; GFR 49 mL/min/1.73 m^2) and worsening of hemoconcentration (Hb 21.4 g/dL; 66.3%). Urinalysis, thorax x-ray and cardiac tests (echocardiogram and biomarkers) were normal. Due to clinical progression with hypotension, a second fluid bolus was administered. There was no need for vasoactive drugs. Ceftriaxone was started and blood cultures collected. The patient was transferred to an intensive care unit.

In the pediatric intensive care unit (PICU) he remained tachycardic (150 bpm), without hypotension, and with abdominal pain. At admission blood gases revealed pH 7.35, $HCO3^-$ 16.8 mEq/L, base deficiency 14.1 mEq/L and lactate 4.3 mmol/L (max. 8 mmol/L). Hemoconcentration (Hb 22.7 g/dL, Htc 68%) persisted and hypoalbuminemia (2.48 g/dL) was revealed. An abdominal computed tomography (CT)-scan revealed intermuscular edema in the abdominal wall and thighs. A few hours later, the renal function worsened (maximum creatinine 1.48 mg/dL), with progression to anuria, and hypoproteinemia. For that reason, albumin 20% 1 g/kg was administered, and a furosemide infusion was started with improvement in the urine output. The patient complained about non-specific pain in the lower limbs.

In the next day, the clinical condition began to improve, with normal urine output and a reduction in heart rate. Inflammatory blood markers, serologic testing and blood cultures were negative, excluding infectious shock causes. Antibiotic therapy was stopped after three days. At the end of the day, lower limb edema suddenly became noticeable, with pale skin and reduced dorsalis pedis pulse, accompanied by worsening of the pain. Compartment syndrome of the extremities was confirmed, with measured tissue pressure around 30 mmHg and diastolic blood pressure of 60 mmHg, and presence of rhabdomyolysis with elevation of creatinine phosphokinase (CK) – max 4340 U/L. After surgical evaluation, fasciotomy was not needed. Ultrasound excluded deep venous thrombosis.

Two days later, the child began to improve, with regression of periorbital and lower limb edema. A second furosemide perfusion was required during the recovery phase. When discharged from the intensive care unit, analytic evaluation showed a normal renal function and complete blood count. The patient fully recovered one week after hospital admission, diagnosis of ISCLS was assumed and prophylactic treatment was started with monthly intravenous immunoglobulin therapy (IVIG) 1 g/kg. Outpatient follow-up was maintained, with no new episodes until the present day.

DISCUSSION

According to the literature, the median age at presentation of pediatric ISCLS is 4.5 years-old, but it has been described in all ages from newborns to adolescence.[2] Around 75% of children affected by this disease, as in our case, had an acute illness preceding the episode.[2,3] Patients typically present with tachycardia, hypotension, hemoconcentration and hypoalbuminemia.[2-5] Differential diagnosis with common causes of distributive shock can be challenging. The most common complications of the acute extravasation phase are uncompensated circulatory shock and rhabdomyolysis – with or without compartment syndrome –, and, in the recovery phase, pulmonary edema.[2,3] Other analytic changes have been described as rise of IL-8, TNF- a and CCL2.[3]

The treatment is not well established, consisting of supportive care during the extravasation and recovery phase.[2-4] In most of the described cases, multiple crystalloid bolus and albumin administrations were used,[3] as in our patient. More specific and successful treatments in the acute phase are described with aminophylline plus terbutaline[2-4] and IVIG.[3,4] In one pediatric case, infliximab appeared effective in reverting symptoms.[4] Prophylactic therapy is well-documented in adults, with IVIG being the treatment of choice,[3,4] and in most recent series it has been equally successful in children.[3] As recurrent episodes can be severe or fatal, even with prompt recognition, we decided to start prophylactic IVIG in our patient.

With this report we aim to raise awareness of a rare but life-threatening disease that mimics other serious conditions such as septic shock, toxic shock syndrome or anaphylaxis. The characteristic triad of hypotension, hypoalbuminemia, and hemoconcentration, along with negative inflammatory markers, helps with the diagnosis. After excluding the previously described conditions, ISCLS should be considered and treated to give support and prevent complications.

AUTHOR CONTRIBUTIONS

JV: Literature review and writing of the manuscript.

FA, FC, ADC: Writing and critical review of the manuscript.

ARTIGO ACEITE PARA PUBLICAÇÃO DISPONÍVEL EM WWW.ACTAMEDICAPORTUGUESA.COM

CE: Critical review of the manuscript.
All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Clarkson B, Thompson D, Horwith M, Luckey EH. Cyclical edema and shock due to increased capillary permeability. Am J Med. 1960;29:193-216.
2. Bozzini MA, Milani GP, Bianchetti MG, Fossali EF, Lava SA. Idiopathic systemic capillary leak syndrome (Clarkson syndrome) in childhood: systematic literature review. Eur J Ped. 2018;177:1149-54.
3. Hsu P, Xie Z, Frith K, Wong M, Kakakios A, Stone KD, et al. Idiopathic systemic capillary leak syndrome in children. Pediatrics. 2015;135:e730-5.
4. Bichon A, Bourenne J, Gainnier M, Carvelli J. Capillary leak syndrome: state of the art in 2021. Rev Méd Interne. 2021;42:789-96.
5. Lee H, Shin J, Kim S, Hwang JH. Idiopathic systemic capillary leak syndrome: a case report. BMC Nephrology. 2023;24:72.
6. 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;154:464-71.

ARTIGO ACEITE PARA PUBLICAÇÃO DISPONÍVEL EM WWW.ACTAMEDICAPORTUGUESA.COM