Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18424
DOI URL: http://dx.doi.org/10.21474/IJAR01/18424

RESEARCH ARTICLE

A MISLEADING FORM OF IDIOPATHIC CAPILLARY LEAKAGE SYNDROME (CLARKSON'S DISEASE): A CASE REPORT

UNE FORME TROMPEUSE DU SYNDROME DE FUITE CAPILLAIRE IDIOPATHIQUE (MALADIE DE CLARKSON) : A PROPOS D'UN CAS

N. Bouhabba, I. Meziane, M. Bouchoual, Z. Hamdani and A. Alayoud

Manuscript Info

Manuscript History
Received: 15 January 2024
Final Accepted: 17 February 2024
Published: March 2024

Key words:-
Clarkson Syndrome, Capillary Leakage, Repetitive Shock, Vascular Filling

Abstract

The idiopathic capillary leak syndrome, commonly referred to as Clarkson's disease, is an uncommon and severe disorder that frequently necessitates intensive care intervention due to recurring episodes of shock.With no established treatment available during the acute phase, the primary approach to management revolves around symptom relief. It seems that the use of vascular fluid resuscitation has an adverse effect on patient outcomes in intensive care, and therefore, there should be endeavors to restrict its usage.As an illustrative case, this article describes the case of a 53-year-old patient who presented to the emergency department with edema following the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and was initially misdiagnosed as anaphylaxis.Laboratory tests revealed hypoproteinemia in contrast to hemoconcentration, and the absence of serum albumin, which raised suspicion of Clarkson's syndrome. This suspicion was confirmed through serum protein electrophoresis, ruling out other diagnoses.

Introduction:

Idiopathic capillary leak syndrome (ICLS) is a rare but severely prognostic entity that can jeopardize the patient's life and whose pathophysiology remains poorly understood.Clinically, ICLS is characterized by the onset of edematous syndrome, oliguria, and arterial hypotension that can progress to repeated hypovolemic shock. From a laboratory perspective, Clarkson's disease is associated with hemoconcentration, paradoxical hypoalbuminemia, and hypoproteinemia.

We report a case of Clarkson's disease mistakenly treated as anaphylaxis, thereby worsening the patient's prognosis.

Case report :

Patient information :

A 53-year-old man, known for iron-deficiency anemia for the past three years, was admitted to the emergency department with sudden-onset asthenia, unquantified fever, and diffuse myalgias, notably more pronounced in the calf muscles. This symptomatology was preceded, one week before his admission, by an episode of mumps orchitis. The patient reports taking nonsteroidal anti-inflammatory drugs (NSAIDs) two days prior, which was followed by the onset of facial edema.

Corresponding Author:- N. Bouhabba

Clinical findings :

The clinical examination revealed a conscious patient who was polypneic at 26 cycles per minute, tachycardic at 125 beats per minute, with a blood pressure of 110/55 mmHg, and a fever of 39°C. There were soft, bilateral lower limb edemas that were pitting and painful on palpation, along with periorbital edema and bilateral inguinal lymphadenopathy. Abdominal palpation revealed painless periumbilical indurations.

Diagnostic Assessment :

Confronted with this clinical finding, as the initial hypothesis, a diagnosis of anaphylaxis with angioedema following NSAID intake was considered, and symptomatic treatment was initiated, including vascular fluid resuscitation with isotonic saline, corticosteroid therapy with methylprednisolone at a dose of 40 mg twice a day, oral antihistamines, and close monitoring of vital signs.

Six hours after his admission to the emergency department, the patient experienced hemodynamic instability characterized by refractory arterial hypotension at 70/40 mmHg, despite well-conducted vascular fluid resuscitation. This necessitated the introduction of vasoactive drugs (noradrenaline at a rate of 0.3 µg/kg/minute), and there was an exacerbation of the edematous syndrome on clinical examination, with no impairment of consciousness.

Subsequently, a series of laboratory tests were requested, including an infectious assessment: normal white blood cell count (WBC), lymphopenia, elevated C-reactive protein (CRP) at 70 mg/L, negative procalcitonin at 0.2 ng/mL, sterile urinary analysis, negative COVID-19 PCR, and negative blood culture.

Abdominal ultrasound showed no anomalies except for a small amount of peritoneal effusion.

Furthermore, the rest of the laboratory tests revealed a surprisingly normal hemoglobin level at 12.9 g/dL with a hematocrit of 50%, an acute kidney injury that appeared to be functional with a creatinine level of 14.9 mg/L, hypoproteinemia at 44 g/L, and hypoalbuminemia at 20 g/L without albuminuria.

The patient underwent a skin lesion biopsy, which favored leukocytoclastic vasculitis, with negative results in the immunological panel (ANCA, antinuclear antibodies, anti-DNA antibodies).

Therapeutics and evolution :

The decision made by the multidisciplinary consultation team was to administer the patient a 1g methylprednisolone bolus for 3 days, followed by oral prednisone at a daily dose of 60 mg.

The evolution was marked by the worsening of the edematous syndrome, along with hemodynamic and respiratory instability.

The diagnosis of proximal pulmonary embolism was ruled out through a thoracic CT angiogram, which also revealed bilateral interstitial syndrome and a small amount of pleuropericardial and peritoneal effusion without any suspicious lesions.

Subsequently, the patient was transferred to the intensive care unit for further management.

Given the combination of hemoconcentration, the persistence of hypovolemic shock without associated acidosis, the normal cortisol level, hypoproteinemia, and paradoxical hypoalbuminemia in the lab results, idiopathic capillary leak syndrome (ICLS), or Clarkson's disease, was strongly suspected.

An etiological investigation was initiated: serum protein electrophoresis revealed a monoclonal IgG kappa gammopathy. Viral serologies (hepatitis B, C, A, HIV, TPHA, VDRL, EBV) were negative, CPK was elevated, rheumatoid factor was normal, and a sternal puncture showed no specific findings.

The secondary management involved reducing vascular fluid resuscitation and adding 100 ml of 20% albumin twice a day, along with preventive anticoagulation using low molecular weight heparin.

The clinical course afterward showed improvement, with a gradual tapering of noradrenaline, an alleviation of dyspnea, and a reduction in edema without the need for diuretics. Follow-up laboratory tests indicated an improvement in renal function parameters with the persistence of hypoalbuminemia characteristic of capillary leak syndrome.

A decision to initiate an etiological treatment with immunoglobulins was made, but three days later, a second crisis occurred, and the patient's condition rapidly deteriorated, leading to multiple organ failures and ultimately resulting in the patient's death.

Discussion:

Affecting middle-aged adults around 50 years old with an even gender ratio [1], Clarkson's disease or ICLS is a rare disease with a poor prognosis, first described in 1960 [2], and to date, fewer than 250 cases have been reported in the literature [3].

With its poorly understood pathophysiology, its diagnosis remains primarily clinical, characterized by the repetitive occurrence of hypovolemic shock alongside hemoconcentration and hypoalbuminemia.

It can occur suddenly or manifest with a prodromal phase featuring non-specific general symptoms (asthenia, fever), or a genuine viral infection (such as viral rhinopharyngitis or gastroenteritis) [1,3]. In our patient's case, it was a mumps virus infection.

After the prodromal phase, this disease is characterized by a state phase and a recovery phase, with the initial, unpredictable phase being the most critical aspect of the condition. It can jeopardize the patient's life due to hypovolemic shock without impairment of consciousness, accompanied by skin and serous membrane infiltration [1,3,4].

The main clinical signs during ICLS crises found in the literature include: [1]

1. Signs related to the triggering factor:
   - Fever
   - Flu-like Syndrome
   - Headaches
   - Cough, runny nose, dyspnea
2. Signs related to hypovolemia:
   - Asthenia and intense thirst, polydipsia
   - Lightheadedness, fainting
   - Mottling, profuse sweating
   - Low blodd pressure, tachycardia
   - Oliguria
3. Signs related to capillary leakage:
   - Myalgia, paresthesia
   - Nausea, vomiting, diarrhea
   - Abdominal pain
   - Widespread edema, in the arms and face
   - Compartment syndromes
   - Myocardial dysfunction

The laboratory presentation is pathognomonic, characterized by the combination of hemoconcentration and paradoxical hypoalbuminemia without albuminuria.

Serum protein electrophoresis reveals a monoclonal gammopathy, most commonly of the IgG kappa type, in over 80% of cases.

During the state phase, compartment syndrome may be observed, often exacerbated by massive fluid resuscitation. Oliguria in the context of functional renal impairment is consistent, typically reversible without lasting effects. Other complications that may arise include seizures due to cerebral edema and cardiac arrhythmias [3,4].

In our case, the patient rapidly developed a state of shock with highly suggestive laboratory findings, and the myalgias were related to a compartment syndrome and rhabdomyolysis. The patient remained vigilant despite the severity of the clinical presentation.
Given the clinical and laboratory profile suggestive of ICLS, it is important to rule out other potential secondary causes of capillary leakage, including hematological disorders, drug and toxic causes, postoperative and post-traumatic contexts, bacterial and viral infections, acute adrenal insufficiency, pheochromocytoma, hypothyroidism, nephrotic syndrome, carcinoid tumors, heart failure, exudative enteropathy, acute mountain sickness, and more [3,4,5].

Our patient underwent a thorough etiological assessment as soon as diagnostic suspicion arose to rule out other secondary causes.

The management of this rare syndrome is currently based on observational data, and treatment during the acute phase is purely symptomatic, as the crisis spontaneously resolves within 48 to 72 hours. The goal is to successfully navigate through the state phase and prevent complications.

The primary therapeutic approaches for severe crises involve intensive care monitoring, invasive blood pressure measurement, with an emphasis on limiting vascular fluid resuscitation to tolerate arterial hypotension. Additionally, regular monitoring of muscle compartment pressure and neurological examination of all four limbs is essential, along with surveillance for the development of pulmonary edema during the recovery phase. [1]

A randomized study comparing 59 ICU admissions among 37 patients with Clarkson's disease reported that vascular fluid resuscitation appeared to be detrimental and correlated with mortality. Moreover, it was strongly associated with the development of compartment syndrome [3]. The authors concluded that it is justifiable to reduce initial vascular fluid resuscitation, tolerate moderate hypotension, and promptly use vasoactive drugs in cases of profound hypotension, thus ensuring organ perfusion. The use of synthetic colloids (hydroxyethyl starch) to reduce the volume of fluid resuscitation may be considered, as well as resuscitation with albumin [3,6]. In our patient, prior to the diagnostic suspicion of ICLS, excessive vascular fluid resuscitation led to an exacerbation of complications and a hastening of multi-organ failures during the second crisis.

Despite advances in understanding the pathophysiology of ICLS, targeted therapies have been implemented in isolated cases but have not proven their effectiveness. Therefore, there is currently no specific treatment available [4,6,7].

Given the risk of recurrent crises, severe forms of the disease warrant the initiation of long-term maintenance therapy as a prophylactic measure. A recommended first-line approach is the use of 2g/kg/month of intravenous immunoglobulin (IV Ig) administered over 48 hours [1]. Prophylaxis also involves regular dental care and vaccination against influenza and pneumococcal infections, as these crises can be triggered by infectious episodes.

Lastly, the prognosis of this disease remains bleak. The majority of patients succumb in the acute phase in the intensive care unit. The ten-year survival rate is 68% in the EurêClark registry as well as in the Mayo Clinic cohort [8]. The rate of progression to myeloma does not appear to be higher compared to other monoclonal gammopathies not associated with ICLS. Therefore, it is important to screen for myeloma at the time of ICLS diagnosis and regularly monitor the progression of the monoclonal gammopathy.

Conclusion:

Given the severity of Clarkson's disease and despite its rarety, a thorough understanding of its clinical and laboratory syndrome is essential to enable early diagnosis, mitigate harmful treatments, and thereby improve the patients' prognosis. Treatment remains primarily symptomatic, with the hope of gaining a better understanding of the underlying pathophysiological mechanisms.

Références:

1. Pineton de Chambrun, ,M.Gousseff , C.E.LUYT , N.Bréchot , A.Combes , Z.Amoura . Diagnostic et prise en charge du syndrome de fuite capillaire idiopathique (SFCI). Méd.Intensive Réa.2017 April26, pages 268–276

2. Clarkson B, Thompson D, Horwith M, Luckey EH, Cyclical edema and shock due to increased capillary permeability. Am J Med 1960 Aug;29:193-216
3. Duron L, delestre F, Amoura Z, Arnaud L. idiopathic and secondary capillary leak syndromes: a systemic review of the literature. Rev Med interne. 2015 Jun ; 36 (6): 386-94.
4. Gousseff M, Amoura Z, Idiopathic capillary leak syndrome.Rev Med interne. 2009 Sep;30(9):754-68
5. Druey KM, parikh SM. Idiopathic systemic capillary leak syndrome (Clarkson disease). J Allergy clin Immunol 2017Sep;140(3):663-670 .
6. George C, Regnier B, Le Gall JR, Gastinne H, Carlet J, Rapin M, Hypovolaemic shock with oedema due to increased capillary permeability. Intensive Care Med 1978 Jul;4(3):159-63
7. Pineton de chambrun M, Goussef M, Mauhin W, Lega J-C, Lambert M, Rivière S, et al. Intravenous Immunoglobulins Improve Survival in Monoclonal Gammopathy-Associated Systemic. Capillary-Leak Syndrome, Am J Med. 2017 Oct;130(10):1219.e19-1219.e27
8. Kapoor P, Greipp PT, Schaefer EW, Mandrekar SJ, Kamal AH, Gonzalez-Paz NC, Kumar S, Greipp PR, Idiopathic systemic capillary leak syndrome (Clarkson's disease): the Mayo Clinic experience. Mayo Clin Proc 2010 Oct;85(10):905-12.