v. 3, n. 13 2023

International Journal of Health Science

SYSTEMIC LUPUS ERYTHEMATOSUS DIAGNOSED AFTER AN EPISODE OF HEMOLYTIC UREMIC SYNDROME - A CASE REPORT

Amanda Moreira Portes
Resident Doctor of the Medical Clinic of the institution: Fundação Universidade Federal do Tocantins
Palmas – TO
http://lattes.cnpq.br/3883772302324578

Izabella Chaves Parreira
Resident Doctor of the Medical Clinic of the institution: Fundação Universidade Federal do Tocantins
Palmas – TO
http://lattes.cnpq.br/1376294317615447

Laíz Soares Silva
Resident Doctor of the Medical Clinic of the institution: Fundação Universidade Federal do Tocantins
Palmas – TO
http://lattes.cnpq.br/3498161493081005

Abstract: Hemolytic uremic syndrome (HUS) is characterized by the presence of microangiopathic hemolytic anemia, thrombocytopenia, generalized microvascular occlusion and acute kidney injury, which can be divided into typical HUS - caused by Escherichia coli producing Shiga toxin; Primary atypical HUS and secondary atypical HUS. Systemic lupus erythematosus (SLE) is a multisystem immune disease associated with activation of immune complexes. These immune complexes may be associated with kidney damage, called lupus nephritis. In clinical practice, it is initially difficult to differentiate between the two diagnoses, as in some cases renal dysfunction may be the first manifestation of Lupus, even before the cutaneous-hematological changes, and it is important to think about the differential diagnoses cited for patients with suggestive clinical and epidemiological history. In this work, we report a clinical case of overlapping of the two pathologies.
Keywords: Systemic lupus erythematosus; Lupus nephritis; Hemolytic Uremic Syndrome.

INTRODUCTION

Hemolytic uremic syndrome (HUS) is characterized by the presence of microangiopathic hemolytic anemia (due to shear stress in the microcirculation), thrombocytopenia (due to platelet consumption) and generalized microvascular occlusion caused by the deposition of platelet-rich thrombi, with mainly renal involvement (POLITO et al, 2010).

HUS is currently divided into typical HUS, which is caused by Shiga toxin-producing Escherichia coli; primary atypical HUS (aHUS), which is related to alterations in the regulation of the alternative complement pathway; and secondary aHUS, which may be associated with infectious, neoplastic, immunological diseases, among others (NIETO-RIOS et al, 2021).

Systemic lupus erythematosus (SLE) is a multisystem immune disease associated with activation of immune complexes. These immune complexes may be associated with kidney damage, called lupus nephritis, which is characterized by progressive renal failure due to focal or diffuse membranous glomerulonephritis. Among patients with lupus nephritis, 17.5% develop microvascular thrombosis with progressive thrombocytopenia, hemolytic microangiopathic anemia and progressive renal failure (PARK et al, 2018), characteristics that, as already described, also define HUS. Thus, the similarity of the clinical and laboratory presentation of complement-mediated thrombotic microangiopathy associated with Lupus Nephritis and HUS is remarkable.

Here we will present the case of a patient who opened the picture of SLE together with a classic hemolytic uremic syndrome.

CASE REPORT

Patient N.C.F, 31 years old, female, G2P2A0 on the 54th postoperative day after cesarean section, previously healthy, from Miracema-TO. Admitted to the Hospital Geral de Palmas on 01/07/2023 complaining of diffuse abdominal pain and abdominal distention after a single episode of mucous-bloody diarrhea, rapidly progressing to oliguria and anasarca. She also refers dyspnea to the efforts she associated with the current situation. Companion and patient reported that neighbors and family members had similar gastrointestinal symptoms.

It refers to good eating habits, denies alcoholism and smoking. He is unaware of any personal or family first and second degree renal, oncological, hematological or rheumatological pathology. Reports uneventful pregnancies, term delivery without

associated complications. She was discharged 48 hours after the last delivery.

Upon physical examination on admission, the patient presented edema in the lower limbs symmetrical associated with facial edema and ascites. Other systems and devices showed no changes.

In the laboratory tests on admission, he presented a blood count with leukocytosis associated with thrombocytopenia (hemoglobin 12.3 g/dL; hematocrit: 34.3%; leukocytes: 16,600/mm^3; Platelets: 76,000/mm^3), significant alteration in renal function (Creatinine: 7.39 mg/dL and Urea: 108 mg/dL) and hypoalbuminemia (Albumin: 2.8 g/dL). During the hospitalization, he developed severe anemia, with hemoglobin equal to 7.0 g/dL, hematocrit of 19.8% and anisocytosis with hypochromia, the presence of schistocytes not being described by the laboratory, but with a considerable increase in serum lactate dehydrogenase.

The urine analysis (EAS) showed cloudy urine, proteinuria +++, hemoglobin ++, pyocytes of 21,000/mL, epithelial cells 28,000/mL and red blood cells of 70,000/mL, leukocyte esterase and negative nitrite. Ultrasonography of the kidneys and urinary tract showed normal-sized kidneys, an ultrasonographically normal bladder, with no alterations or signs of chronicity.

A computed tomography scan of the entire abdomen was performed with intravenous administration of iodine contrast, which identified moderate bilateral pleural effusion, greater on the right, a small amount of fluid in the pelvic cavity and normodistended intestinal loops, noting a slight increase in diffuse parietal thickness and fat blurring adjacent mesenteric membrane, which may correspond to an inflammatory/infectious process (colitis?).

Due to the renal failure identified in the initial exams, a consultation with the nephrology team was requested, which raised a diagnostic hypothesis of HUS. Concomitantly, due to the patient's epidemiological profile and clinical case compatible with lupus nephritis, rheumatological tests were also requested to investigate Systemic Lupus Erythematosus (SLE).

During hospitalization, the dyspnea that was previously reported on exertion evolved to dyspnea at rest, requiring the initiation of oxygen therapy through a nasal catheter due to pulmonary congestion with little response to diuretic therapy. Renal replacement therapy (RRT) by hemodialysis was then started on January 9th to control metabolic and fluid balance, due to clinical worsening and low responsiveness to conservative measures.

The patient remained undergoing RRT until January 21, the date of her last session. After this period there was recovery of spontaneous diuresis, in addition to permanent improvement of respiratory symptoms and anasarca.

After releasing the results of the rheumatological markers (Table 1), the patient was evaluated by the Rheumatology team, confirming the diagnosis of Systemic Lupus Erythematosus, initiating drug treatment with hydroxychloroquine, prednisone and calcium carbonate.

Exams	Result	Reference value
FAN	Core: Fine Dotted Nuclear 1/320 Homogeneous Nuclear 1/80 Nucleolus: Reagent Cytoplasm: Non-Reactive Mitotic Apparatus: Non-Reactive Chromosomal metaphase plate: Non-Reagent	Non-reagent
Anti DNA	1/40	Non-reagent
C3	89 mg/dL	Newborn: 58 to 108 mg/dL 3 months: 67 to 124 mg/dL 4 to 6 months: 74 to 124 mg/dL 7 to 9 months: 78 to 144 mg/dL 10 to 12 months: 80 to 150 mg/dL 1 to 10 years: 80 to 150 mg/dL 11 to 19 years: 85 to 160 mg/dL 20 to 30 years: 82 to 160 mg/dL 31 to 39 years: 84 to 160 mg/dL 40 to 70 years: 90 to 170 mg/dL
C4	25,3 mg/dL	12 a 36 mg/dL
CH50	38,3 U/CAE	Greater than 60 U/CAE
lupus anticoagulant	< 1/2	Reference values Absent: Less than or equal to 1.2 Present: Greater than 1.2
Beta 2 glycoprotein I IGG and IGM antibodies	IgG antibodies: 2.8 Elia U/mL / IgM antibodies: 15 Elia U/mL	Negative: Less than 7 Elia U/mL Indeterminate: 7 to 10 Elia U/mL Positive: Greater than 10 Elia U/mL
Anticardiolipin IgG	0,8 GLP U/ml	Non-reactive: Less than 10.0 GPL U/mL Weakly reactive: 10.0 to 40.0 GPL U/mL Reagent: Greater than 40.0 GPL U/mL
Anticardiolipin IgM	less than 0.9 MPL U/ml	Non-reagent: Less than 10.0 MPL U/mL Weakly reactive: 10.0 to 40.0 MPL U/mL Reagent: Greater than 40.0 MPL U/mL
Anti RNP	1,3 Elia U/ml	Reagent: Above 10 U/ml Non-Reagent: less than 5.0 U/ml Undetermined: 5.0 to 10 U/ml
Rheumatoid Factor	less than 8.0 IU/ml	less than 8.0 IU/ml
Anti-SM	less than 8 Elia U/ml	Non-Reagent: < 7.0 Elia U/mL Inconclusive: 7.0 to 10.0 Elia U/mL Reagent: > 10.0 Elia U/mL
Anti- SSA	Greater than 240 Elia U/m	Non-Reagent: < 7.0 Elia U/mL Inconclusive: 7.0 to 10.0 Elia U/mL Reagent: > 10.0 Elia U/mL
Anti- SSB	88 Elia U/m	Non-Reagent: < 7.0 Elia U/mL Inconclusive: 7.0 to 10.0 Elia U/mL Reagent: > 10.0 Elia U/mL
Coombs direct	Negative	Negative
24 hours proteinuria	3380 mg/24h	<100.0 mg/24 hours
24-hour creatinine clearance	23,3 mL/min/1,73 m^2	Adults: 75 to 115 mL/min/1.73 m^2 Child: 70 to 140 mL/min/1.73 m^2

Table 1 - Antibodies and other tests performed in the investigation.

He was discharged from the hospital for outpatient follow-up in Rheumatology and Nephrology in good general condition and with improvement of the initial complaints. On the day of discharge, the patient had a mild anemia (hemoglobin 11.1 g/dL; hematocrit: 31.7%; leukocytes: 3,600/mm^3; Platelets: 375,000/mm^3) and significant improvement in renal function compared to admission (Creatinine: 2.24 mg/dL and Urea: 34 mg/dL).

DISCUSSION

The association of SLE with HUS, although rare, has already been reported by several authors. Our patient presented symptoms of HUS simultaneously with those of SLE and, therefore, received both diagnostic hypotheses.

Typical HUS is more frequent in children, but it has also been reported in adults, although in smaller numbers. Its etiology and pathogenesis in childhood and adults are the same, but the prognosis of HUS in adults is worse, renal and neurological involvement are usually more severe and sequelae are more frequent (RUGGENENTI et al, 2021). Our patient, being a young adult, quickly evolved with severe kidney damage, requiring RRT.

The incidence of typical HUS is higher in the hot summer months, when there are more cases of E. coli infection. The mean interval between Shiga toxin exposure and illness ranges from 1 to 8 days, and initially presents with abdominal cramps and non-bloody diarrhea that can become bloody in 70% of cases, usually within a day or two (RUGGENENTI et al, 2021). As in the present case.

Although our patient developed a clinical picture of typical HUS, SLE is also associated as a secondary cause of atypical HUS. There are several hypotheses that try to explain the mechanism of the association between HUS and SLE, although this pathogenic relationship is still uncertain. Among the already presumed factors there is the presence of circulating antiplatelet antibodies, antiendothelial antibodies, immunocomplexes, anticardiolipin antibodies and antiphospholipid antibodies (RABBANI et al, 2005. ESPINOSA et al, 2004).

SLE was the first autoimmune disease in which the association of microangiopathic hemolytic anemia with antiphospholipid antibodies was recognized. But this relationship is intriguing, as antiphospholipid antibodies are present in up to 50% of patients with SLE and a positive test can be expected in a proportion of patients with SLE who develop thrombotic microangiopathy without necessarily implying an existing causal relationship. (ESPINOSA et al, 2004).

To establish a causal link between SLE and HUS in this case was not possible, and only their coexistence was determined. As already described the HUS clinic, the patient also closed the diagnosis of SLE according to the EULAR/ACR criteria (2019), presenting the entry criterion (ANA greater than or equal to 1:80) and scoring another 21 points: 4 (thrombocytopenia) + 5 (pleural effusion) + 4 (proteinuria) + 2 (positivity for anti-beta2-glycoprotein I IgM) + 6 (Anti-DNA reagent).

Renal impairment in SLE occurs in about 60% of patients and can indicate tubular, interstitial, vascular and glomerular alterations, the latter being the one that determines most of the signs and symptoms of lupus nephritis. In most cases it is not possible with clinical and laboratory tests alone to differentiate the probable causes of kidney disease. Performing a renal biopsy has the role of differentiating and determining the histological class, which helps to guide the therapeutic choice (KLUMB et al, 2015).

Despite being a simple procedure, in practice performing a renal biopsy is not always feasible, both in our service and

in several others. For these situations, it is possible to use clinical and laboratory markers to help determine the severity and activity of the disease and direct the treatment with immunomodulatory and/or immunosuppressive agents (KLUMB et al, 2015).

CONCLUSION

The reported case demonstrated that when two pathologies have similar clinical presentations, it is difficult to determine a causal relationship between the two when they manifest at the same time. It is not possible to differentiate whether there is a coincidence or a dependence of one on the other.

Defining the case with only one pathology would not be wrong, but failing to consider other diagnostic hypotheses would be imprudent. Upon identifying the presence of hemolytic uremic syndrome and following the investigation, another diagnosis was made, and a new treatment instituted. This proves the importance of considering more than one diagnostic hypothesis and not restricting clinical reasoning, as the conduct can be different and change the patient's life.

REFERENCES

1. ARINGER, Martin. **EULAR/ACR classification criteria for SLE**. Seminars in Arthritis and Rheumatism, [S. l.], p. S14-S19, 25 nov. 2019. DOI https://doi.org/10.1016/j.semarthrit.2019.09.009. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0049017219306444?via%3Dihub. Acesso em: 5 fev. 2023.

2. ESPINOSA, G et al. **Thrombotic microangiopathic haemolytic anaemia and antiphospholipid antibodies.** Annals of the Rheumatic Diseases, [S. l.], v. 63, p. 730–736, 14 jun. 2004. DOI 10.1136/ard.2003.007245. Disponível em: https://ard.bmj.com/content/63/6/730. Acesso em: 25 jan. 2023.

3. KLUMB, Evandro Mendes et al. **Consenso da Sociedade Brasileira de Reumatologia para o diagnóstico, manejo e tratamento da nefrite lúpica.** Revista Brasileira de Reumatologia, [S. l.], p. 1 - 21, 1 fev. 2015. Disponível em: https://doi.org/10.1016/j.rbr.2014.09.008. Acesso em: 3 fev. 2023.

4. NIETO-RIOS, John Fredy et al. **Síndrome hemolítico-urêmica causada por Escherichia coli produtora de toxina Shiga em um relato de caso de receptor de transplante renal.** Brazilian Journal of Nephrology, [S. l.], p. 591-596, 11 nov. 2020. Disponível em: https://doi.org/10.1590/2175-8239-JBN-2020-0048. Acesso em: 24 jan. 2023.

5. PARK, Mi Hee et al. **Complement-mediated thrombotic microangiopathy associated with lupus nephritis.** Blood Advances, [S. l.], p. 2090–2094, 28 ago. 2018. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113612/. Acesso em: 24 jan. 2023.

6. POLITO, Maria Goretti; KIRSZTAJN, Gianna Mastroianni. **Microangiopatias trombóticas: púrpura trombocitopênica trombótica e síndrome hemolítico-urêmica.** Brazilian Journal of Nephrology, [S. l.], p. 303-315, 25 out. 2010. Disponível em: https://doi.org/10.1590/S0101-28002010000300013. Acesso em: 31 jan. 2023.

7. RABBANI, Malik Anas et al. **Systemic Lupus Erythematosus presenting as Hemolytic Uremic Syndrome: a case report.** Journal of Pakistan Medical Association, [S. l.], p. 84-87, 1 fev. 2005. Disponível em: https://ecommons.aku.edu/pakistan_fhs_mc_med_pulm_critcare/122. Acesso em: 31 jan. 2023.

8. RUGGENENTI, Piero et al. **Thrombotic microangiopathy, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura.** Kidney International, [S. l.], p. 31-46, 1 set. 2021. DOI 10.1046/j.1523-1755.2001.060003831.x. Disponível em: https://pubmed.ncbi.nlm.nih.gov/11532079/. Acesso em: 1 fev. 2023.