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CASE REPORT: PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND MANIFESTATIONS OF LUPUS NEPHRITIS

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Abstratc: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology. It has a very varied clinical picture, which may involve skin, joint, vascular, renal, neurological and other systems. Renal involvement is prevalent and serious, requiring careful clinical management. Therefore, this article is a case report of a patient whose follow-up and treatment were carried out in the Nephrology department of Santa Casa de Misericórdia de Passos. Data were collected from the patient's medical records and literature. The patient's informed consent form was obtained. The evolution of a patient with SLE was described, from suspicion, diagnosis, treatment, correlating with data from the literature.
Keywords: systemic lupus erythematosus; lupus nephritis; early diagnosis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an inflammatory, chronic, autoimmune disease. (BORBA et al, 2008). It compromises organs and tissues in the most diverse combinations and in varying degrees of severity. (IMBODEN; HELLMANN; STONE, 2014). Renal involvement is one of the main determinants of morbidity and mortality in patients with SLE. It is clinically evident in 50 to 70% of patients with SLE. (ORTEGA, 2010) SLE is more prevalent in women of reproductive age, with the first signs and symptoms beginning between the second and third decades of life. (NELSON, 2009; SCHUR; GLADMAN, 2011).

For the diagnosis of lupus nephritis, according to the American College of Rheumatology, some criteria are considered. (Hahn BH et al 2012). The treatment of lupus nephritis is targeted (RODOVALHO, H. O. P, 2023) and the goals established in the therapy of the disease is to induce complete renal remission (FALK, R.J., et al, 2023).

Considering the severity of the disease, the need for diagnosis and introduction of early treatment, the objective of this case was to report the case, from diagnosis to the final result.

METHODOLOGY

This case report is characterized as descriptive, exploratory, with a qualitative approach (Pereira, Shitsuka, Parreira, & Shitsuka, 2018), where the identification, diagnosis and treatment stages of a patient with Lupus Nephritis are presented.

The data described were collected and disclosed after the patient read, agreed and signed the informed consent form (TCLE), authorizing the completion of this report and the collection of information contained in her medical record.

CLINICAL CASE

A.M.F.S, 52 years old, female, was admitted to the service reporting pain and edema for 5 months in the lower limbs, upper limbs, face and abdomen, associated with progressive paresthesia of the lower limbs, foamy urine, weakness and dyspnea. She denied fever, weight loss and other symptoms. During the time of evolution, she sought other health services several times, using anti-inflammatories and painkillers, without improving her condition. She also reported that around 20 years ago she had experienced an episode of nephritis, at the time, she received in-hospital treatment and used oral corticosteroids for around 8 years, discontinuing the medication on her own. She reported a recent diagnosis of systemic arterial hypertension (SAH) and was continuously taking spironolactone 25mg (1-0-1) and furosemide 40mg (1-0-0).

On physical examination:

Ectoscopy: Regular general condition, mucocutaneous pallor (2+/4+), hydrated, anicteric and acyanotic, edema in the lower

limbs (2+/4+) and periorbital edema,

Cardiovascular: Rhythmic, normophonetic sounds in 2 beats, without murmurs, tachycardia (HR: 108 bpm).

Respiratory: Vesicular murmur present with crackles on the right base.

Abdomen: flaccid abdomen, painful on palpation in the left lower quadrant, bowel sounds present.

Neurological: lethargic, but responsive and lucid and with paresthesia in the left lower limbs.

Laboratory tests, AP chest X-ray and USG of kidneys and urinary tract were requested:

EXAMS	RESULT
Hemoglobin	7.3
Hematocrit	25.2
V.C.M	81
H.C.M	24
A.D.H	15.3
Leukocytes	10.600
Segmented	71
Rods	0
Platelets	343 mil
Urea	103
Creatinine	1.8
Sodium	135
Potassium	5
Calcium	7.5
Magnesium	1.90
TSH3 ULTRA	7.90
T4 LIVRE	0.73
PCR	12
VHS	87
TGO	22
TGP	12
Total bilirubin	0.20
Direct bilirubin	0.10
Indirect bilirubin	0.10
Protein	7.8
Albumin	2.2
Globulin	5.6
Prothrombin time (activity)	79%
Prothrombin time (RNI)	1.15
TTPA	1.1
Urine Routine	Protein +, hemoglobin +++, leukocytes
Urine culture	No bacterial growth
Protein/creatinine ratio	1.37
Total cholesterol	108
HDL	24
Triglycerides	213
LDL	56
FAN	Reagent
C3 serum complement	32
C4 serum complement	5
Ferritin	955
Iron	51
Total iron binding capacity	118
Venereal Disease Research Laboratory	Negative
Anti- HCV	Negative
Hepatitis B – HBsAg	Positive
Anti - HIV	Negative

The findings on the chest X-ray did not show signs of pulmonary congestion or findings that would justify dyspnea.

Given the clinical picture and laboratory evaluation, the hypothesis of glomerulonephritis due to systemic lupus erythematosus (SLE) was raised.

We started iron replacement, transfusion of 1 packed red blood cell and renal surveillance. Two days after admission, pulse therapy with methylprednisolone 500 mg/day and prophylactic antiparasitic treatment with coverage for strongyloidiasis with albendazole were started for five days. During the course of corticosteroid therapy, the patient continued to experience dyspnea. Therefore, we requested a transthoracic echocardiogram and a new chest X-ray. The X-ray showed no changes and the transthoracic echocardiogram showed: Significant left ventricular concentric hypertrophy, preserved systolic and diastolic function, presenting type 1 dysfunction – relaxation alteration. Mild enlargement of the left atrium, right ventricle with

preserved systolic function, mild mitral and tricuspid reflux, mild pericardial effusion and pulmonary artery pressure estimated at 24 mmHg.

After the end of pulse therapy, clinical and laboratory improvement improved. The patient's breathing pattern improved and kidney function normalized, however, pain persisted in the lower limbs, making walking difficult. He was discharged from hospital with a request for outpatient motor physiotherapy, follow-up at the nephrology outpatient clinic and new pulse therapy scheduled in 12 days and prescribed prednisone 40 mg in the morning.

RESULTS AND DISCUSSION

Systemic lupus erythematosus (SLE) is a chronic inflammatory, autoimmune disease, of little known etiology. It is due to an imbalance in the immune system and the production of antibodies directed against the body's own protein. This generates the formation of immunocomplexes which, when deposited in small vessels, result in vasculitis and dysfunction in the affected area. (BORBA et al, 2008).

It compromises organs and tissues in the most diverse combinations and in varying degrees of severity, it can affect different organs, such as the skin, joints, lungs, heart, kidneys, nervous system, among others. (IMBODEN; HELLMANN; STONE, 2014). This pathology may include constitutional symptoms, arthritis, serositis, nephritis, vasculitis, myositis, mucocutaneous manifestations, immunological hemocytopenias, various neuropsychiatric conditions, reticuloendothelial hyperactivity and pneumonitis (LOPES, 2006)

SLE is more prevalent in women of reproductive age, with the first signs and symptoms beginning between the second and third decades of life, which demonstrates a potential effect of estrogen on the pathophysiology of the disease. In relation to children, in whom the effect of estrogen is minimal, the ratio between female and male sex is 4:1 before puberty, 8:1 from that stage onwards, with a predominance in females during their reproductive phase. (NELSON, 2009; SCHUR; GLADMAN, 2011). In Brazil, an approximate incidence of 4.8 and 8.7 cases per 100,000 inhabitants/year is estimated. SLE is a universal disease affecting all ethnicities, affecting one in every 1000 white people and one in every 250 black people, but it is more common in people of African descent. The characteristics of the disease and its severity as well as its prevalence may differ in different groups ethnic groups. (NELSON, 2009; SCHUR; GLADMAN, 2011).

Lupus nephritis is common in SLE, as 74% of patients will be affected at some point in the course of the disease. This renal pathology occurs due to the deposit of circulating immune complexes or local formation of these complexes in the glomeruli, leading to complement activation and subsequent recruitment of inflammatory cells. In addition to the inflammatory process, necrosis and the formation of scars in the glomeruli, renal pathology is characterized by lesions vascular diseases such as thrombotic microangiopathy and extraglomerular vasculitis, in addition to tubulointerstitial involvement with tubular atrophy and interstitial fibrosis. (CECIL, 2009).

Renal involvement is one of the main determinants of morbidity and mortality in patients with SLE. It is clinically evident in 50 to 70% of patients, but practically 100% of them have kidney disease by electron microscopy. In general, kidney diseases appear within the first 2 to 5 years of the onset of the disease and, when they appear as the initial manifestation of the disease, they worsen the prognosis of these patients. Clinical manifestations

underestimate the true frequency of renal involvement, as some patients with SLE may have significant histopathological changes on renal biopsy without any clinical sign of renal involvement. (ORTEGA, 2010)

For the diagnosis of lupus nephritis, according to the American College of Rheumatology, criteria are considered to be persistent proteinuria (demonstrated by proteinuria greater than 0.5g/day in 24-hour urine collection, proteinuria greater than 3+ and, protein/creatinine ratio located in urine greater than 0.5 g/g), together with the presence of cellular casts in the urinary sediment examination plus dysmorphic hematuria. (Hahn BH et al 2012). The gold standard for diagnosis is renal biopsy demonstrating immune complex-mediated glomerulonephritis compatible with lupus nephritis. (Schwartz N et al, 2014; Borchers AT et al, 2020) Biopsy must be performed in all patients with clinical evidence of lupus nephritis untreated unless strongly contraindicated. Indications include proteinuria greater than 500 mg/day, active urinary sediment (5 or more dysmorphic red blood cells per high power field or cell casts) or increasing serum creatinine without a clear explanation. (Hahn BH et al, 2012; Fanouriakis A et al, 2019). The patient under study presents criteria for completion, as she has a protein/creatinine ratio of 1.37 g/g and the presence of hematuria in the urinary sediment. However, our service does not allow early biopsy, so it was requested and the patient is awaiting the procedure. It is important to highlight that the biopsy must be performed as soon as clinical signs are evident, as it is associated with a better prognosis. (Faurschou M et al, 2006). In 2003, the International Society of Nephrology/Renal Pathology Society classified LN into 6 classes, which are even used as a parameter to direct treatment:

To support the diagnosis of lupus nephritis and to monitor both its activity and that of the disease lupus erythematosus, immunological tests can be performed. Among them, serum measurement of C3/C4 and anti-double-stranded DNA is performed in all patients with suspected nephritis and in addition, other optional markers of lupus nephritis activity include anti-C1q and antinucleosome antibodies. (Tunnicliffe Dj et al, 2015; Heidenreich U et al, 2009; Moroni G et al, 2009). An increase in the titer or positivity of anti-dsDNA antibodies and Hypocomplementemia are considered, mainly a decrease in C3 levels, signs of renal activity, a characteristic present in the laboratory tests of the patient in question, C3 of 32 and C4 of 5, reinforcing the diagnostic findings (KLUMB, Evandro Mendes et al, 2015). As LN is a manifestation of SLE, it is important to consider its diagnostic criteria to rule out possible differential diagnoses that could explain the clinical presentation. Remembering that the entry criteria for SLE begin with a positive antinuclear antibody greater than 1:80 (Aringer M et al, 2019).

The treatment of lupus nephritis is directed and determined by the result and histological class obtained in the kidney biopsy. In general, classes I and II do not require specific therapy, however, classes III, IV and V require immunosuppressive therapy. In the terminal stage of the disease, defined as class VI, there is no indication for drug treatment as it is an irreversible condition that can only be resolved through renal replacement (RODOVALHO, H. O. P, 2023).

The goals established in the therapy of the disease are to induce complete renal remission, observed through the reduction of proteinuria below 0.5g/day or protein creatinine ratio in urine below 0.5g/g, in addition to the absence of hematuria at the glomerular level and normalization or stabilization of GFR. Another objective is the prevention of renal "flares" of

– Minimal mesangial LN	Glomeruli normal to light microscopy (MO), but with immune deposits to immunofluorescence (IF).
– Proliferative mesangial LN	Pure mesangial hypercellularity of any degree or expansion of the mesangial matrix by the BM with immune deposits in the mesangium. There may be few and isolated subepithelial or subendothelial deposits visible on IF or electron microscopy (EM), but not on BM.
III – NL focal	Focal active or inactive, segmental or global, endo- or extra-capillary glomerulonephritis (GN) involving ≥ 50% of all glomeruli, typically with subendothelial immune deposits with or without mesangial changes. It is further classified into: A, active; Active/chronic A/C; C, chronic inactive.
– diffuse NL	Focal active or inactive, segmental or global, endo- or extra-capillary glomerulonephritis (GN) involving ≥ 50% of all glomeruli, typically with subendothelial immune deposits with or without mesangial changes. It is divided into diffuse segmental (IV-S) in which ≥ 50% of the glomeruli involved present segmental lesions (involving less than half of the tuft. This class includes cases with diffuse wire-loop deposits with little or no glomerular proliferation. It is also classified as: A, active; A/C active/ chronic; C, chronic inactive.
Class V – membranous NL	Global or segmental subepithelial immune deposits or their morphological sequelae to MO and IF or ME, with or without mesangial changes. It can occur in combination with classes III or IV.
Class V – membranous NL	Global or segmental subepithelial immune deposits or their morphological sequelae to MO and IF or ME, with or without mesangial changes. It can occur in combination with classes III or IV.
VI – advanced sclerosis	Global glomerular sclerosis in ≥ 90% without residual activity.

Table 1: Classification of lupus nephritis by the International Society of Nephrology/Renal Pathology Society 2003. (ZAMITH, Luiza Magalhães et al, 2018)

the disease, which are defined by an increase in serum creatinine of at least 30% and an active urinary sediment with glomerular hematuria increased by 10 or more red blood cells per field, independent of changes in proteinuria (FALK, R.J., et al, 2023).

Initial drug therapy for classes III and IV consists of the administration of high-dose intravenous glucocorticoids, the choice being 500 to 2500 mg of methylprednisolone in combination with mofetil-mycophenolate (MMF) with a target dose of 2-3g/day or IV cyclophosphamide. in low doses, with a total of 6 fortnightly doses of 500mg IV. Then, the choice is the oral route with prednisolone 0.3-0.5mg/kg/day until the 4th week, gradually reducing to less than 5-10mg/day in the 3rd month. In the patient reported, immediate pulse therapy was administered with significant improvement in symptoms and, subsequently, outpatient follow-up with prednisone 40 mg/day (RODOVALHO, H. O. P, 2023).

After the patient progresses to a complete or partial response to the disease, therapeutic maintenance of LN is implemented for at least 3 years, based on the use of MMF 2g/day or azathioprine (AZA) 2mg/kg/day and less possible dose of oral prednisolone (FALK, R.J., et al, 2023). Studies show that combined therapy has increasingly proven to be effective, through the association of some drugs, including MMF and calcineurin inhibitor – TAC or vaclosporin; MMF and belimumab (BEL), an anti-CD20 monoclonal antibody with better effect than rituximaben (RODOVALHO, H. O. P, 2023).

In addition to treatment using drugs, it is extremely important to highlight that for all patients, general measures are indicated, including dietary restriction of sodium and protein and physical exercise. (FALK, R.J., et al, 2021). Furthermore, the satisfactory evolution of patients who use ACE inhibitors or ARBs to reduce proteinuria and assist in blood pressure control, vitamin D and calcium supplementation to prevent the side effects of corticosteroids, statins depending on cardiovascular risk, immunization against pneumococcus is well known. and influenza and antiparasitics for empirical treatment with broad-spectrum anthelmintics, as in the case reported, the chosen one was albendazole

(KLUMB, Evandro Mendes et al, 2015).

Finally, the prognosis of LN is influenced by histological class, with renal biopsy classified as an indicator of chronicity. It is also known that in black patients, the risk of progression to end-stage renal disease is increased. Furthermore, patients with LN have a greater chance of developing cancer, primarily B-cell lymphomas, in addition to atherosclerotic complications, vasculitis, hypertension and dyslipidemia (KLUMB, Evandro Mendes et al, 2015).

FINAL CONSIDERATIONS

Early diagnosis and treatment directly impact the evolution of patients with lupus nephritis. In the present report, the patient was underdiagnosed for months, being referred to our service with a longer evolution. With targeted treatment and follow-up, complete renal remission was possible.

The purpose of this report is to inform the medical profession and enable similar cases to be promptly diagnosed and treated.

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