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NEUROPSYCHIATRIC IMPAIRMENT IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

Flavia Cristina de Freitas Maia
São Carlos, SP
http://lattes.cnpq.br/2233042202677369

Fernanda Cristine Zanotti
São Carlos, SP
http://lattes.cnpq.br/7578163817956320

Larissa Pimentel Guimarães
São Carlos , SP

Júlia Eduarda Nóbrega de Melo e Castro
São Carlos- SP
http://lattes.cnpq.br/6100548633657846

Caroline de Oliveira Bertuccio
Campinas
http://lattes.cnpq.br/3723921766901200

Willian Kenji Reis Watanabe
Clementina -Sp
http://lattes.cnpq.br/5752583889178257

Gustavo Roberto Lourenço
Araraquara- SP
http://lattes.cnpq.br/190984438656684

Abstract: Patient A.S.D.A., 59 years old, female, with a previous diagnosis of Systemic Lupus Erythematosus (SLE), hypertension and hypothyroidism, all under regular drug treatment. Admitted to the Santa Casa de Misericórdia de São Carlos in June 2022 with a complaint of mental confusion and fever. Laboratory and imaging tests showed no changes, except for the cerebrospinal fluid, which suggested an inflammatory process. Unable to rule out meningoencephalitis, empirical antibiotic therapy was started with Ceftriaxone for 7 days and, after completion, pulse therapy with methylprednisolone and cyclophosphamide was performed due to evidence of clear activity of renal disease. She was discharged asymptomatic. She returned to the service after 16 days, with worsening neurological status, when, then, the hypothesis of neurolupus was raised. Imaging confirmed changes in white matter secondary to vasculitis. Thus, a new pulse therapy was performed and, due to the absence of clinical improvement, human immunoglobulin was started as a therapeutic test. Remained in Glasgow 7, evolving with decerebrate. As a result of the refractoriness of all treatments instituted, agreed with the family, palliative care. The report in question is a Catastrophic Neurolupus, a rare case, with severe evolution and unfavorable prognosis.
Keywords: Neuropsychiatric Systemic Lupus Erythematosus; Systemic lupus erythematosus; Central Nervous System; Methylprednisolone.

INTRODUCTION

Systemic Lupus Erythematosus is an autoimmune disease with a polymorphic and polygenetic profile, present in the group of connective tissue diseases, which is characterized by a multisystem chronic inflammatory process with periods of exacerbation and remission (ASANO et al, 2013). It has an estimated incidence of 1 to 22 cases per 100,000 people per year in the world, and in Brazil it is around 8.7 cases per 100,000 people per year, with a higher prevalence in females of childbearing age and black race (KEISERMAN et al, 2012).

Due to the wide variety of clinical presentations and in order to improve the detection of early/recent Lupus, the diagnostic criteria were re-established in 2019 by Eular (the European League Against Rheumatism), and steps were proposed for the final diagnosis. As a first step, the entry criterion must have FAN ≥ 1:80 (HEp-2 cell method or equivalent) and then proceed to the next step, when adding the domains: constitutional(fever); hematological (leukopenia < 4,000/mm3, thrombocytopenia < 100,000/mm3, autoimmune hemolysis); neuropsychiatric (delirium, psychosis, seizures); mucocutaneous (non-scarring alopecia, oral ulcers, subacute or discoid cutaneous lupus, acute cutaneous lupus); serositis (pleural or pericardial effusion, acute pericarditis); musculoskeletal (joint involvement); renal biopsy (proteinuria >0.5g/24 hours, Renal biopsy with class II or V lupus nephritis, renal biopsy with class III or IV lupus nephritis. Laboratory findings (antiphospholipid antibodies, C3 and C4 complements, as well as as specific antibodies.) Finally, if the sum is ≥10, the diagnosis is confirmed.

Among the manifestations of SLE, the most frequent result from the deposition of immune complexes in tissues, blood vessels, kidneys and skin, and neurological alterations may occur, which are rarer and difficult to confirm. The most common complication of the pathology itself is glomerulonephritis, which is often associated with the presence of positive anti-DNA (LOPES et al, 2016).

It is estimated that 75% of patients had neurological manifestations that can range

from milder cases with headaches and mood disorders, to severe alterations characterized by acute confusional state, myelopathy and stroke. The diagnosis of Neuropsychiatric Systemic Lupus Erythematosus (NPLE) is a medical challenge, since it can promote focal and diffuse changes (JOSEPH et al, 2010).

The treatment of SLE must always be individualized taking into account case by case. At first, non-pharmacological measures associated with hydroxychloroquine sulfate, an antimalarial, are used in order to induce remission of the disease. In addition to prednisone, a glucocorticoid, with the aim of controlling the disease, its dosage being variable and defined depending on the involvement, ranging from low dose to pulse therapy, as well as immunosuppressants such as azathioprine and cyclophosphamide, in addition to immunoglobulin in more extreme cases. (BORBA et al, 2008).

The present study aims to report the case of a 59-year-old female patient, admitted to an Intensive Care Unit (ICU) with severe neurological manifestations associated with renal impairment.

REPORT

Patient, female, 59 years old, hypertensive, with systemic lupus erythematosus and hypothyroidism, using prednisone 40 mg/day, hydroxychloroquine 400 mg/day and Puran 100 mcg/day. Natural and from São Carlos, in the interior of São Paulo. Admitted to the Santa Casa de Misericórdia de São Carlos in June 2022 under the care of the rheumatology and neurology teams, due to mental confusion and fever. Upon physical examination, she presented disorientation in time and space, psychomotor agitation, in addition to a fever of 38.1º Celsius and diffuse reddened plaques throughout her body, including her trunk and face.

Entry laboratory tests showed no changes. She performed a cranial tomography with no evidence of acute alterations, and then we chose to collect CSF, whose result showed a clear and colorless aspect; bacterioscopic absent; negative aerobic culture; search for bacillus of Koch (PBK): negative; global count: 350 nucleated cells/mm^3 (reference value (RV): up to 3/mm^3); 20 red blood cells/mm^3 (RV: absent); lymphocytes 57% (RV: 70-80%); neutrophils 43% (RV: 20-30%); negative ink; glucose 41 mg/dL (RV: 40-75 mg/dL); chloride 116 mEq/L (RV: 120-130 mEq/L); total proteins 158 mg/dL (RV: 15-45 mg/dL); Venereal Disease Research Laboratory (VDRL): non-reactive. Unable to rule out an infectious condition, empirical treatment for meningoencephalitis was started with ceftriaxone 2 grams, intravenously, every 12 hours for 7 days.

The investigation continued, and the following laboratory tests were performed: blood count with evidence of normochromic and normocytic anemia; serology for HIV, hepatitis B, hepatitis C and non-reactive syphilis; complement C3: 41 mg/dL (RV: 90-180 mg/dL), complement C4: 6 mg/dL (RV: 10-40 mg/dL) and anti-DNA: reagent. Quantitative urinalysis revealed proteinuria of 4.46 g in 24 hours (RV: 0.04-0.23 g/24h). Thus, class V renal activity was suggested, representing membranous lupus nephritis, even without biopsy. For this reason, we opted for pulse therapy with 1g methylprednisolone once a day for 3 days and then 1.3g cyclophosphamide for one day (0.7g/m2). Patient after 14 days of hospitalization, with the end of treatment, is discharged, with total improvement of the condition.

Returns to the service after 16 days, presenting a decline in general condition, loss of capacity for basic and instrumental activities of daily living, speech and gait slowing down. He denied fever or any other sign/symptom involved. Initial laboratory tests again

without acute changes. In a dialogue with her daughter, she reported interruption of the use of hydroxychloroquine on her own since her last hospitalization. A cranial tomography was performed, showing a small brain volume reduction associated with widening of fissures and sulci, marked hypoattenuation of supratentorial periventricular white matter and in subcortical foci (figures 1 and 2).

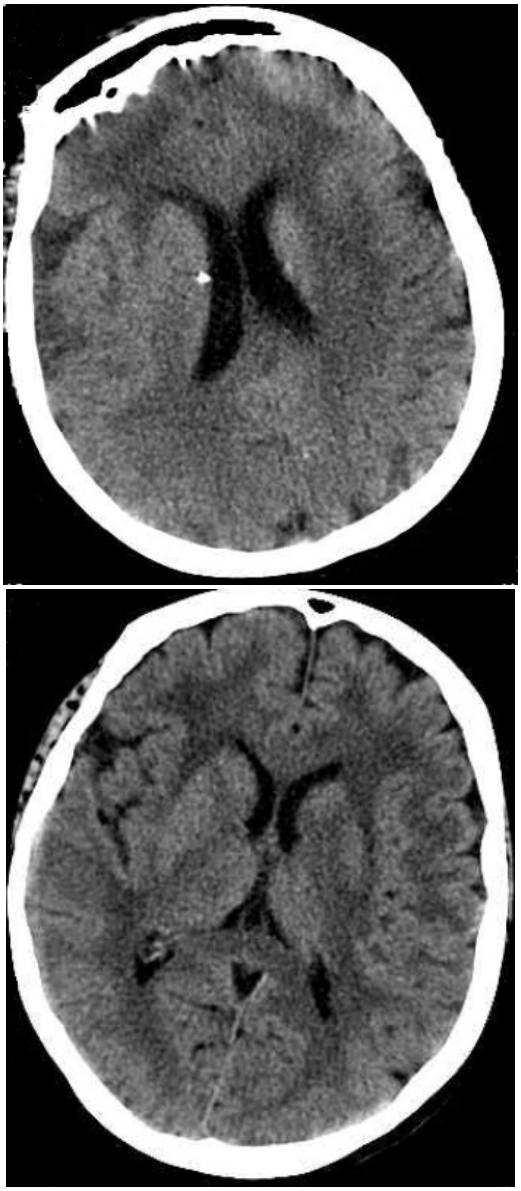

Figure 1 and 2: Marked hypoattenuation of supratentorial periventricular white matter and in subcortical foci, nonspecific, most commonly attributable to areas of microangiopathy.

Patient in ICU was monitored by the neurology team, maintained Glasgow 7, absence of eye opening to any stimulus, absence of verbal response, maintaining movements of withdrawal to pain. A new CSF collection was performed which maintained the normal parameters. As a diagnostic complement, brain venesonance was performed and nonspecific alterations of signals in the cerebral white matter were confirmed, which may be related to foci of gliosis and/or myelin alterations, compatible with diffuse leukopathy secondary to vasculitis (figures 3 and 4).

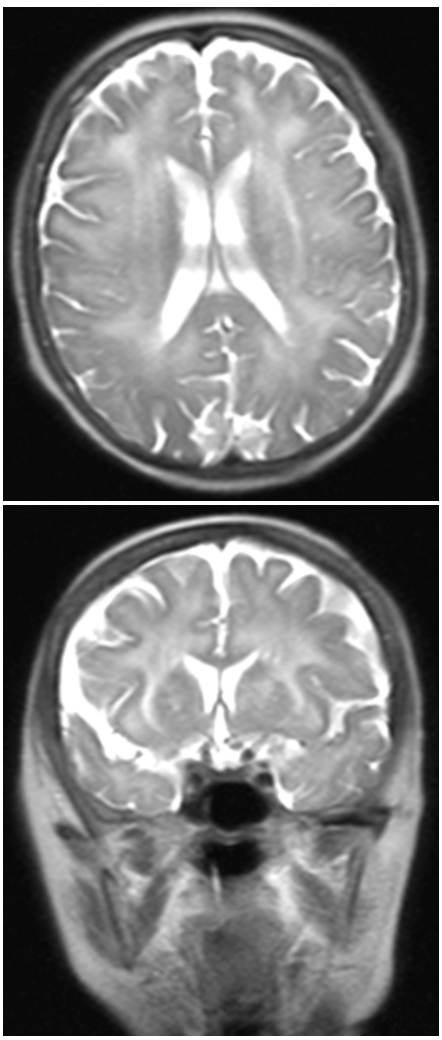

Figure 3 and 4: Magnetic Resonance Imaging with High T2/FLAIR signal of cerebral white matter with confluence in periventricular and deep regions as well as subcortical white matter mainly in frontal and temporal regions.

Thus, the hypothesis of NPLES was raised, with the decision to perform a new cycle of methylprednisolone 1g, once a day, for 3 days and, due to lack of response, human immunoglobulin was started at a dosage of 7.5 g, once a day for 5 days. The condition was so severe, the patient evolved with clinical deterioration, with episodes of decerebration and worsening of the level of consciousness. Opted for palliative care provided between medical staff and family members due to poor clinical prognosis.

After a few days of hospitalization, the patient remains hemodynamically stable in the ward. Hospital discharge was defined together with family members due to an irreversible neurological condition and referred to an outpatient clinic, for periodic monitoring of the underlying pathology.

DISCUSSION

The case described is a female patient with SLENP, with a compatible clinic and with an imaging test showing nonspecific changes in the white matter that corroborates this rare diagnosis.

LENSP can affect up to 75% of patients with SLE, both the profile and severity vary over the years, regardless of disease activity. It is known that in 40% of cases, the pathology is secondary to the cause of SLE in other regions of the body other than the central nervous system or due to the side effect of drugs (CENTURION-WENNINGER, 2021). The neurological manifestations that can be found are difficult to diagnose, including, among other symptoms, cognitive dysfunction, headache (most common), seizures, peripheral neuropathy and stroke (BELTRÃO et al, 2013). These manifestations are attributed to a primary process that directly results from vascular occlusion due to vasculopathy mediated by immune complexes or by antineuronal antibodies (COGO, 2016).

Some antibodies have been studied and correlated to LESNP, the main anti-N-methyl-d-antibodies of the aspartate receptor (anti-NMDAR), more specifically the anti-NR2 subtype, being able to differentiate a diffuse central involvement from peripheral involvement and anti-P ribosomal disorders related to central nervous system involvement and psychosis. Both antibodies are of significant importance, anti-NMDAR causes neuronal damage by an excitotoxic mechanism and anti-ribosomal P induces apoptosis (CARRIÓN-BARBERÀ et al, 2021). It is difficult to define whether the symptoms that the patient presented were due to the underlying disease, for example SLE, or to other diseases that could be developing at that time.

For this reason, the help with imaging techniques can help in the diagnosis, Magnetic Resonance Imaging (MRI) is the exam of choice because it has a specificity of 60-80% to identify acute lesions present in the white matter in patients with NSPLE. There is still no exact location of the lesions that can be found, but about 19-70% of patients with the disease have alterations (TOLEDANO et al, 2013).

Given the complexity of the pathology, its diagnosis must initially exclude other more common diseases, in addition to being based on selected clinical criteria, autoantibody dosage, CSF evaluation, electrophysiological studies, imaging tests and neuropsychiatric evaluation (CENTURION-WENNINGER, 2021).

The catastrophic neurological manifestations described in the case, which were the main involvement, suggested numerous diagnostic hypotheses. Meningoencephalitis was initially suspected on the first hospitalization, having been treated as such. However, in a second step, with a further clinical investigation of the case, the real

hypothesis of NSPLE associated with grade V (membranous) lupus glomerulonephritis can be confirmed.

Renal involvement represents one of the severe manifestations of SLE known as lupus nephritis (LN) whose pathophysiology is the deposition of immune complexes in renal tissues, with the glomeruli being the most affected, which promote the activation of the classical complement pathway, thus reducing the levels of C3 and C4 proteins. In adults, renal involvement is associated with high levels of anti-dsDNA antibodies and low levels of C3 and C4. It is defined as renal impairment in patients with SLE proteinuria ≥ 500 mg in 24 hours; or urinary protein to creatinine ratio ≥ 0.5; or erythrocyte casts in the urine (PINHEIRO et al, 2018).

The presence of proteinuria greater than 1g/day may represent more severe renal impairment, as seen in the case in question. Among the classifications of NL, there are VI groups defined from the site of involvement, in which only types III and IV are considered proliferative (ZAMITH et al, 2018). In this report, it was suggested to be a class V, membranous type.

The treatment of NSPLE ranges from symptomatic therapy to more specific interventions with the use of anticoagulants and/or immunosuppressants, depending on the immunopathogenic mechanism. It is worth mentioning, importance in the treatment of comorbidities that corroborate neuropsychiatric events, as a key point in preventing the onset of crises (ZEMBA et al, 2020).

With the therapeutic approaches for SLENP reviewed recently, pulse therapy with intravenous cyclophosphamide is available, being indicated in non-thrombotic acute cases. Some studies have shown that cyclophosphamide has been more effective than methylprednisolone in the treatment of these syndromes, but more grounded clinical studies in the area must be performed (VIEIRA et al, 2008).

Finally, since all appropriate measures were performed for the case in question, and the patient was hemodynamically stable and had severe neurological injuries. With the family members, we opted for medical discharge and follow-up on an outpatient basis.

REFERENCES

ASANO, Nadja Maria Jorge et al. Comorbidades psiquiátricas em pacientes com lúpus eritematoso sistêmico: uma revisão sistemática dos últimos 10 anos. Revista Brasileira de Reumatologia, v. 53, n. 5, p. 431-437, 2013.

BELTRÃO, Sônia Maria da Rosa et al. Sintomas psiquiátricos em pacientes com lúpus eritematoso sistêmico: frequência e associação com atividade da doença com o uso do Questionário de Morbidade Psiquiátrica em Adultos. **Revista Brasileira de Reumatologia**, v. 53, n. 4, p. 328-334, 2013.

BORBA, Eduardo Ferreira et al. Consenso de lúpus eritematoso sistêmico. **Revista Brasileira de Reumatologia**, v. 48, p. 196-207, 2008.

CARRIÓN-BARBERÀ, Irene et al. Envolvimento neuropsiquiátrico no lúpus eritematoso sistêmico: uma revisão. **Autoimmunity Reviews,** v. 20, n. 4, 2021.

CENTURION-WENNINGER, C. Lupus neuropsiquiátrico. **Rev. parag. reumatol.**, Asunción , v. 7, n. 2, p. 41-48, 2021.

COGO, Antônio Carlo Klug et al. Lúpus eritematoso sistêmico com acometimento neurológico grave: Relato de Caso. **Blucher Medical Proceedings**, v. 2, n. 7, p. 237-242, 2016.

LOPES, Eduardo et al. Lúpus eritematoso sistêmico com acometimento neurológico grave: Relato de Caso. **Blucher Medical Proceedings,** v. 2, n. 7, p. 237-242, 2016.

JOSEPH, Fady G.; SCOLDING, Neil J. Neurolupus. **Practical neurology**, v. 10, n. 1, p. 4-15, 2010.

KEISERMAN, Briele. Isotipos IgG e IgM anti-dsDNA em pacientes com lúpus eritematoso sistêmico. **Dissertação de Mestrado.** Pontifícia Universidade Católica do Rio Grande do Sul. 2012.

PINHEIRO, Sergio Veloso Brant et al. Nefrite Lúpica em Pediatria. **Jornal Brasileiro de Nefrologia**, v. 41, n. 2, p. 252-265, 2019.

TOLEDANO, Pilar et al. Neuropsychiatric systemic lupus erythematosus: Magnetic resonance imaging findings and correlation with clinical and immunological features. **Autoimmunity Reviews**, v.12, n. 12, p. 1166-1170, 2013.

VIEIRA, Walber Pinto et al. Análise de prevalência e evolução das manifestações neuropsiquiátricas moderadas e graves em pacientes com lúpus eritematoso sistêmico internados no serviço de reumatologia do Hospital Geral de Fortaleza. **Revista Brasileira de Reumatologia**, v. 48, p. 141-150, 2008.

ZAMITH, Luiza Magalhães et al. NEFRITE LÚPICA: CLÍNICA, DIAGNÓSTICO E TRATAMENTO. **Cadernos da Medicina-UNIFESO**, v. 1, n. 1, 2018.

ZANEVAN, Ivan Rosso et al. Lúpus Eritematoso Sistêmico: limitações da classificação atual e perspectivas diagnósticas Systemic Lupus Erythematosus: limitations of the current classification and diagnostic perspectives. **Brazilian Journal of Health Review**, v. 5, n. 1, p. 237-249, 2022.

ZEMBA, Diane et al. Neurolupus: a propósito de um caso observado no serviço de medicina interna do centro hospitalar universitário Yalgado OUEDRAOGO et revue de la littérature. **Rhumatologie Africaine Francophone**, v. 1, n. 2, p. 13-18, 2020.