MANIC EPISODE AS A RARE NEUROPSYCHIATRIC MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS: CASE REPORT

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Abstract: Systemic lupus erythematosus (SLE) is a pathology capable of affecting several organs and systems of the human body, including the central nervous system. The most common psychiatric manifestations addressed in studies are acute confusional state, mood disorders, cognitive dysfunction, psychosis, among others. However, there are few documented case reports associating lupus with an episode of mania, mainly because this neuropsychiatric symptom usually precedes the onset of typical SLE symptoms, such as malar rash or arthralgias. The objective of this study is to describe the case of a patient hospitalized for diagnostic investigation of SLE who presented with mania.

Keywords: Neuropsychiatric Systemic Lupus Erythematosus; Mania;

INTRODUCTION

Diagnosis and management of neuropsychiatric manifestations (NPM) of systemic lupus erythematosus (SLE) are still a challenge, especially since they can appear at any time during the course of the disease. The prevalence of MNP in SLE reported in studies is variable, from 14-75%. (1, 3, 4)

The etiology of neuropsychiatric systemic lupus erythematosus encompasses multiple factors, including microangiopathy, autoantibodies and release of pro-inflammatory cytokines. Any portion of the central or peripheral nervous system can be affected, leading to localized or generalized involvement. (3, 4)

There are 19 clinical syndromes defined by the American College of Rheumatology (ACR) of NPM in lupus, which were divided into two groups, the first, manifestations of the Central Nervous System (CNS) - aseptic meningitis, cerebrovascular disease, demyelinating syndrome, headache, disorders of the movement, myelopathy, seizure, acute confusional state, anxiety disorders, cognitive
dysfunction, mood disorders and psychosis – the second, manifestations of the Peripheral Nervous System (PNS) - acute inflammatory and demyelinating polyradiculoneuropathy, autonomic changes, mononeuropathy multiplex, polyneuropathy, myasthenia gravis, cranial neuropathy and plexopathy. (15)

However, the management of PMN in lupus is not uniform, considering the broad spectrum of involvement, leading to high morbidity and impact on the quality of life of affected individuals. (4) In this sense, this study aims to report the case of a patient who was hospitalized for diagnostic investigation of SLE when she presented with mania.

**CASE REPORT**

Patient, female, 23 years old, born in the interior of the State of Ceará, Brazil, started 6 months ago, before hospital admission, a condition of vomiting, diffuse abdominal pain in colic and twinges, consumptive syndrome (weight loss of 13 kg in 5 months), chronic diarrhea, xerostomia, xerophthalmia, xeroderma and photosensitivity. Faced with these symptoms, she was hospitalized in a health unit in her hometown, where she was hospitalized for 10 days. Later, on 04/14/2022, she was transferred to a hospital with a tertiary level of health care, a reference in rheumatology, in the capital of the State of Ceará, Brazil, because, in addition to the clinical symptoms presented, she had additional tests showing antinuclear factor ( ANA) with titre 1:320 and fine dotted pattern and anti-double-stranded DNA antibodies (anti-dsDNA) 1:80, being referred to the rheumatology service for diagnostic investigation of Systemic Lupus Erythematosus/Sjogren’s Syndrome.

The patient was admitted to the referral hospital already using hydroxychloroquine 400mg/day, amoxicillin 2000mg/day/clarithromycin 1000mg/day/lansoprazole 60mg/day (treatment for Helicobacter pylori) and prednisone 20mg/day, weighing 37 kg, emaciated, with Regular general condition, eupneic, normocardic, presenting malar rash and frontal alopecia, referring persistence of diarrhea, five bowel movements in the last 24 h, alternating between liquid and pasty consistency, associated with abdominal discomfort. On the third day of hospitalization, she evolved with an episode of mania, manifested by disorientation, reduced need for sleep, staying almost 24 hours awake, in addition to distraction, psychomotor agitation, flight of ideas, emotional lability and tachylia. After psychiatric evaluation, valproic acid 500mg/day and clonazepam 2mg/day were associated, and later risperidone 1mg/day. However, there was a worsening of the psychiatric condition, with significant psychomotor agitation, with risk to third parties, which prevented the performance of a lumbar puncture, requiring restraint in bed. In addition, she started to refuse food and medicine, with a loss of 4 kg (33 kg). As a result, it was necessary to feed her through a nasoenteric tube and administer medications parenterally. She also manifested hydroelectrolytic disturbances, possibly related to refeeding syndrome and severe malnutrition.

He had the following immunological panel, anti-Smith autoantibodies (anti-Sm), Anti-dsDNA, anti-ribonucleoprotein (anti-RNP), anti-SSA/Ro, positive anti-SSB/La and negative antiphospholipid antibodies, complement consumption ( C4 5.98 C3 52.9), serology for hepatitis B and C, HIV, VDRL negative. It scored, according to the EULAR/ACR criteria for the classification of systemic lupus erythematosus, 10 points (2). And six points on the disease activity index - SELENA-SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), featuring moderate flare. (11)
Due to the chronic diarrheal condition, the following complementary exams were performed: colonoscopy (05/04/22) where colonic and colorectal mucosa were found to be within normal limits and whose histopathology showed mild chronic ileitis; upper digestive endoscopy (03/26/22), where histopathological chronic pangastritis in severe activity, with positive Helicobacter pylori research. Computed tomography (CT) of the abdomen (04/19/22), with no retroperitoneal lymph node enlargement, small-volume ascites. mild dilation of the pancreatic duct and CT of the head (04/19/22), with focal enlargement of the CSF space, in the medial region of the left temporal fossa (2.0x1.0 cm) and an arachnoid cyst. There were no masses or signs of cranial hypertension.

Conducted investigation for celiac disease (03/12/22), with non-reagent anti-endomysial IgG and IgM and anti-transglutaminase IgG and IgA antibodies. Plus lactose tolerance test (02/14/22): baseline 93; 30min 103 mg/d; 60min 110mg/d; 90min 112 mg/dL. In addition to performing multiplex PCR of feces and PCR for cytomegalovirus (CMV) on 04/20/2022, both non-reactive.

It was not possible to perform calprotectin, due to the improvement of diarrhea after the use of corticosteroids and antimalarials.

In view of the increasing severity of the picture suggestive of neuropsychiatric involvement, associated with the positivity of anti-antibodies for systemic lupus erythematosus and ruling out other diagnoses, such as infection by syphilis, HIV, CMV and viral hepatitis, it was prescribed, on 04/27/2022, pulse therapy with methylprednisolone 500mg/day for 3 days, after which methylprednisolone equivalent to 1mg/kg/day of prednisone was prescribed. After pulse therapy with methylprednisolone, the patient progresses in improvement, and it is decided to start immunosuppression with cyclophosphamide, monthly dose of 750mg/m², on 05/05/2022 (1st cycle). Evolved in 2 weeks with significant improvement, oriented in time and space, flow of thought and language, normal form and content, without clinical complaints, opted not to perform a lumbar puncture, being discharged after a month of hospitalization. Patient attended the first follow-up appointment on 05/27, without new episodes of mania. After 6 monthly infusions of cyclophosphamide, from May to September 2022, maintenance therapy with azathioprine 2mg/kg/day was prescribed. During the last outpatient consultation, in January 2023, the patient continues to have no psychiatric complaints or diarrhea, had regained weight (at that time, she weighed 67 kg), and with a zero SELENA-SLEDAI disease activity index, without clinical disease activity, in use of hydroxychloroquine 1600mg/week, azathioprine 150mg (started on November 22), valproic acid 1g/day, olanzapine 5mg/ day, prednisone 5mg/day.

**DISCUSSION**

The nervous system is commonly affected in all age groups of patients with SLE. Such involvement is strongly related to a worse prognosis and cumulative damage in children. In adults, 28% to 40% of lupus NPM present before or close to the diagnosis of SLE, but may occur in the absence of serological activity or other systemic manifestations. The most common lupus NPMs are: headache, seizures, cerebrovascular events, psychosis, and movement neuropathy. Of these, only seizures and psychosis meet the American College of Rheumatology criteria for SLE. In a study carried out in Fortaleza, the same location as this one, in another Rheumatology reference center, the prevalence of NPM...
in lupus was 16.4%. However, the reported prevalence in studies usually ranges from 14 to 75%. This discrepancy reflects the wide variation that exists, especially considering the dimensions of studies carried out at the population level, as well as the underdiagnosis of this disease spectrum

Postmortem studies reveal a wide range of brain histopathological changes in patients with SLE, with variable etiologies, such as the multifocal microinfarcts, cortical atrophy, macroscopic infarcts, hemorrhage, ischemic demyelination, and irregular demyelination similar to multiple sclerosis. In addition, the deposition of immune complexes seems to be important in microscopic changes. However, there are no findings that are pathognomonic of neurological involvement by lupus. It is possible that, in such post-mortem studies, macroscopic or microscopic alterations are not perceived, which may infer that SLE is capable of triggering neurophysiological alterations, even without altering the anatomical structure. More recent studies prove that the integrity of the blood-brain barrier, as well as the presence of some antibodies, can directly interfere with the occurrence of MNP in SLE, such as the antiphospholipid antibody, which is associated not only with thrombotic events, but also with seizures, chorea and other movement disorders.

The diagnosis of SLE must be confirmed using traditional diagnostic criteria for the disease, as well as a detailed anamnesis and physical examination to exclude other sources of neuropsychiatric manifestations. Some immunological studies are performed mainly to know the diagnosis of SLE and nuances of the disease, such as antiphospholipid antibodies and anti-P research, strongly associated with lupus psychosis, especially when using c22 peptide.

For this work, the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM) were used, in association with the diagnostic criteria for SLE, in which mania is defined as a period of ≥ 1 week of altered mood (elevated, expansive or irritable) and excessive, persistent activity directed towards a fixed goal or a noticeable increase in energy associated with ≥ 3 of the following symptoms: inflated self-esteem or grandiosity, decreased need for sleep, tachylalia, flight of ideas or racing thoughts, hypervigilance, increased activity goal-directedness and involvement in activities with a high potential for negative consequences.

Due to the diversity of neuropsychiatric manifestations in SLE with diverse pathogenesis, until the present moment, there are no therapies directed towards psychiatric involvement, being indicated the use of antipsychotics and antidepressants as symptomatic and/or immunosuppressants to inhibit the systemic disease. The treatment is based on the cause that generates the MNP, which may be of inflammatory or ischemic origin. In severe cases of inflammatory NPM or cerebral vasculitis, the first line of treatment is high-dose glucocorticoids, associated with cyclophosphamide 0.5 -1 g/m2 monthly for 6 months. If there is a good response, maintenance can be performed with azathioprine 2mg/kg/day or mycophenolate 3g/day or cyclosporine 5mg/kg/day and oral glucocorticoids. If partial response, cyclophosphamide 0.5 -1 g/m2 quarterly for 18 months. If there is no response, rituximab 375 mg/m2, weekly, twice or 1g repeated in 15 days. No response, plasmapheresis daily or every other day, 1 to 1.5 times total plasma volume 3 to 6 times, or immunoglobulin 2g/kg for 2 to 5 days. Without response, evaluate autologous stem cell transplantation.
In cases of ischemic origin, with positive antiphospholipid antibodies, oral anticoagulation for a prolonged period is indicated. If a new ischemic event, add acetylsalicylic acid 100mg/day. In the absence of these antibodies, acetylsalicylic acid 100mg/day is indicated. In the presence of a new event, use, as an alternative, antiplatelet agents, clopidogrel 75mg/day (4,7,8,10).

**CONCLUSION**

After the article presented, it is concluded that further studies are needed regarding SLE and the associated neuropsychiatric manifestations, especially when it comes to mania, aiming to enable an early diagnosis, as well as adequate intervention, with greater objectivity for the therapy, which must be instituted. In addition, it is necessary, based on the above, greater summarization of treatment and appropriate sequence in the management of mania in SLE.

**STUDY LIMITATIONS**

At the health center where the case was approached, it is not possible to request anti-P, making it difficult to associate it with serological studies.

The rarity of the association between SLE and mania makes clinical practice with the patient difficult and there are few studies on the subject.

**REFERENCES**


