

Catatonia due to systemic lupus erythematosus

Catatonia secundária a lúpus eritematoso sistêmico

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ABSTRACT

Objectives: Discuss neuropsychiatric aspects and differential diagnosis of catatonic syndrome secondary to systemic lupus erythematosus (SLE) in a pediatric patient. **Methods:** Single case report. **Result:** A 13-year-old male, after two months diagnosed with SLE, started to present psychotic symptoms (behavioral changes, hallucinations and delusions) that evolved into intense catatonia. During hospitalization, neuroimaging, biochemical and serological tests for differential diagnosis with metabolic encephalopathy, neurological tumors and neuroinfections, among other tests, were performed. The possibility of neuroleptic malignant syndrome, steroid-induced psychosis and catatonia was also evaluated. A complete reversal of catatonia was achieved after using benzodiazepines in high doses, associated with immunosuppressive therapy for lupus, which speaks in favor of catatonia secondary to autoimmune encephalitis due to lupus. **Conclusion:** Although catatonia rarely is the initial clinical presentation of SLE, the delay in recognizing the syndrome can be risky, having a negative impact on prognosis. Benzodiazepines have an important role in the catatonia resolution, especially when associated with parallel specific organic base cause treatment. The use of neuroleptics should be avoided for the duration of the catatonic syndrome as it may cause clinical deterioration.

Keywords

Catatonia, systemic lupus erythematosus, benzodiazepines, differential diagnosis.

RESUMO

Objetivos: Discutir aspectos neuropsiquiátricos e o diagnóstico diferencial da síndrome catatônica secundária a lúpus eritematoso sistêmico (LES) em paciente pediátrico. **Métodos:** Relato de caso individual. **Resultado:** Adolescente do sexo masculino com 13 anos de idade iniciou, após dois meses de diagnosticado com LES, quadro psicótico (alterações comportamentais, alucinações e delírios) que evoluiu para franca catatonia. Durante internação hospitalar foram realizados, entre outros, exames de neuroimagem, bioquímicos e sorologias para diagnóstico diferencial com encefalopatia metabólica, tumores neurológicos e neuroinfecções. Foi avaliada também a possibilidade de síndrome neuroléptica maligna, psicose e catatonia induzida por corticoides. Houve reversão completa da catatonia após o uso de benzodiazepínico em altas doses associado à terapia imunossupressora para o lúpus, o que fala a favor de uma catatonia secundária a uma encefalite autoimune de base lúpica.

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Palavras-chave

Catatonía, lúpus eritematoso sistêmico, benzodiazepínicos, diagnóstico diferencial.

Conclusão: Apesar de a catatonía ser raramente apresentação clínica inicial do LES, o atraso no reconhecimento da síndrome pode ser arriscado, tendo impacto negativo no prognóstico. Os benzodiazepínicos têm papel importante na resolução da catatonía, principalmente quando associada ao tratamento específico em paralelo para a causa orgânica de base. O uso de neurolépticos deve ser evitado durante a vigência da síndrome catatônica, podendo agravar o quadro clínico.

INTRODUCTION

Catatonía has been reported in the clinical spectrum of systemic lupus erythematosus neuropsychiatric (SLENP) manifestations. It represents a complex syndrome characterized mainly by stupor, mutism, negativism, waxy flexibility, stereotypy, automatic obedience, echo phenomena (including echolalia and echopraxia)¹. Catatonía can be caused by a large variety of metabolic, neurologic, psychiatric and intoxication conditions, including neuroleptic malignant syndrome². Although catatonía as an expression of a pure mental disorder is a diagnosis of exclusion³ and it has usually a recognizable organic component⁴, when placing it into an organic mental syndrome, psychiatrist evaluation is valuable since the clinical manifestations are mainly mental and behavioral⁵. Often, there is an association with previous psychiatric conditions⁶ and need of treatment with benzodiazepines or electroconvulsive therapy in refractory cases⁷⁻⁹.

Catatonía has been rarely reported as an SLENP manifestation in pediatric patients^{9,10}. This article is apparently unique at medical database since it reports the case of the first young male with catatonía due to lupus.

CASE REPORT

A thirteen-year-old Brazilian male without any previous psychiatric disorders was brought to the pediatric emergency unit of the hospital by his mother, who reported generalized anxiety with social withdrawal and outside world strangeness. In the prior day he had presented low fever (38 °C) and psychotic symptoms characterized by visual Lilliputian hallucinations with macropsia and micropsia. He also presented persecutory delusions involving hospital staff during the clinical screening and developed hypervigilant mental status.

An investigation of his prior medical history revealed he met the criteria of the American College of Rheumatology (ACR) for Systemic Lupus Erythematosus (SLE) two months before, during past hospitalization. At the time of diagnosis, he had lupus photosensitivity rash, arthritis in knees and elbows and some typical laboratory findings (Table 1). He was in use of prednisone 20 mg/day, hydroxychloroquine 400 mg/day and was discharged after clinical improvement.

Table 1. Complementary exams revealed auto antibodies profile suggestive of SLE, complement consumption, leukopenia and thrombocytopenia

Parameter	Title/count
Antinuclear factor (FAN)	> 1:160 – homogeneous nuclear and metaphase plate
Platelets	115.000/mm ³
Auto-antibodies native DNA	1:20 – Reagent
Complement – C3, C4, CH50 (respectively)	39.5 mg/dl; 13.1 mg/dl; 54 u/CAE
Leulocytes	3.640/mm ³

On the first day of current hospitalization treatment was kept with hydroxychloroquine and prednisone. Ophthalmologic evaluation resulted with no corneal deposits, maculopathy or retinitis. Thus, visual hallucinations couldn't be explained by hydroxychloroquine poisoning. Risperidone 2 mg/day was given for the lupus psychosis presentation. Next day progressive difficulties appeared, involving deambulation, food refusal and urinary incontinence. Patient developed tachycardia (132 bpm), tachypnea (30 ipm) and catatonía itself: extreme hypoactivity, stopped verbal communication (silence), stare, waxy flexibility with discrete spastic stiffness members.

Neuroleptic Malignant Syndrome (NMS) was dismissed by insidious onset, very low fever, muscle rigidity being only mild (not in "lead pipe"), CPK being less than 1.000 UI/l (172 UI/l), absence of leucocytosis, electrolyte disturbances or elevated liver transaminases. Although it can happen with risperidone, which affects more dopamine D2 receptors, NMS is more common with typical neuroleptics used parenterally.

The first diagnostic hypothesis was Catatonic Disorder Due to a General Medical Condition (International Classification of Diseases – F06.1), specifically caused by SLE. Differential diagnosis for catatonía like cerebral vasculitis, neurological infections, meningoencephalitis were discussed. Other blood cultures were requested, as toxoplasmosis, measles, cytomegalovirus, hepatitis B and syphilis. We performed electroencephalogram (EEG), skull computed tomography (CT), lumbar puncture followed by collection of cerebrospinal fluid for biochemical analysis. Before lumbar puncture, cefepime 2 g 12/12h was empirically started to avoid germ ascension. Metabolic encephalopathy was properly dismissed due to lack of hydroelectrolyte, glucose, liver and urinary biochemical alterations.

On the third day of hospitalization the level of consciousness decreased and tachycardia increased (162 bpm), associated with generalized tremors. Because of convulsive status, we performed 10 mg of diazepam IV. Amazingly, seconds after the catatonic state completely reversed and level of consciousness improved. Patient was able to communicate by speech and walked. However, short lived response was noted, with complete return to catatonia after thirty minutes.

Prednisone was increased to 30 mg/day due to clinical lupus decompensation. Risperidone was prescribed due the emergence of catatonic syndrome and to dismiss neuroleptic-induced catatonia. Valproic acid was prescribed for seizures prophylaxis since it increases brain metabolism with more consumption of oxygen and energy.

EEG tracing was compatible with acute encephalopathy (Figure 1).

CT scan showed no specific findings, only mild enlargement of the cerebral lateral ventricles. An intracranial magnetic resonance imaging (angio-MRI) was performed for additional differential diagnosis, but the findings were nonspecific (Figure 2). Repeatedly negative blood and urine cultures, lack of white cell changes, negative serology for infections and normal cytological, biochemical and mycobacteriological analysis of cerebrospinal liquid ruled out the possibility of ongoing infection.

We started with 1 g methylprednisolone pulse therapy for three days because of target organ injury (brain). Diazepam was adjusted for 20 mg/day, trying to reverse catatonia. Fever resolution was observed, partial improvement of catatonia occurred (patient was able to sit in bed and talk), but some clouding of consciousness remained. The patient partial improvement after methylprednisolone pulse dismissed the possibility of corticosteroid-induced neurologic lesion. We started 1 g/day pulse with cyclophosphamide for supporting role in lupus nephritis. Despite of the higher frequency of awakenings, patient always remained with a hypoactivity baseline, hipoprosexia, echopraxia and stereotyping.

Catatonia was probably not induced by risperidone used for three days only, because this secondary catatonia is reversible in a few days by the discontinuation of the precipitating agent.

Due to the unavailability of lorazepam and in light of the complexity of the case, patient was transferred to a reference general hospital. He stayed hospitalized there for 13 days, prednisone dose was adjusted to 40 mg/day, hydroxychloroquine to 400 mg/day and diazepam was replaced for lorazepam 10 mg/day. The catatonia was completely resolved during this hospitalization, and he returned to outpatient assessment in the primary hospital using lorazepam 1 mg/day and olanzapine 10 mg/day. Eight months after his last discharge, with periodical follow-up, patient has not returned to catatonic status.

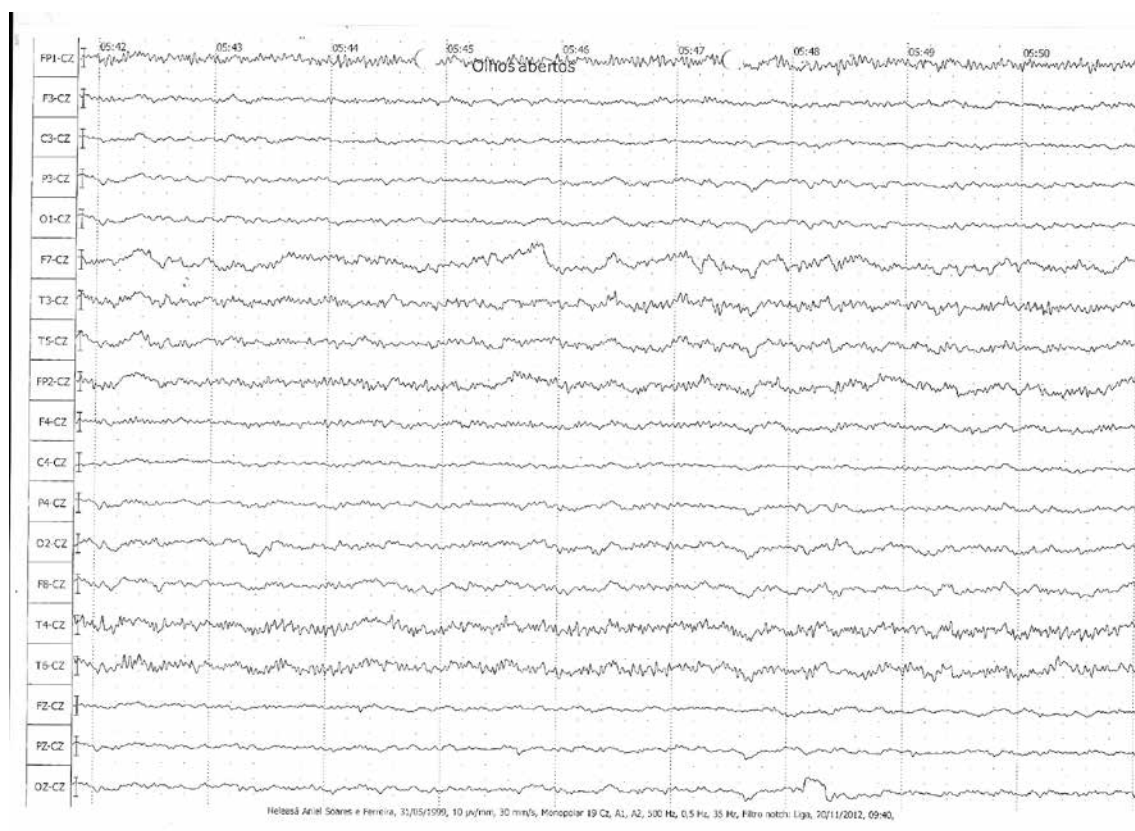


Figure 1. Patient's EEG tracing shows regular basis beta low amplitude rhythm interspersed by theta waves with moderate voltage, increasing suspicion of an organic mental disorder worsening the catatonic syndrome.

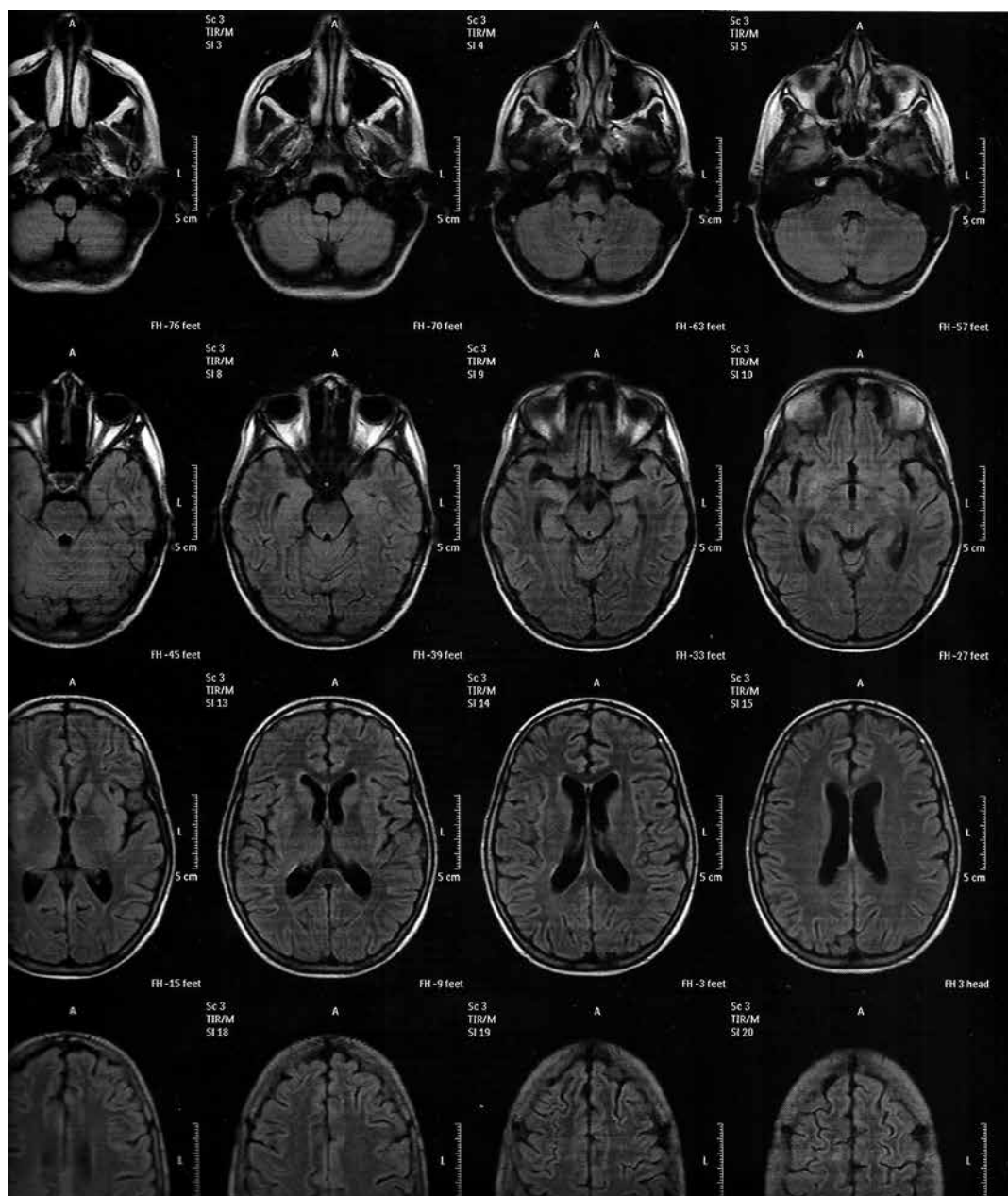


Figure 2. Angio-MRI shows foci of change in the FLAIR sequence on lenticular nucleus, right superior frontal gyrus and left corpus callosum forceps.

DISCUSSION

The concern to validate clinical spectrum of SLENP manifestations led to studies that revealed the presence of these signs and symptoms in up to two thirds of the patients, and it may include psychosis, cognitive dysfunction and delirium¹¹. Due to large variability in prevalence and the low specificity for SLE, the final validation of the ACR by the Systemic Lupus International Collaborating Clinics (SLICC) did not include all such manifestations as diagnosis value, but admits that it may occur due to SLE¹². As it seems, despite of the high incidence, SLENP manifestations are not common as the initial clinical presentation, which was consistent with

the reported case since the teenager presented arthritis and photosensitivity rash and psychiatric symptoms appeared only months later.

A prospective study with 256 patients confirmed morbidity and cumulative damage to target organs in juvenile SLENP manifestations, warning that failure to observe the immunological and structural brain differences between adults and children makes it risky to implement the conclusions of the scientific data obtained from adults to children and adolescents¹⁰.

Although somatic factors do not have a definitive role, juvenile catatonia is associated with a high prevalence of general medical conditions^{13,14}, being psychiatric disorders

interpreted as accompanying factors⁶. The case described here confirms this hypothesis of mental disorder derived from organic cause, as there was acute autoimmune encephalitis due to lupus, culminating with catatonic psychiatric syndrome.

There are no conclusive studies regarding the pathophysiology SLE catatonia. However there is evidence of microvascular injury and autoimmune central nervous system lesion, as like complement-mediated response and nuclear antibodies as anti-DNA and anti-P ribossomal. There are also evidences that anti-NMDA-receptor encephalitis can cause catatonia^{13,14}.

The available literature instructs lupus catatonia treatment with benzodiazepines in high doses⁶, especially after Zolpidem 10 mg or 1 mg intravenous lorazepam positive test, associated with specific treatment for general medical condition, if present. Antipsychotics should be done only after the catatonia remission and only if necessary^{6,7,13}. The use of risperidone for lupus psychosis by our patient was prescribed just after the installation of the catatonic syndrome, and other neuroleptic restarted only after its improvement, due to persistent delusional episodes. After resolution of catatonia, the use of neuroleptic in even larger doses (10 mg/day) showed no sign of relapse, helping to dismiss that catatonia could be neuroleptic-induced.

Zolpidem was not available at the medical service, and the benzodiazepine (diazepam), used primarily due to seizure, also had positive effect in catatonia symptoms. Our patient had no complete response to pulse therapy with corticosteroids. The patient overcame catatonia only after using lorazepam 10 mg daily. The explanation for this may lie in functional neuroimaging study with Single Photon Emission CT (SPECT) which revealed lower binding of GABA-A alpha-1 subunit receptors in catatonic patients when compared with healthy controls. Thus, lorazepam would be more effective than other benzodiazepines because the higher binding affinity for GABA-A¹⁵, implicated in pathophysiology of catatonia.

CONCLUSION

Although catatonia is rare as initial clinical presentation in SLENP manifestations, the delay in its recognition may be risky. Benzodiazepines have a role in the reversal of catatonia, and should always be associated with the specific treatment of underlying organic cause as soon as possible, preferably without the use of antipsychotics during the catatonia term.

INDIVIDUAL CONTRIBUTIONS

Francisco de Assis Pinto Cabral Júnior Rabello – Was responsible for the introduction, case report and discussion.

Daniel Calich Luz – Was responsible for translation and data collection.

Evânia Claudino Queiroga de Figueiredo, Edmundo de Oliveira Gaudêncio, Larissa Cristina Queiroga Mendonça Coutinho and Waldeneide Fernandes de Azevedo – Helped with bibliography, discussions on the theme and ethic procedures.

CONFLICT OF INTERESTS

The authors have no conflicts of interests to report.

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