Subacute cerebellar ataxia as presenting symptom of systemic lupus erythematosus

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Abstract. – Neuropsychiatric manifestations are commonly observed in systemic lupus erythematosus (SLE) patients. In particular, neurological involvement is known to be more common in patients with positive anticardiolipin antibodies and lupus anticoagulants. Nevertheless, cerebellar ataxia has rarely been reported, especially as the first clinical manifestation of this systemic autoimmune disorder. Cerebral vascular infarction or ischemia, vasogenic oedema and antibody-mediated cerebral vasculopathy or vasculitic process have been supposed as possible aetiologies of acute cerebellar ataxia related to SLE. We report the clinical and radiological features of a woman who developed a rapidly progressive cerebellar syndrome as first sign of SLE; no other cause explaining her cerebellar ataxia was found. The patient improved after high-dose steroids. The appearance of a cerebellar syndrome with unknown aetiology with associated features of possible systemic autoimmune dysfunction, should be taken into account in clinical practice for appropriate diagnostic workup in order to provide effective therapeutic options.

Key Words: Cerebellar ataxia, LES, neurolupus.

Introduction

Neuropsychiatric manifestations are present in 50-70% of the patients with systemic lupus erythematosus (SLE) and include a wide variety of central and peripheral neurological manifestations. Cerebellar ataxia is one of the less described neurological features of SLE. Its prevalence in SLE has been estimated to occur in less than 2% of the cases, even more uncommon as the first clinical manifestation of such autoimmune systemic condition. Several possible aetiologies of acute cerebellar syndrome related to SLE have been postulated, including cerebral infarction or ischemia, antibody-mediated dysfunctions and vasculopathy or vasculitis. However, the definite nature of the neurological manifestations of SLE is not fully understood and diagnostic doubts, related to different clinical phenotypes and therapeutic options, are common. We report the clinical and radiological features of a patient who showed signs of subacute cerebellar syndrome associated to MRI evidence of the left cerebellar hemisphere atrophy. Other possible causes, including infective, metabolic or paraneoplastic causes, drugs, alcohol and demyelinating diseases, are excluded by medical history, physical examination and appropriate investigations. The cerebellar ataxia, which was the main clinical feature in our patient, improved following steroids administration.

Case Description

A 42 years-old woman was admitted to our Neurological Unit for evaluation of a six-weeks history of unsteady gait, slurred speech and clumsiness and tremor of hands. Her symptoms developed gradually and were characterized by mild unsteadiness of gait, but they rapidly progressed over the next few weeks, when she presented marked ataxia and postural tremor involving her upper extremities. She had no visual symptoms, headache, nausea, vomiting, sphincteric disturbances, weakness or other neurological symptoms. No family history of neurological disease was reported. She has been treated for high blood pressure in the previous 2 years. Recently she complained of intense asthenia and diffuse arthralgias; she denied fever, skin rashes, mouth ulcers. Physical examination revealed tenderness and swelling involving both the wrist joints. Tenderness with no swelling was also evident when examining the remaining joints.

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Neurological examination showed marked limb and truncal ataxia. She presented kinetic tremor involving both arms and dysdiadokinesia. Mild bilateral nystagmus was also present. Deep tendon reflexes were brisk and symmetrical. No muscle weakness or sensory disturbance was noted. Mental functions, cranial nerve examination, including fundus examination, were normal. Meningeal signs were absent. Examinations of other systems including cardiovascular, chest and abdominal were unremarkable. Laboratory work-up included complete blood count, which showed leukopenia (3.63 x10^3/μL; normal values: 4.80-10.80 x10^3/μL) and thrombocytopenia (98 x3.μL; normal values: 150-400 x3.μL), already present in a previous test; immunological investigations revealed increased ANA and ENA indexes, 4.40 (normal values: <1.5) and 3.30 (normal values: <1.0) respectively, with ENA profile showing positive nRNP/sm, SS-A Native and Ro-52. Blood glucose, thyroid tests, renal and liver functions were normal. Tumour markers were negative as well as complete panel for anti-neuronal antibodies associated to paraneoplastic syndrome of CNS. The results of cerebrospinal fluid (CSF) examination showed a mild increased level of leucocytes (7 μL; normal values: <5), Link index 0.91 (normal values: <0.65) and presence of oligoclonal bands. Brain MRI scan showed exclusively a marked atrophy of left cerebellar hemisphere also involving the vermis (Figure 1, panels A, B and C). On the basis of clinical and serological findings a diagnosis of SLE was suspected. She was treated with intravenous methylprednisolone (1 g for 3 days), followed by oral prednisone 1 mg/kg with progressive tapering over the next 6 months, with slight improvement of symptoms. Unfortunately the patient refused further neurological visits and laboratory investigations as well as alternative therapeutic options with other immunomodulant agents.

Discussion

The present case confirm that, although neurological involvement in SLE is so frequent to be considered one of the American Rheumatism Association criteria for diagnosis of SLE, cerebellar dysfunction has been rarely observed. Indeed, cerebellar ataxia due to focal or diffuse cerebellar atrophy is estimated as occurring in less than 2% of definite SLE cases, but it is only anecdotally reported as presenting symptom of such autoimmune condition. To our knowledge, few SLE cases with cerebellar ataxia has been reported. In our case the subacute clinical presentation of a cerebellar dysfunction, associated with immunological findings, allowed us to hypotize the diagnosis of SLE. Therefore, the patient fulfilled four (arthritis, leucopenia occurring in two occasions, presence of antinuclear antibodies as well as other immunological dysfunctions) out of the eleven American College of Rheumatology revised criteria for the classification of SLE. Other causes of cerebellar syndrome, such as infective, toxic, metabolic, paraneoplastic and demyelinating, were excluded by reviewing medical history and performing careful physical examination as well as laboratory and neuroimaging investigations. As far as physiopathological aspects are concerned, several mechanisms are postulated for central nervous system (CNS) involvement in pa-

Figure 1. Brain MRI scan. Axial (A), coronal (B) and sagittal (C) T2-weighted images showing left cerebellar hemisphere atrophy.
tients with SLE. Although neurological manifestations are commonly associated with serological detection of lupus anticoagulant and anticardiolipin antibodies in these patients, the exact pathogenetic mechanism is not to date fully elucidated. It may be related to a vascular process consisting of widespread thrombosis of small cerebral vessels. Alternatively, an antibody-mediated reaction has been hypothesised: antiphospholipid antibodies may cross-react with epitopes on CNS phospholipids such as sphingomyelin. In this context, previous studies reported that antibodies against the NR2 subtype of the NMDA-receptor are detected in patients with SLE and primary Sjögren’s syndrome. These antibodies, as previously demonstrated in mice with autoimmune disease, can cause focal hippocampal atrophy and cognitive impairment when they gain access to the brain. Recently, similar findings of focal hippocampal subfield atrophy in chronic voltage-gated potassium channel (VGKC) complex antibody-mediated limbic encephalitis have been observed.

Conclusions

Patients with SLE may rarely present with cerebellar dysfunction as first clinical sign. The appearance of an acute or subacute cerebellar syndrome with no obvious cause, especially together with emerging associated autoimmune systemic features during the clinical course, should suggest for possible SLE. Such diagnostic hypothesis, albeit not frequent, is crucial due to implications for clinical practice in order to provide a prompt therapy and to improve clinical outcome.

Conflict of Interest

The Authors declare that they have no conflict of interest.

References