

# A rare association of multiple sclerosis and systemic lupus erythematosus - A case report

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## ABSTRACT

Although both systemic lupus erythematosus (SLE) and multiple sclerosis (MS) are autoimmune diseases, their simultaneous presence in the same patient is rare.

**Case report.** We present the case of a 26-year-old woman who was diagnosed with MS and underwent treatment with interferon beta 1-alfa. After 2 years, she developed cutaneous lesions subsequent to a systemic disorder. After multiple serological tests were conducted, the diagnosis of SLE was established and hydroxychloroquine was added to the patient's treatment.

**Conclusion.** The presented case report is one of only a few cases published on the association of the two autoimmune diseases.

**Keywords:** systemic lupus erythematosus, multiple sclerosis, autoimmune, interferon, systemic

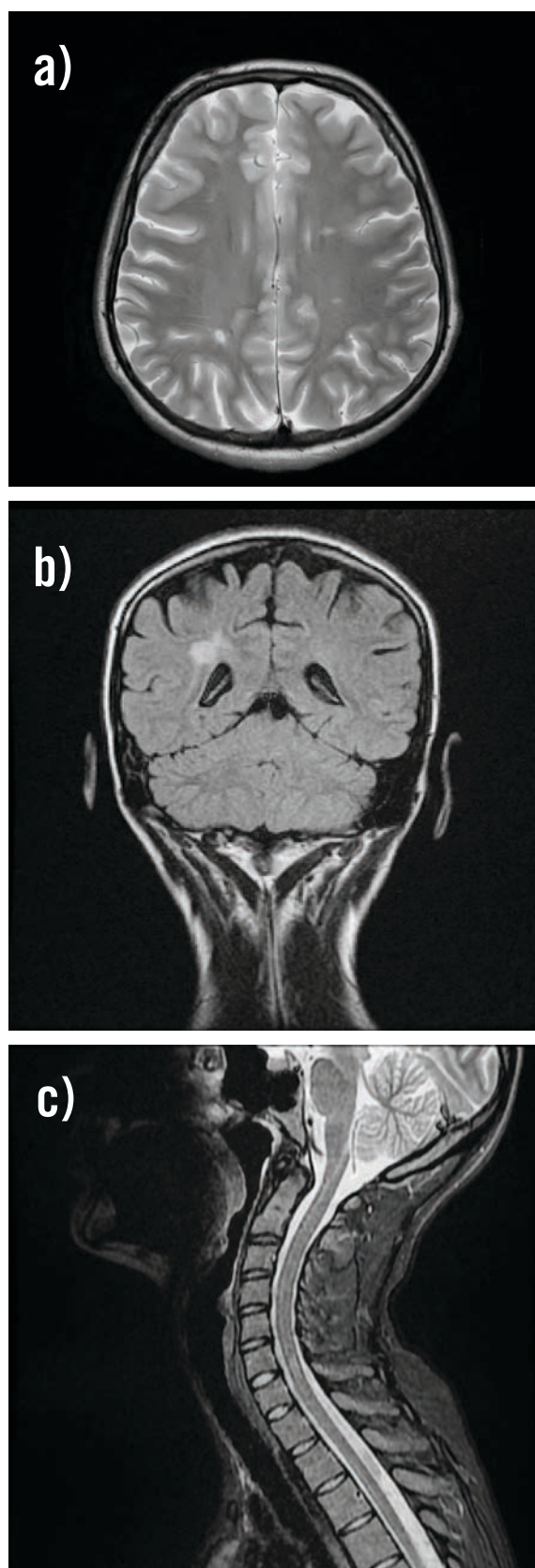
## INTRODUCTION

Multiple sclerosis (MS) and systemic lupus erythematosus (SLE) are both chronic, autoimmune disorders that primarily affect young adults. Their etio-pathogenesis is still largely unknown [1]. MS is the most common immune-mediated inflammatory demyelinating disease of the central nervous system. Clinical manifestations in MS are secondary to inflammation, demyelination and axonal degeneration. Altered interactions between T cells, B cells and other immune cell populations represent the cellular immunopathology of MS [2]. LES is a B-cell-mediated autoimmune disease in which the clinical manifestations are secondary to antibody formation against nuclear antigens and the formation of immune complexes, thus leading to tissue damage. However, the exact etiology of SLE still remains uncertain [3,4]. The diagnosis of LES in a patient with MS represents a real challenge bearing in mind that the association between the two diseases is rare, only 19 other case

reports have been published so far, from our knowledge [3,5].

## CASE REPORT

We present the case of a 26-year-old woman with no significant previous diseases or known family history of autoimmune abnormalities. At the age of 23, she was diagnosed with relapsing-remitting MS (RRMS). Prior to the diagnosis, the patient had suffered from a single episode of paresthesia in the lower limbs, ascending from the plantar region to the upper territories. Serum immunological tests, including antinuclear antibodies (ANA), anti-double-stranded DNA antibodies (anti-dsDNA), antiphospholipid antibodies (aPLa), aquaporin 4 antibodies (anti-AQP4), Venereal Disease Research Laboratory (VDRL) tests and Human immunodeficiency virus (HIV) tests were negative. Vitamin B12 levels were normal. At the time of the diagnosis, oli-



**FIGURE 1** - MRI showing signs of CNS involvement in MS  
**a)** Axial T2-weighted image shows multiple hyperintense, ovoid, fairly well demarcated in a juxtacortical and periventricular location; **b)** Coronal FLAIR weighted right periventricular lesion; **c)** MRI shows a single area of T2 hyperintensity which extends for a single vertebral level and involves both grey and white matter in the lateral-posterior part of the spinal cord (C6)

goclonal bands (OCBs) were identified in the cerebrospinal fluid (CSF). Magnetic resonance imaging (MRI) examination was performed and 10 demyelinating lesions were identified in the supratentorial region (frontal lobe and both parietal lobes), associated with lesions in the infratentorial region (right cerebellum hemisphere and left bulbar region) and 1 lesion with similar characteristics in the spine (C6 level of the vertebral column; Figure 1). The patient met the diagnostic criteria of RRMS [6] and started treatment with interferon beta 1-alfa (INFB1a). She underwent annual MRI investigations, which did not reveal any change in the already existing lesions, nor did they reveal any new demyelination.

After almost two years of treatment, she began developing cutaneous manifestations (Figure 2), such as papules that turned into edematous, erythematous plaques that would disappear at vitropresure. During their evolution, the lesions presented a tendency of desquamation. A cutaneous biopsy revealed leukocytoclastic vasculitis. She received intravenous methylprednisolone resulting in complete recovery. The patient stopped treatment with INFB1a. However, two months later the cutaneous manifestations reappeared associated also with polyarthralgia and asthenia. Laboratory investigations showed leukopenia (2720/ $\mu$ L) and lymphopenia (1250/ $\mu$ L). C3 complement low levels were identified. Serum immunological tests were reevaluated, as follows: positive ANA (6.3 times the upper limit of normal - ULN; ELISA), positive anti-dsDNA antibodies (8 times the ULN), positive anti-Sm antibodies (5.2 times the ULN), anti-U1RNP antibodies (3.9 times the ULN). Extractable nuclear antibodies (ENA) and anti-ribosomal P protein (anti-P) antibodies also tested positive. Anti-Ro antibodies, anti-La antibodies, aPLa and anti-histone antibodies were negative. The angiotensin-converting enzyme was negative. Other laboratory findings, including renal function tests, were normal. Thyroid tests identified autoimmune thyroiditis with normal thyroid function. Echocardiogram was normal. A second cutaneous biopsy was taken, which revealed a histopathological pattern compatible with chronic cutaneous lupus erythematosus.

Considering the clinical symptoms (arthralgia) and the laboratory findings (leukopenia, low complement and increased anti-dsDNA and anti-Sm antibodies), the SELENA-SLEDAI disease activity index [7] had a moderate value of 9. The patient started treatment with methylprednisolone low dose, hydroxychloroquine 300mg/day and topical glucocorticoids. After 6 months of treatment with hydroxychloroquine, there was complete clinical response and there have been no clinical relapse symptoms.



FIGURE 1 - Evolutive phases of the cutaneous manifestations

## DISCUSSION

In the presented case report, the main focus is the differentiation between the natural clinical and paraclinical evolution of MS associated with late development of LES versus early onset neurological manifestations of SLE. The demyelinating process can be a direct manifestation of SLE or a comorbid autoimmune condition such as MS [8]. The diagnosis of MS in our patient met the 2017 McDonald Criteria for the diagnosis of MS [6]. She had presented one episode of paresthesia in the lower limbs and more than two lesions in two different regions were identified on the cerebral and spine MRIs. Also, OCBs were present in the CSF [8]. At the time of the diagnosis, serological tests for other autoimmune or infectious diseases were all negative. However, OCB can be present in the CSF in 15-50% of patients diagnosed with SLE and up to 98% of patients diagnosed with MS [1,5]. The absence of systemic disease in the first two years and the small percentage of reported cases of demyelinating lesions in LES support the hypothesis of the two diseases coexisting [9].

In patients with SLE, aPLa have a key role in the neurologic manifestations. With the ability to mimic myelin at a molecular level, they produce vasculopathy and autoimmune vasculitis, thus producing a disease similar to MS [3,10]. However, in our patient's serum aPLa were negative, throughout the evolution of the case.

Our patient has received treatment with INFb1a for the treatment of RRMS, which has been shown to promote the activation of the immune system in patients with LES. High circulating levels of IFN ac-

companied by the multitude of genes it regulates have been shown to contribute to autoimmunity and tissue damage. High levels of IFN in patients diagnosed with SLE determine a more active disease, with a higher probability of developing nephritis and other severe manifestations [11,12]. Drug-induced SLE (DISLE) was taken into consideration when debating the case. DISLE can have similar clinical and paraclinical manifestations as SLE, except for central nervous system and renal disorders which are rare. The drug-induced systemic disorder can be characterized by arthralgia, myalgia and rash and can present positive ANA and anti-histone antibodies in the serum. Despite their similarities, DISLE usually reverts weeks after stopping the treatment that caused it [13], unlike the case we presented, where the systemic manifestations did not revert after the MS treatment ended. What is more, few cases of SLE development in patients suffering from MS and being treated with IFN have been published [14-16].

Treatment guidelines for the association of MS and SLE should be established. Rituximab can be an option for both pathologies. It is recommended in SLE with neurological, renal, or hematological manifestations who failed to respond to first-line therapies [17-19]. Its effectiveness for patients with RRMS who were identified as non-responders to first and second lines of treatment, is shown in an observational study, that also reports its efficacy for patients with associated autoimmune pathologies, as in our presented case [20].

## CONCLUSION

In conclusion, even though the concomitant presence of MS and SLE in one patient is a rare occurrence,

LES should be taken into consideration when confronted with a case of systemic manifestations in a patient prior diagnosed with MS.

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