

# Inflammatory myopathy and autoimmune hepatitis in a patient with a flare of systemic lupus erythematosus: An exceptional association

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## Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease with a wide clinical expression, and musculoskeletal manifestations are the most frequent manifestations of the disease. Digestive manifestations, however, are less prevalent, appearing in only 2%-30% of the patients. Among these cases, the association of SLE with autoimmune hepatitis (AIH) is considered to be rare, with only a few cases documented in the medical literature. We present the only reported case to date of a patient diagnosed with SLE suffering from a flare with a simultaneous hepatic and muscular inflammatory involvement, both evidenced by biopsy.

**Keywords:** Systemic lupus erythematosus, inflammatory myopathy, autoimmune hepatitis, SLE activity

## Introduction

In systemic lupus erythematosus (SLE), the musculoskeletal manifestations are the most frequent manifestations, arthritis and arthralgias being the most common. Myalgias and muscular weakness are not uncommon, while inflammatory myopathies and polymyositis in particular are less frequent. Apart from the overlap with authentic inflammatory myopathies, cases of steroid myopathy, hydroxychloroquine-induced myopathy, and even vacuolar myopathy, have been reported (1). Digestive manifestations are less frequent in SLE, occurring in only 2%-30% of patients. Among these cases, the association of SLE with autoimmune hepatitis (AIH) is rare, with only a few cases being documented in the medical literature (2). In this manuscript, we present the case of a patient diagnosed with SLE suffering from a flare of the disease with simultaneous hepatic and muscular inflammatory involvement.

## Case Presentation

A 46-year-old woman from Uruguay was diagnosed with SLE 22 years ago. She initially presented with bilateral hand polyarthritis and, at the time of diagnosis, she fulfilled clinical and analytical criteria for SLE (arthritis, presence of ANA, anti-dsDNA, and anti-Sm antibodies, photosensitivity, malar rash, and oral ulcers). In the years before moving to Barcelona, she had only received treatment with corticosteroids occasionally. In 2003, she received follow-up care in the Rheumatology Department at the Hospital del Mar/Parc de Salut Mar (Barcelona), where she started treatment with Dolquine (hydroxychloroquine) at a dose of 400 mg/day. Corticotherapy was withdrawn, with no need for reintroduction at any time during her follow-up. With this therapy, the patient remained clinically and analytically stable, with no new flares or presence of another symptomatology attributable to SLE. We would like to highlight the persistent negativization of anti-dsDNA and of the rest of autoantibodies since 2007.

In December 2014, the patient was admitted to the emergency department due to fever that had lasted for three days, associated with arthralgias in proximal interphalangeal joints and both wrists, discrete malar rash, and pain focused in the region of the left quadriceps, with slight muscle weakness as well as pain at the palpation of the mentioned zone. Given these findings, the patient was admitted at the Rheumatology Department with the suspicion of an SLE flare. Serological findings revealed ANA 1/320, negative anti-dsDNA, and positivity for anti-Sm and anti-RNP antibodies, no proteinuria or hematuria, and mild lymphopenia (1050 cells/L) as the only alteration of the hemogram. Muscle enzymes were elevated (creatinine kinases [CK] of 309 IU/L and aldolase of 12.8 IU/L), and there was an increase in acute phase reactants, with an ESR



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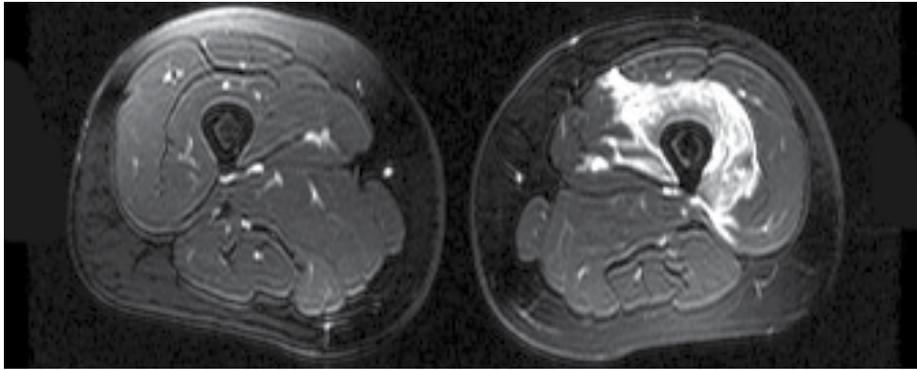
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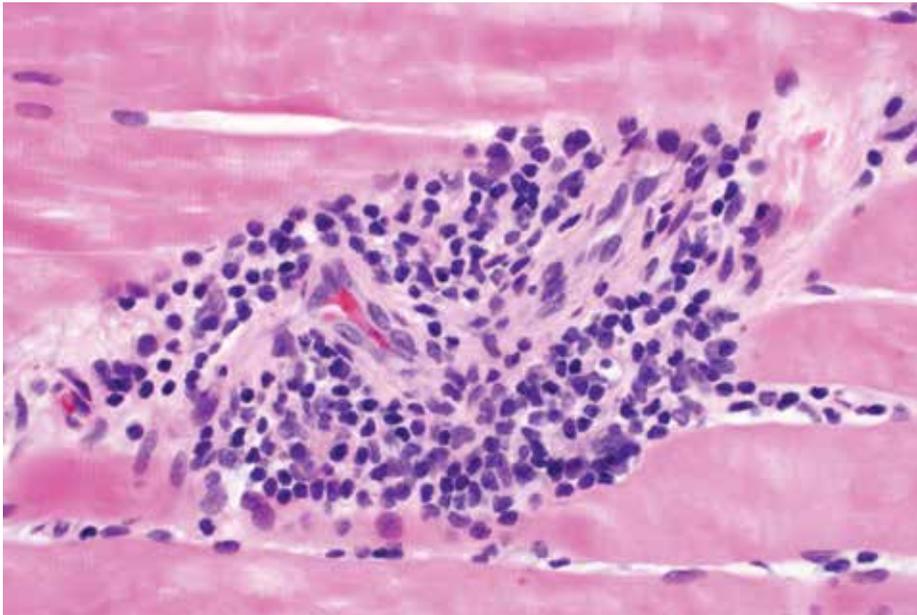
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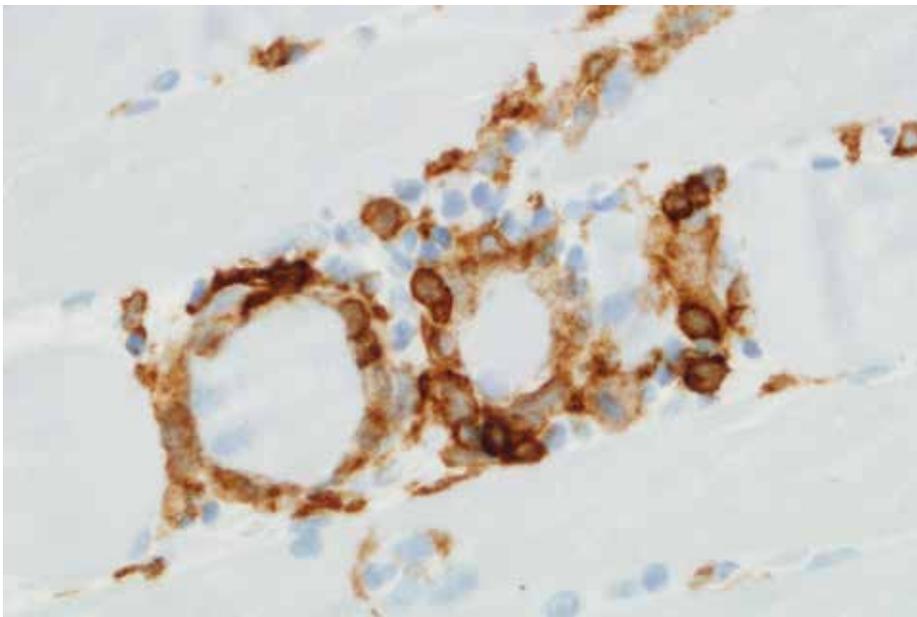
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**Figure 1.** Lower limbs MRI, coronal cut: extensive muscle involvement in left quadriceps, affecting intermediate vastus and partially lateral and medial vastus



**Figure 3.** Histological study of the muscle (HE, 40x); detail of a group of muscular fibers showing a perivascular aggregate of chronic inflammation



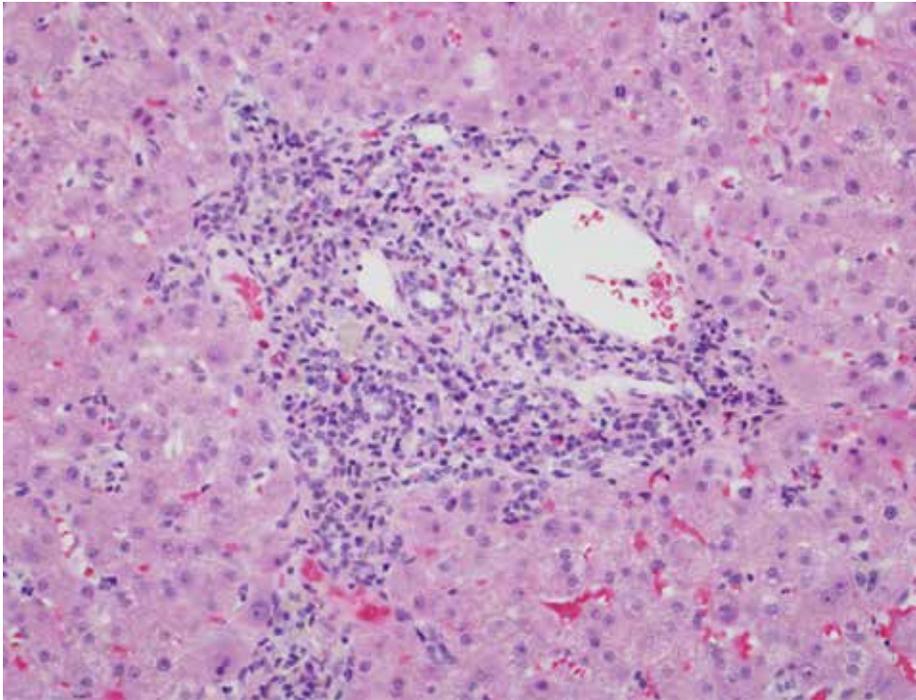
**Figure 4.** Histological study of the muscle (IHC anti-CD4, 40X); the lymphoid aggregates detected were predominantly composed of CD4+ T lymphocytes



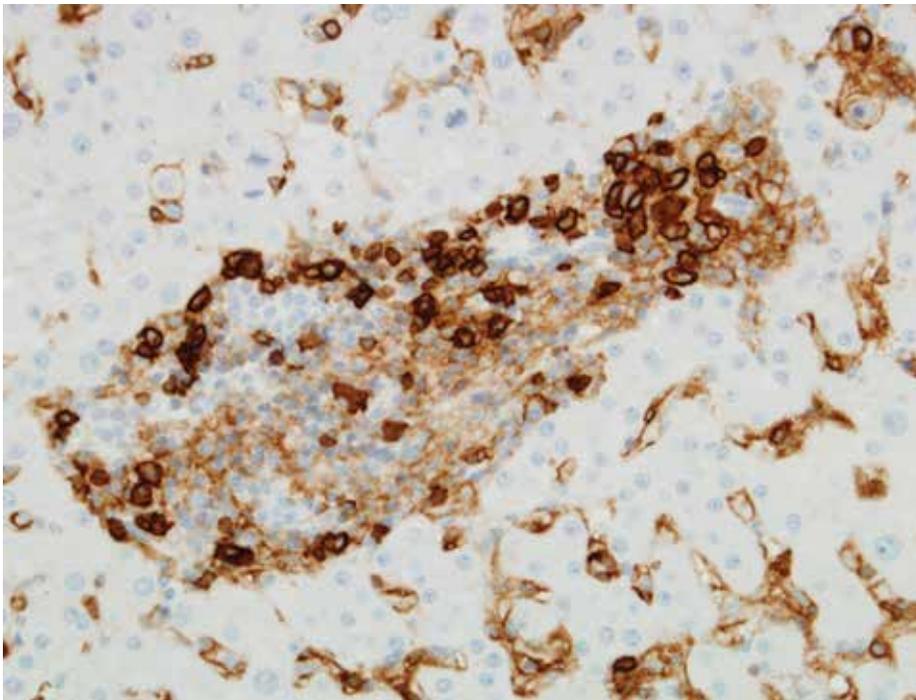
**Figure 2.** Lower limbs MRI, axial cut: muscular alterations similar to the descriptions in coronal cuts, compatible with edema/inflammatory changes/myositis

of 34 mm/h, PCR of 4.09 mg/dL, and ferritin of 614 ng/mL. There was also an increase in hepatic enzymes (GOT 694 IU/L, GPT 1044 IU/L, FA 130 IU/L). The serologies of the hepatotropic viruses (HAV, HBV, HCV) as well as the most common antibodies associated with autoimmune hepatitis (ASMA, anti-LKM1, anti-SLA, and anti-LP) were negative. In terms of complementary examinations, an MRI (magnetic resonance imaging) of the lower limbs was performed, which showed extensive muscular involvement of the left quadriceps, affecting the intermedius vastus and partially the lateralis and medialis, compatible with edema, inflammatory changes, or myositis (Figures 1 and 2).

Three tissue fragments were obtained by muscle biopsy. The results of this study were consistent with an inflammatory myositis (Figures 3 and 4). In view of the possibility of concomitant hepatic involvement, a percutaneous liver biopsy was performed, and two tissue cylinders were obtained and submitted for histological study. The biopsy results showed a pattern of lobule and portal hepatitis with plasma cell aggregates compatible, in the clinical context, with an active autoimmune hepatitis and without signs of chronicity (Figure 5 and 6). Prednisone was started at a dose of 1 mg/kg (60 mg/day). Following the American guidelines for the clinical management of autoimmune hepatitis in young adult patients, no immunosuppressant treatment was applied at the beginning. Nevertheless, after a new increase in the values of muscular and liver enzymes during the descending regimen of corticosteroids, treatment with azathioprine at a dose of



**Figure 5.** Histological study of the liver (HE, 20X); Detail of portal inflammatory infiltrates with interface activity



**Figure 6.** Histological study of the liver (IHQ anti-CD 38, 40X); presence of plasma cells aggregates constituting the periportal inflammatory infiltrate

50 mg/24 h was started, pending the results of the thiopurine methyltransferase (TPMT) polymorphism studies.

### Discussion

To date, the current case represents the first reported case of an overlap involving systemic lupus erythematosus, autoimmune hepatitis, and inflammatory myopathy. Autoimmune

liver disease may be associated with extrahepatic inflammatory manifestations (3). Several associations between autoimmune hepatitis, and polymyositis/dermatomyositis with other diseases have been documented: with thyroiditis and antiphospholipid syndrome; systemic sclerosis and cerebral vasculitis; primary biliary cirrhosis and thrombocytopenic purpura; myasthenia gravis and thymoma; membranous

nephropathy and Sjögren's syndrome; and, finally, with systemic sclerosis and sarcoidosis of mediastinal lymphoid nodules (3-8). In the case described, the GOT/GPT ratio was not indicative of an acute process exclusively. Muscle pain in the lower extremities lead to an MRI of the lower limbs, with findings indicating focal myositis of the quadriceps muscle, results later confirmed by the muscle biopsy.

The diagnosis of autoimmune hepatitis was made by combining clinical, analytical (absence of other etiologies such as hepatotrope virus positivity, enolic intake or recently new introduced drugs) and histological data (liver biopsy compatible with presence of plasma cell aggregates in the portal regions). The pre-treatment index for detecting autoimmune hepatitis scored 13 points (9).

Currently, the patient's progress is satisfactory, with azathioprine applied at a dose of 50 mg/24 h and hydroxychloroquine 400 mg/24 h. At present, she is stable without elevated liver enzymes or myalgias suggestive of persistent inflammatory myopathy.

### Conclusion

When assessing a patient with SLE and evidence of clinical activity (acute flare) with elevated transaminases, it is essential to examine muscle enzymes and to rule out a possible myopathic involvement, isolated or even concomitant with autoimmune hepatitis, as in the case presented.

**Informed Consent:** Written informed consent was obtained from the patient who participated in this study.

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