ANTI-SRP ANTIBODIES ASSOCIATED NECROTIZING AUTOIMMUNE MYOPATHY AND MULTIPLE SCLEROSIS: A CASE REPORT

A.Marangi, A.Gajofatto, D.Marastoni, F.Gobbin, P.Tonin, MD.Benedetti

Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Introduction

Necrotizing autoimmune myopathy (NAM) is characterized clinically by subacute onset of muscle weakness and histologically by muscle necrosis and regeneration with minimal or absent inflammation. Autoantibodies directed to 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) or to signal recognition particle (SRP) are detected in about two-third of cases[1]. Different associations between NAM and malignancies or rheumatologic disorders have been reported.[1]

We herein describe the **association between multiple sclerosis** (MS) and **anti-SRP related NAM** in a 61-year old man who presented with subacute onset of diffuse myalgias and asthenia and increase in creatine kinase levels up to 3400 IU/L. The neurological examination revealed, besides of lower limbs weakness, sensory impairment and pyramidal signs in the left limbs. At the time of hospitalization the patient recalled a history of long-term, undiagnosed paresis of the left lower limb and dyslipidemia.

Methods

A wide laboratory work-up was performed. The patient underwent EMG of the four limbs, muscle biopsy and brain and spinal cord MRI. Neurophysiological tests, lumbar puncture and total body PET-CT completed the diagnostic work-up.

Results

EMG of the four limbs revealed the presence of a myopathy. Consequent muscle biopsy showed a histological picture consistent with a necrotizing myopathy (Fig. 1 a-c), with blood tests positive for anti-SRP antibodies. At the same time, MRI revealed several inactive demyelinating lesions. (Fig. 2 a-c) Multimodal evoked potentials showed increased latency of central conduction. CSF oligoclonal bands were detected, while total body PET-TC was negative for malignancies. The final diagnosis was **NAM associated with MS**. Consequent therapy with steroids (only for the first six months) and, afterwards, azathioprine (gradually increased to 150 mg/daily) resulted in the resolution of the myopathic syndrome and in a complete stability of MS during the follow up.

Conclusions

- The co-occurrence of CNS demyelinating syndrome and NAM might firstly suggest a paraneoplastic aetiology[1,2], but the diagnostic work up, besides of the long time lapse between the onset of symptoms and the negative screening for cancer during the follow-up, ruled out this hypothesis.
- Mitochondrial disorders such as MELAS were also excluded in light of MRI and muscle biopsy findings.[3]
- MRI picture showed dissemination in space typical of MS, and the history of a long-term neurological impairment suggests a possible primary progressive indolent course of the disease.
- Although a chance association between NAM and MS may not be ruled out, it appears reasonable to hypothesize the presence of an immunological dysregulation with consequent phenomena of molecular mimicry.

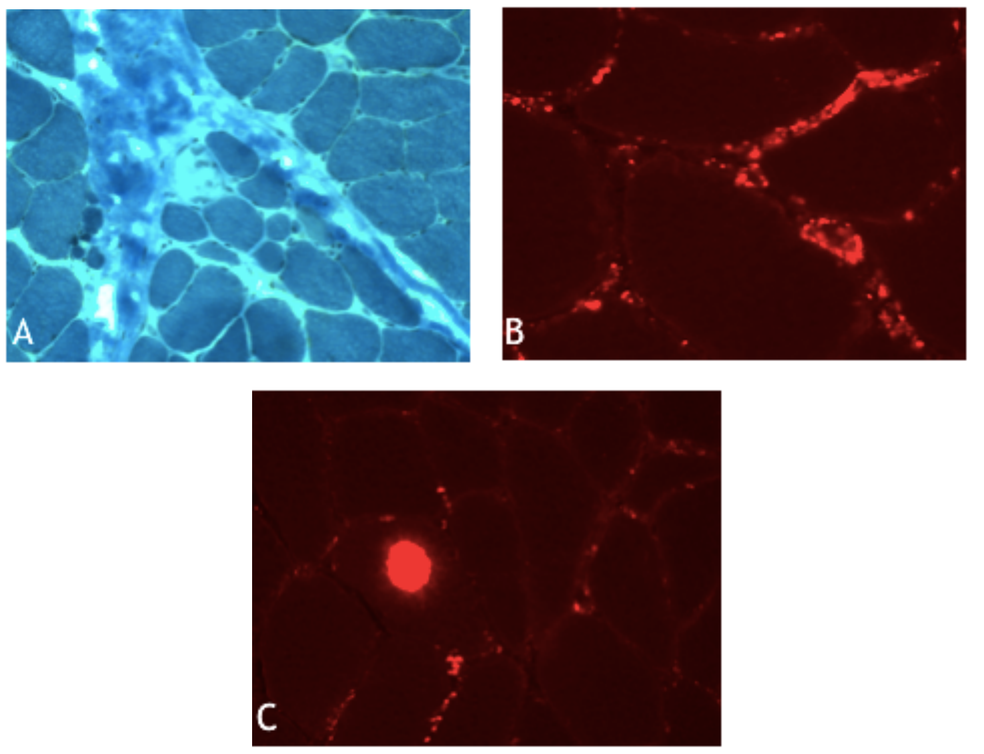

Figure 1 a-c. Biopsy of gastrocnemius muscle: few necrotic fibers without inflammatory infiltrates, some regenerating fibers along with deposition of MAC on small vessel walls, on the membrane of rare fibers and in the cytoplasm of one necrotic fiber.

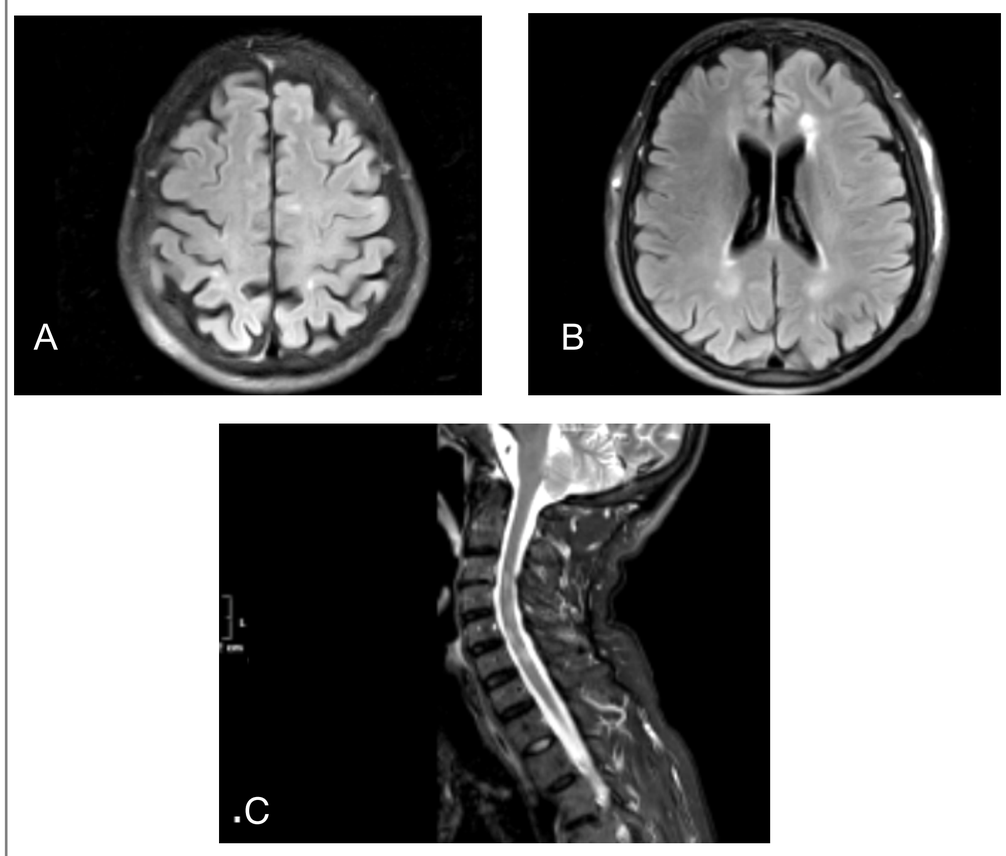

Figure 2 a-c. Axial fluid attenuation inversion recovery (FLAIR) images (3T) (a-b) showing bilateral areas of hyperintensity suggestive of demyelinating lesions in the juxtacortical and periventricular regions. Short T1 inversion recovery (STIR) image (c) revealed multiple demyelinating lesions in the cervical cord

Bibliography

1) Basharat P, Christopher-Stine L. Immune-mediated necrotizing Myopathy: Update on Diagnosis and Management. Curr Rheumatol Rep. 2015 feb 14;17

2) Jaster JH, Dohan FC Jr, O'Brien TF. Demyelination in the brain as a paraneoplastic disorder: candidates include some cases of seminoma and central nervous system lymphoma. J Neurol Neurosurg Psychiatry 2002;73:352

3) Weisfeld-Adams JD, Katz Sand IB, Honce JM,Lublin FD. Differential diagnosis of Mendelian and mitochondrial disorders in patients with suspected multiple sclerosis. Brain 2015 Mar;138(Pt 3):517-39