The puzzle of brain autoimmunity: recurrent myelitis associated to lupus anti-coagulant, anti-β2GPI and anti-aquaporin-4 antibodies

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Introduction

Neuromyelitis optica spectrum disorder (NMOSD) syndromes are autoimmune water channelopathies that predominantly target astrocytes or oligodendrocytes and are associated with anti-aquaporin-4 (AQP4-IgG) or anti-myelin oligodendrocyte glycoprotein antibodies. Longitudinally extensive transverse myelitis (LETM) with MRI lesions spanning ≥3 vertebral segments is one of major features of NMOSD. Anti-phospholipid syndrome (APS) is a systemic autoimmune pro-thrombotic disease that has been historically associated with a myelitis whose pathogenesis is still poorly understood. We describe a patient with recurrent LETM who was diagnosed as APS-associated myelitis in 2005 and recognized as NMOSD in 2011.

Case Report

2005

In March 2005, a 72-year-old man, with a medical history remarkable for ischemic cardiopathy and retinopathy, presented with left arm and leg paresthesia. Laboratory tests disclosed high titres of anti-β2-glycoprotein-I (aβ2GPI [IgG/M/A]) antibodies. Cervical spine MRI revealed a LETM. Head MRI was unremarkable.
He was diagnosed with "APS-associated myelitis" and treated with high dose methylprednisolone and lifelong anticoagulation with warfarin.

2009

In 2009 he had a second episode of LETM and the diagnosis of "APS-associated recurrent myelitis" was done. At that time the diagnostic test for AQ4-IgG antibodies was not available.

2011

In 2011 he had a third episode of myelitis. The search for AQP4-IgG gave positive result. A high titre of aβ2GPI (IgG/M/A) antibodies was confirmed. Moreover, he was also positive for lupus anticoagulant (LA) and for anti-nuclear antibody (>1:320), but the search for anti-double stranded DNA antibodies and SSA/SSB gave negative results. Although the patient met the criteria of APS, on the base of the serological findings the diagnosis of AQP4-IgG-positive NMOSD was finally achieved.

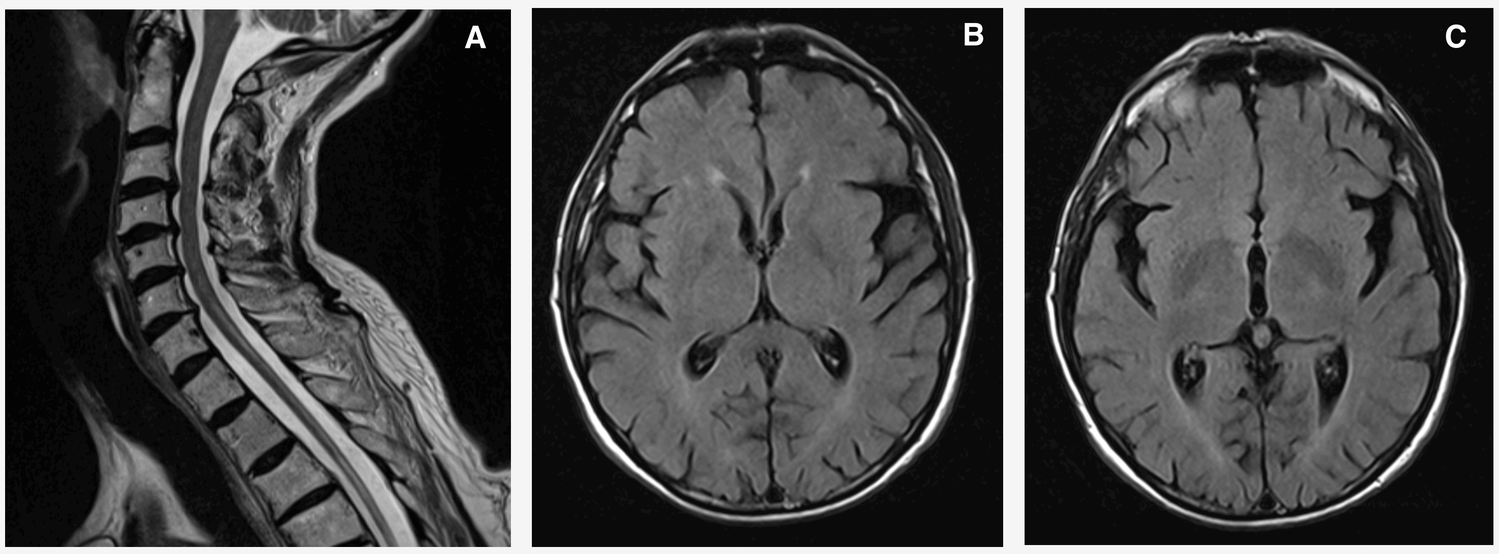

Fig 1. *Cervico-dorsal (A) and brain MRI (B,C)*

Discussion

This case illustrates that a puzzle of autoreactive antibodies can be detected in patients having neurological syndromes belonging to the NMOSD. Patients with recurrent LETM and anti-phospholipid antibodies may be erroneously diagnosed as APS-associated myelitis if anti-AQP4 and anti-MOG antibodies are not investigated. Thus, the search for AQP-4 and MOG IgG are mandatory in LETM even when other autoreactive antibodies are present, since the therapeutic rebounds are considerable. Indeed, long-term immunosuppression is the standard therapy for NMOSD-associated LETM and should be initiated as soon as the diagnosis in achieved, in order to prevent relapses and the accumulation of irreversible disability.