Reactivation of neuromyelitis optica: is natalizumab the guilty?

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Introduction

Neuromyelitis optica (NMO) is an inflammatory-demyelinating autoimmune disease of the central nervous system (CNS), with predominant involvement of optical nerves and spinal cord. NMO, long regarded as a variant of multiple sclerosis (MS), has been recently classified as separate disease. NMO is associated to anti-AQP4 antibodies, derived from B cells and targeting the astrocyte water channel acquaporin-4.

Natalizumab is a humanized monoclonal antibody, binding the adhesion molecule α4 integrin and stopping the leukocyes migration into the CNS across the blood brain barrier. The efficacy of natalizumab in relapsing MS has been demonstrated in several trials, whereas previous reports showed that natalizumab is ineffective in NMO.

Methods

We describe the case of a 50-year-old woman with multiple sclerosis diagnosis, who developed a clinical reactivation of neuromyelitis optica and anti-AQP4 seroconversion, under treatment with natalizumab.
Patient first presented with optic neuritis in 1991; two years later she developed acute dorsal pain with urinary retention and lower limbs weakness. The magnetic resonance imaging showed a T2-weighted hyperintensity with contrast enhancement, involving spinal cord from C-7 to T-7 vertebral levels, suggestive of a longitudinally extensive transverse myelitis. The cerebrospinal fluid analysis revealed intrathecal synthesis of oligoclonal IgG, with increased IgG index.
In 1997, after a new episode of contralateral optic neuritis and the evidence of new inflammatory-demyelinating MRI brain lesions, the diagnosis of relapsing-remitting MS was made and patient started subcutaneous interferon beta-1a treatment. In 2008 blood sampling for anti-AQP4 antibodies was performed, resulting negative.
After six years of clinical stability in the 2013 a clinical and neuroradiological *(fig. 1-2)* worsening occurred and patient was switched to second-line treatment with natalizumab.
In October 2014, after her 14th dose of natalizumab, patient experienced a relapse with acute worsening of lower limb weakness: MRI showed spinal cord oedema with deep contrast enhancement at T7-T9 level, within the tract of pre-existent transverse myelitis *(fig. 3).* The anti-natalizumab antibodies in serum was negative, as well as the JC viral genome in liquor.
The anti-AQP4 antibodies follow-up analysis was positive and the diagnosis of neuromyelitis optica was defined, replacing natalizumab with immunosuppressant treatment.

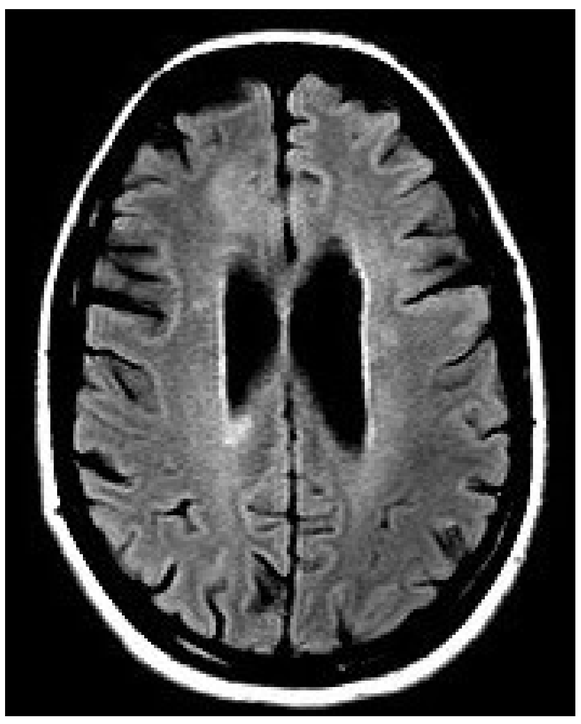

Fig. 1

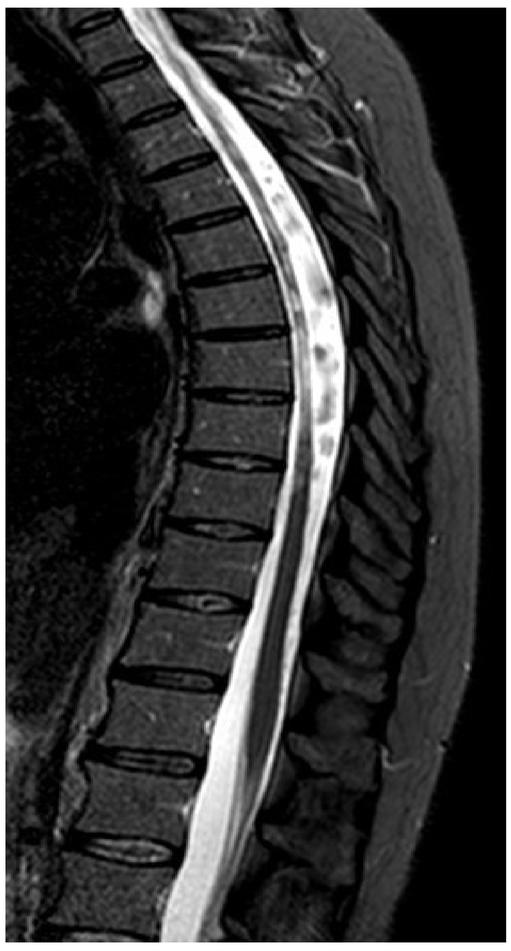

Fig. 2

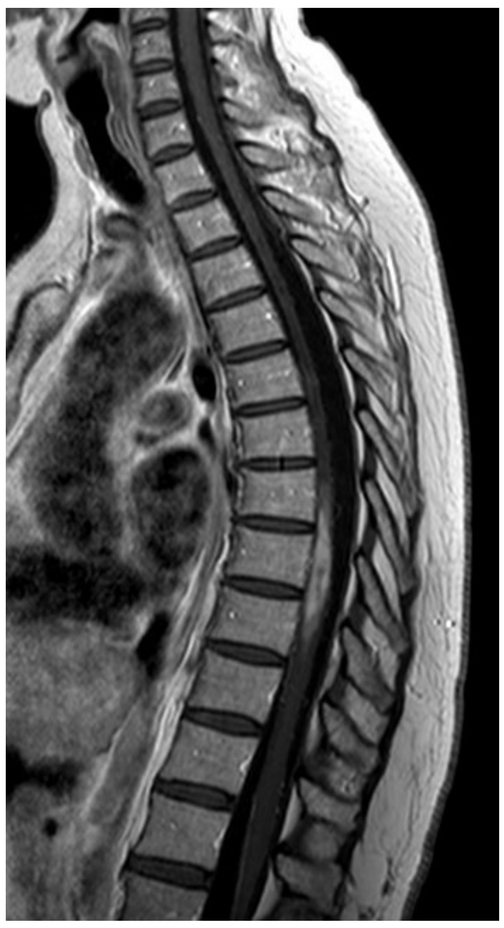

Fig. 3

Conclusions

Some studies suggest that natalizumab increases the proportions of circulating B cells, involved in humoral autoimmunity of NMO pathological pathway. Moreover natalizumab is not effective to prevent CNS migration of Th17 lymphocytes, which are demonstrated highly activated in patients with NMO.

This case remark the importance of differential diagnosis between MS and NMO and confirm the evidence that natalizumab is ineffective in NMO, even reactivating its inflammatory mechanisms.

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