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Case report

First report of coexistence of MOG-antibody-positive disease and Crohn's disease

Marie Philippart[a], Sophie Fastré[a], Jean-François Rahier[b], Frédéric London[a,*]

[a] Department of Neurology, CHU UCL Namur site Godinne, Université catholique de Louvain (UCLouvain), Avenue G. Thérasse 1, 5530 Yvoir, Belgium
[b] Department of Gastroenterology, CHU UCL Namur site Godinne, Université catholique de Louvain (UCLouvain), Avenue G. Thérasse 1, 5530 Yvoir, Belgium

1. Introduction

Myelin oligodendrocyte glycoprotein (MOG) antibody disease has recently emerged as a new inflammatory demyelinating condition of the central nervous system. MOG autoimmunity is increasingly categorised as a distinct entity from aquaporin-4 (AQP4)-IgG-mediated neuromyelitis optica spectrum disorders (NMOSD), although it is still under debate because there is a substantial phenotypic overlap between these two disorders. In contrast to AQP4 positive NMOSD, polyautoimmunity is less common in MOG-IgG-positive disease (Jarius et al., 2016; Cobo-Calvo et al., 2018). We report herein the first case of simultaneous occurrence of MOG-IgG-positive disease and Cohn's disease (CD) in a young male presenting with recurrent myelitis and brainstem syndrome.

2. Case presentation

A 33-year-old male was admitted in February 2017 because of subacute onset of paraparesis with T7 sensory level and urinary retention requiring an indwelling catheter. His medical history was remarkable for a longstanding CD treated with adalimumab and azathioprine (AZA) for 5 and 4 years respectively. Due to persistent disease activity, these treatments were withdrawn and vedolizumab, a gut selective anti-integrin, was started in November 2016. Two months prior to presentation (December 2016), he reported dysesthesia on the left side of T1-T3 dermatomes that did not alarm the treating physician.

On admission, clinical examination showed unsteady gait, left extensor plantar response and hyperreflexia of lower limbs. Spine magnetic resonance imaging (MRI) demonstrated a non-enhancing T2 hyperintense lesion extending from T4 to T6 and a second T2 hyperintensity at the T2 level (Fig. 1(A)). Brain MRI was unremarkable. Negative blood tests included antinuclear antibody panel, lupus anticoagulant, complement level and serology tests (Lyme disease, HIV, CMV, EBV, syphilis). AQP4 antibodies were negative but MOG antibodies were identified in serum (using cell-based assay with live HEK293 cells). Cerebrospinal fluid analysis showed lymphocytic pleocytosis (39 cells/µl; $N < 5$) and absence of oligoclonal bands. Neuro-ophtalmological examination and visual evoked potentials were normal. Because of acute cholecystitis requiring prompt cholecystectomy, corticosteroids were contraindicated. The patient's condition improved with plasmapheresis (5 exchanges). Vedolizumab was stopped, AZA was resumed and ustekinumab, an anti-interleukin 12/23, was initiated.

Three months later, a subsequent relapse occurred with diplopia and paresis of the left upper limb. Repeated MRI showed a new T2 hyperintensity extending from C3 to C4 (Fig. 1(B)) and two T2 hyperintense brainstem lesions (Fig. 1(C) and (D)), without gadolinium-enhancement. He was treated with intravenous methylprednisolone 1 g daily for 5 days and plasmapheresis (5 exchanges). On last follow-up (14 months after diagnosis), while on AZA 200 mg daily and ustekinumab 90 mg/2 months, EDSS was 4.0. The patient was unable to pursue his previous job.

3. Discussion

MOG antibody-associated demyelination is associated with a broad clinical spectrum, including monophasic acute disseminated encephalomyelitis, transverse myelitis, optic neuritis, brainstem syndromes and encephalitis. MOG-IgG related autoimmunity mainly affects the spinal cord and optic nerves, but extra-opticospinal manifestations are not uncommon and the current case underlines that brainstem involvement is also part of the clinical phenotype. Patients with MOG autoimmunity have often a relapsing disease course, indicating that long-term immunotherapy treatment is required especially since severe attack-related disability such as severe motor and sphincter dysfunction or significant bilateral optic nerve damage is not unusual.

Although MOG autoimmunity has different pathophysiology and prognosis than the AQP4-seropositive patients, they share numerous features questioning of whether they are two distinct entities or not. In addition to sharing similarities in clinical and neuroimaging features, both are associated with concomitant autoimmunity but polyautoimmunity seems to be less common in MOG-IgG-positive

* Corresponding author.
E-mail addresses: marie.philippart@student.uclouvain.be (M. Philippart), fastre.sophie@gmail.com (S. Fastré), jean-francois.rahier@uclouvain.be (J.-F. Rahier), frederic.london@uclouvain.be (F. London).

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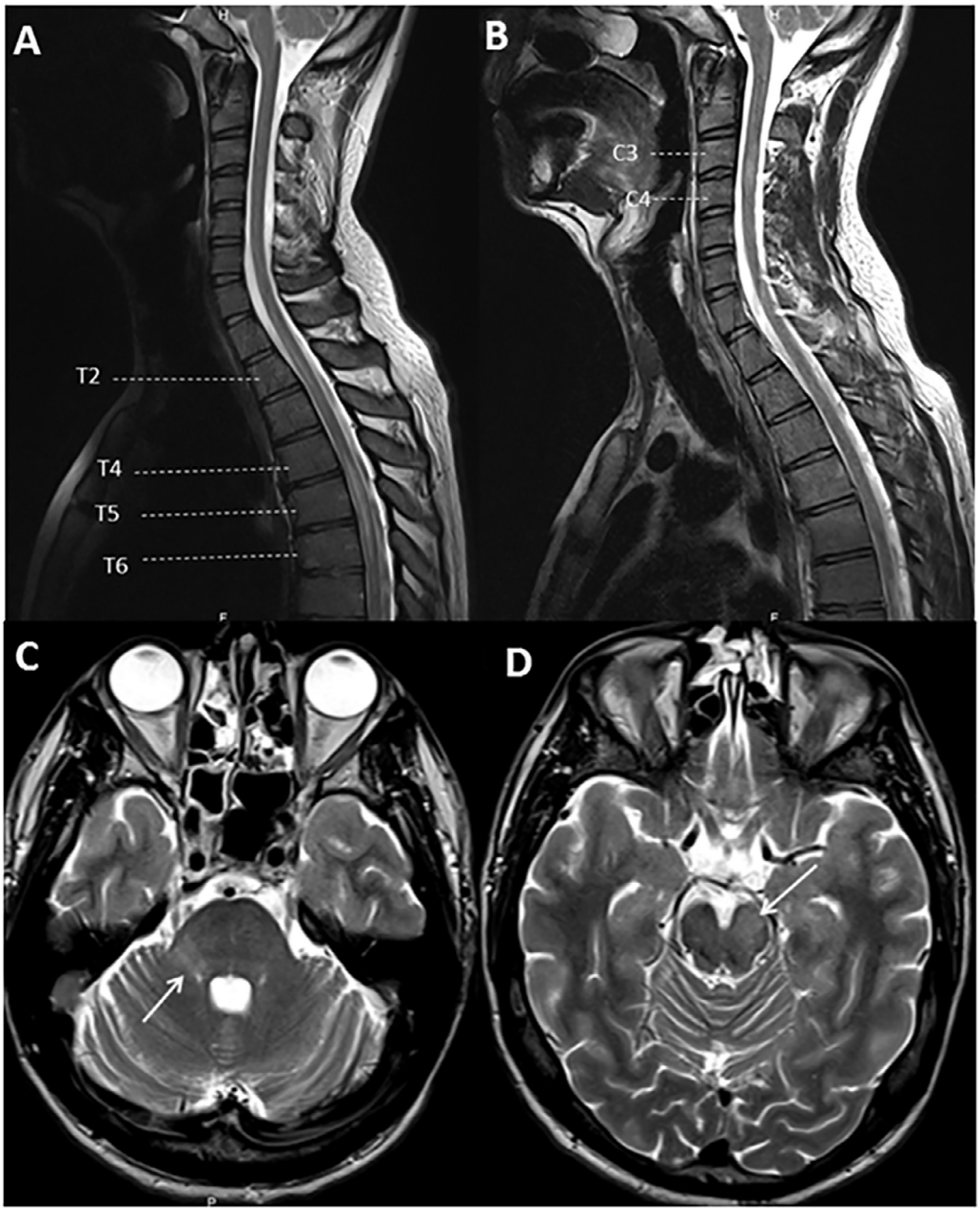

Fig. 1. Spinal cord and brain MRI First spinal cord MRI assessment showed a T2 hyperintensity extending from T4 to T6 and a second T2 hyperintensity at the T2 level (A, T2-weighted images). MRI 3 months later revealed a new T2 hyperintensity at the C3-C4 level (B, T2-weighted images). Axial T2-weighted images showing 2 hyperintense brainstem lesions (arrows) involving the right cerebellar peduncle (C) and the left cerebral peduncle (D).

demyelination. Nearly 20–30% of patients with AQP4 antibody-positive NMOSD have coexisting autoimmune disorders such as Sjögren's syndrome, systemic lupus erythematosus, thyroid disease, celiac disease, and myasthenia gravis (Iyer et al., 2014). In contrast, a minority of patients with MOG antibody-positive disease have a coexisting autoimmune disorder. Indeed, two large cohorts including respectively 50 and 197 adults with MOG autoimmunity found concomitant autoimmune diseases such as hypothyroidism, Grave's disease, rheumatoid arthritis, psoriasis, Sjögren syndrome, autoimmune hepatitis, and myasthenia gravis, in 9 and 11% of patients respectively (Jarius et al., 2016; Cobo-Calvo et al., 2018).

We report herein the first case of simultaneous occurrence of MOG-IgG-positive disease and CD. The interrelationship between MOG-autoimmunity and CD has relevant clinical implications. First, evaluation for MOG-antibodies should be considered in CD patients presenting a clinical and radiological phenotype atypical for multiple sclerosis (MS). Second, rituximab, a monoclonal anti-CD20 antibody found to be effective in MOG autoimmunity, should be avoided since it can induce or exacerbate CD (Fraser et al., 2016; Varma et al., 2017). Third, anti-tumor necrosis factor (TNF) alpha therapies should be avoided since their role in induction or exacerbation of CNS demyelinating disorders is well established. Here, a potential role of adalimumab in the development of CNS demyelination cannot be excluded but seems however unlikely, mainly because the patient still had evidence of active CNS demyelination 7 months after withdrawal of adalimumab. Indeed, one would expect the neurological disorder to resolve after discontinuation of the anti-TNF alpha therapy. However, it is not excluded that the patient had developed a relapsing-remitting course despite discontinuation of the offending agent. In the literature, we found only one report describing a case of NMOSD with positive MOG antibodies

following anti-TNF alpha therapy for psoriasis (Lommers et al., 2018). In this report, as in our case, the patient had a further relapse several months after discontinuation of adalimumab. In this peculiar situation, the question whether NMOSD with positive MOG antibodies is a distinct entity unrelated to anti-TNF alpha therapy or whether the patient just has anti-TNF alpha demyelination from adalimumab with coincidental presence of MOG antibodies remains a matter of debate. Last but not least, by preventing leukocyte trafficking into the central nervous system and the intestinal mucosa, natalizumab is indicated for the treatment of both CD and MS, and is therefore of strong interest in patients with CD and suspected MS. However, natalizumab might be ineffective or even have a detrimental effect in AQP4 antibody-positive NMOSD, owing to differences in immunopathogenesis (Kleiter et al., 2012).Although there is limited data, natalizumab has also failed to reduce relapse in patients with MOG-IgG and is therefore not recommended (Jarius et al., 2016). Given NMOSD may be frequently mistaken for MS, a careful diagnostic work-up is of paramount importance to avoid misdiagnosis of MS, which might lead to potentially harmful risks to patients.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest regarding this case report.

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Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study formal consent is not required. References

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