Coexistent anti-GFAP and anti-MOG antibodies presenting with isolated meningitis and papillitis: more support for overlapping pathophysiology

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ABSTRACT

Background Anti-myelin oligodendrocyte glycoprotein (MOG)-associated disorders are heterogeneous and associated predominantly with central nervous system demyelination. Anti-gial fibrillary acidic protein (GFAP) conditions are much rarer and involve meningoencephalomyelitis with papillitis in addition to characteristic imaging findings and are generally a severe condition. Multiple autoantibodies can exist in patients and may support overlapping pathophysiological mechanisms. The co-occurrence of MOG and GFAP antibodies, however, is rare, with only two cases previously reported.

Case A 53-year-old man presented with headache and fevers, with quick resolution, though with the later development of asymptomatic papillitis. He had a full recovery without the need for immunotherapy. He underwent extensive investigations and was found to have both anti-GFAP and anti-MOG antibodies in the cerebrospinal fluid. Extensive other immunological and infectious investigations were negative. Imaging was largely unremarkable.

Conclusions This is the third case of overlapping anti-GFAP and anti-MOG antibody-associated syndrome of self-limited lymphocytic meningitis, serving to expand the phenotype. Clinicians should consider testing for GFAP and MOG antibodies in otherwise unexplained meningitis, particularly with associated papillitis. This case may also help provide future insights into the pathophysiology of each condition.

INTRODUCTION

Autoimmune glial fibrillar acidic protein (GFAP) astrocytopathy is a recently described autoimmune disorder characterised by a severe meningoencephalomyelitis associated with papillitis and which tends to follow a relapsing course. Anti-myelin oligodendrocyte glycoprotein (MOG) antibody-associated diseases are a heterogeneous group of conditions associated predominantly with central nervous system (CNS) demyelination. The coexistence of anti-GFAP and anti-MOG antibodies is extremely rare, with only two cases previously reported. We present here a patient who presented initially with isolated meningitis, only later developing asymptomatic papillitis and following a benign course without a need for immunotherapy, and who was found to have both anti-GFAP and MOG antibodies. This may further help illustrate common pathophysiological links between the two conditions.

CASE PRESENTATION

A 53-year-old man presented with a 1-week history of headaches, new-onset insomnia, anxiety and fevers but without other neurological or systemic symptoms. There was no infectious prodrome or medical history of note. Initial neurological examination, including funduscopics, was normal. Cerebrospinal fluid (CSF) analysis showed normal glucose of 2.7 mmol/L, with elevated protein at 1.33 g/L. There were 798 leucocytes, with 776 monocytes and 22 polymorphs. Extensive infectious studies were negative, including PCR and culture of viral, bacterial and mycobacterial organisms. Fevers resolved quickly, though headaches continued for some weeks.

Repeat CSF was done on several occasions. Opening pressure was always normal, as was glucose. There was a persistently elevated protein and a reducing mononuclear-predominant pleocytosis. Extensive antibody tests, including anti-NMDA and AQP4, were all negative. CSF oligoclonal bands were positive. Metagenomic next generation sequencing testing for infectious organisms (at UCSF) was negative. Imaging of the brain and spinal cord with contrast on several occasions was unremarkable, though with questionable perivascular radial enhancement. There was no leptomeningeal enhancement (figure 1).

Flow cytometry, however, showed a persistent small monoclonal B cell population (0.3% of lymphocytes), expressing CD19,
AQP4 antibodies, and both with a more severe phenotype and, more rarely, infections, has also been described. MOG is located on the cell surface, while GFAP is found in the cytoplasm, and it may be that MOG antibodies may coexist with a different pathophysiology. This, however, remains speculative given so few cases described to date. MOG antibodies are recommended to be tested on serum rather than CSF, as titres in the CSF are generally lower, although the significance if detected in the CSF likely remains the same.

Our patient had a much milder phenotype, with headache and asymptomatic papillitis, but no other deficits. He also had new-onset insomnia and anxiety, as has been reported in GFAP astrocytopathy, and likely to relate to hypothalamic involvement. Normal brain and spine imaging, as in our patient, is reported in up to one-third of those with GFAP astrocytopathy. Monophasic illness can occur in both, though up to 50% of GFAP astrocytopathy cases may need long-term immunotherapy.

Our patient had no clear associated infections or malignancy. There was a small, isolated and transient CSF monoclonal B cell population, the significance of which is unclear, but unlikely to represent a haematological malignancy. The exact role and pathogenicity of the antibodies in this patient is unclear, particularly given the improvement without immunotherapy and the relatively mild clinical picture, though while the phenotype was mild, has features reported in patients with either anti-GFAP or anti-MOG-associated disorder. We cannot completely discount the possibility that the MOG antibodies in particular represent an epiphenomenon, however.

Clinicians should be aware as to the possibility of multiple overlapping antibody-associated conditions, even with a relatively mild phenotype, and should consider testing for such antibodies in otherwise unexplained lymphocytic meningitis, particularly with associated papillitis.

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