Interferon Beta Treatment in Neuromyelitis Optica

Increase in Relapses and Aquaporin 4 Antibody Titers

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**Objective:** To describe a patient with neuromyelitis optica (NMO) whose aquaporin 4 (AQP4) antibody levels increased following treatment with interferon beta.

**Design:** Prospective clinical and laboratory case report.

**Setting:** Institutional referral center for multiple sclerosis (MS).

**Patient:** One patient with an initial diagnosis of MS that was later revised to NMO.

**Interventions:** A course of interferon beta-1a followed by conventional immunosuppression. Blood samples were collected from the onset of treatment, and clinical and laboratory assessment was performed.

**Main Outcome Measures:** Serum levels of AQP4 antibody and number and characteristics of neurological relapses.

**Results:** After 3 relapses during a 10-month period despite interferon beta-1a treatment, the diagnosis of AQP4 antibody–positive NMO was made and treatment was switched to prednisolone and methotrexate. The AQP4 antibody titers rose dramatically during treatment with interferon beta, and then fell when conventional immunosuppressive therapy was substituted; the patient has remained relapse-free for the subsequent years.

**Conclusions:** Although previous articles have suggested that interferon beta may increase relapses in NMO, this is the first to illustrate an increase in AQP4 antibodies associated with such treatment.

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**NEUROMYELITIS OPTICA (NMO)** is a rare inflammatory demyelinating condition that predominantly affects the optic nerves and spinal cord. It has recently been associated with aquaporin 4 antibodies (AQP4-Abs), which are found in up to 85% of patients with NMO and are very rare in multiple sclerosis (MS). Neuromyelitis optica is a chronic relapsing condition that is now treated with immunosuppressive therapies in a similar manner to myasthenia gravis.

Neuromyelitis optica can present with a similar phenotype to MS, and thus patients may be initially misdiagnosed and treated with disease-modifying therapies such as interferon beta. Indeed, 1% of patients in an interferon beta-1a trial for clinically isolated syndromes (ie, first attack of MS-like symptoms) retrospectively tested positive for serum AQP4-Abs.

In contrast to MS, articles have suggested no effect or even an increase in the relapse rate when patients with AQP4-Ab–positive phenotypes are treated with interferon beta. This might be explained by a shift in the immunological profile toward a T-helper type 2–dominated system that is likely to enhance autoantibody production, but there have been no data to support this. Here we show the results of quantitative analysis of AQP4-Abs in a patient with NMO who was given interferon beta and was subsequently treated successfully with conventional immunosuppressive therapy.

**REPORT OF A CASE**

A 46-year-old woman presented with an inflammatory brainstem attack with transverse myelitis and subsequently had 2 further relapses during the next 3 years. She was diagnosed with MS and started receiving interferon beta-1a. She had 1 relapse shortly after treatment initiation and a further 3 during a 10-month period, which led to a review of the medical records. The diagnosis was revised to NMO, supported by positive testing for serum AQP4-Abs. Her interferon beta-1a treatment was stopped, and she started taking prednisolone and methotrexate; she has remained relapse-free during the subsequent 3 years of follow-up. Serum samples stored from the onset of interferon beta-1a treatment were tested for AQP4-Abs titers in a single assay run. The titers rose...
dramatically during treatment with interferon beta and then fell when conventional immunosuppressive therapy was substituted (Figure).

Although clinical reports have suggested that interferon beta has no effect on or exacerbates NMO, and there is a mechanistic theory to explain this, this is the first article to show an increase in AQP4 antibodies and lack of a clinical response in association with interferon beta treatment. This was in direct contrast to the serological and clinical effect of subsequent immunosuppressive therapy. This article supports the view that NMO has a different pathogenesis to MS and that more conventional immunosuppression should be used to treat this antibody-mediated condition.

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REFERENCES