Case report

Two patients with neuromyelitis optica but contrasting clinical courses

Thashi Chang[1], **M T M Riffsy**[2], **Padma S Gunaratne**[2]

Sri Lanka Journal of Neurology, 2012, **1**, 54-56

Abstract

Neuromyelitis optica (NMO) is an idiopathic, relapsing, demyelinating disease of the central nervous system that preferentially affects the optic nerve and spinal cord. Diagnostic criteria for definite NMO require optic neuritis, myelitis, and at least two of three supportive criteria: onset brain MRI non-diagnostic of MS; spinal cord lesion extending over 3 or more vertebral segments; or seropositive for NMO-IgG. We report two Sri Lankan patients who fulfil the above diagnostic criteria but have contrasting clinical courses over a 4-year follow-up period. The NMO-IgG seropositive patient demonstrated a more severe, relapsing disease course whilst the seronegative patient did not relapse despite not being on long-term immunosuppressive therapy. Given that para-infectious NMO is often monophasic and seronegative, discerning guidelines in recommending maintenance immunosuppression in NMO is required particularly in settings where incriminatory infections are prevalent.

Index words: neuromyelitis optica (NMO), multiple sclerosis (MS), optic neuritis (ON), transverse myelitis, NMO-IgG

Introduction

Neuromyelitis optica (NMO), also known as Devic disease, is an idiopathic, severe, relapsing, demyelinating disease of the central nervous system that preferentially affects the optic nerve and spinal cord leading to cumulative disability. Although previously thought to be a variant of multiple sclerosis (MS), the recent discovery of antibodies to the aquaporin-4 channel (NMO-IgG) in the serum has led to the redefining of NMO as a distinct clinical and pathological entity[1]. Accordingly, the revised diagnostic criteria for definite NMO require optic neuritis, myelitis, and at least two of three supportive criteria: onset brain MRI non-diagnostic of MS; spinal cord lesion extending over 3 or more vertebral segments; or seropositive for NMO-IgG[2].

We describe two patients with NMO with contrasting clinical courses and discuss the need for discerning guidelines in prescribing maintenance immunosuppressive therapy.

Patient A

A 35-year old housewife presented in January 2008 with paraparesis. She has had two episodes of optic neuritis, first in the right eye in 2005 that completely recovered following treatment with intravenous methylprednisolone and the second in the left eye in 2006 that did not recover. She had not sought treatment for the second episode since she had been pregnant at that time. Apart for hypothyroidism for which she was on replacement therapy, her past medical history was unremarkable.

On examination, she had bilateral optic disc pallor L > R. Visual acuity was 6/18 on the right whilst she could only perceive finger movements with the left eye. Other cranial nerves and upper limbs were normal. She had spastic paraparesis (power 4/5) with a sensory level of D5 and bladder incontinence.

MRI of the brain was normal but the MRI of the cord showed a contrast-enhancing inflammatory lesion extending > 3 vertebral segments in the thoracic cord (Figure 1). CSF showed a mild lymphocytic pleocytosis with 18 lymphocytes and 42 mg/dl of protein. Routine haematological and biochemical investigations including inflammatory markers were normal whilst the vasculitic and viral screens were negative. Aquaporin-4 antibodies were detected in serum.

A diagnosis of NMO was made. She was treated with intravenous methyl prednisolone pulses followed by a combination of oral prednisolone and azathioprine. Her symptoms gradually improved apart for residual spastic weakness in her lower limbs. She subsequently defaulted treatment and relapsed in February 2009 with a longitudinally extensive transverse myelitis around D8 that improved with intravenous steroid pulses. She has since been on oral prednisolone and azathioprine and has not had any relapses as of May 2012.

[1]*Department of Clinical Medicine, University of Colombo, Sri Lanka,* [2]*Institute of Neurology, National Hospital of Sri Lanka, Colombo.*

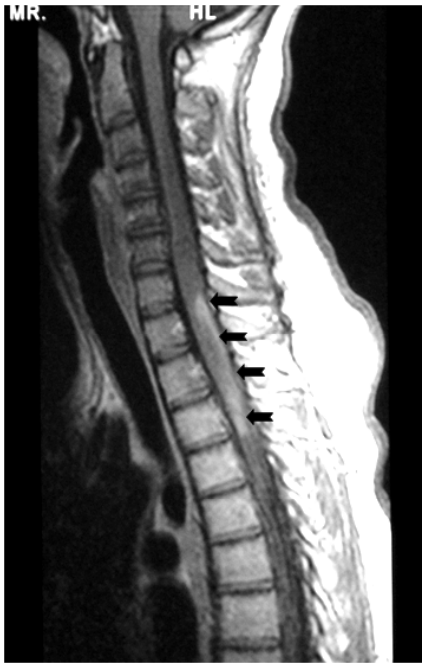

Figure 1. Satgital T1-weighted MR image of the spine shows a longitudinally-extensive, expansile lesion in the upper thoracic cord with enhancement following intravenous gadolinium administration (arrows).

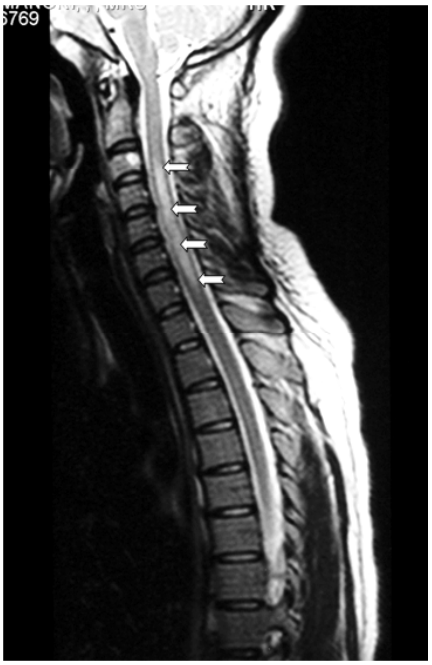

Figure 2. Satgital T2-weighted MR image of the spine shows a longitudinally-extensive, centrally located lesion in the cervical cord (arrows).

Patient B

A 28-year old housewife presented in January 2008 with paraparesis. Five weeks earlier, she has had retrobulbar neuritis in the right eye that completely resolved within 3 weeks following treatment with intravenous methylprednisolone. Her past medical history was unremarkable.

Examination revealed right-sided optic disc pallor. Visual acuity was 6/18 on right and 6/6 on left. She had spastic paraparesis (power 4/5) with a sensory level at D2 and sphincter involvement. Rest of the neurological examination was normal.

MRI of the brain was normal but the MRI of the cord showed a contrast-enhancing inflammatory lesion extending > 3 vertebral segments in the cervical cord (Figure 2). Visual evoked potential showed a delay in P100 in the right eye. CSF showed 5 PNL, 54 lymphocytes and 53 mg/dl of protein. Routine haematological and biochemical investigations including inflammatory markers were normal whilst the vasculitic and viral screens were negative. Aquaporin-4 antibodies were not detectable in her serum.

She was treated with intravenous methylprednisolone pulses followed by a two-week taper of oral prednisolone. She was not prescribed long term immunosuppressive therapy. She made a complete recovery and has not had any recurrences up to May 2012.

Discussion

Eighty- to ninety-percent of patients with NMO have relapsing episodes of optic neuritis (ON) and myelitis, rather than a monophasic course[3]. Frequent and severe relapses lead to incremental disability with more than 50% of patients becoming blind in one or both eyes or dependent for ambulation within 5 years of disease onset[3]. This is in contrast to MS in which relapses recover almost completely and patients accrue disability only during the later, secondary progressive phase of MS. Furthermore, NMO do not benefit with immunomodulatory therapies effective for MS (eg, interferon beta, glatiramer acetate)[4], but long-term immunosuppression has shown to reduce relapses. Hence, establishing a diagnosis of NMO has both therapeutic and prognostic implications.

According to the revised criteria, the presence of NMO-IgG is not essential for the diagnosis of NMO. Both patients in this report fulfill the criteria for diagnosis although NMO-IgG was negative in patient B. Interestingly, in the four-year follow-up period, patient B did not have any relapses despite not being on long-term immunosuppressive therapy whilst patient A followed the typical course described for NMO. Patients with nearly simultaneous ON and myelitis as in patient B are less likely to relapse than patients who have index events that are several months apart[5]. Nonetheless, it must be noted that ON and or longitudinally-extensive myelitis can occur secondary to infections such as varicella, EBV,

CMV, dengue, mycoplasma, *Treponema pallidum* and tuberculosis[6]. These 'para-infectious NMO syndromes' are often monophasic and negative for aquaporin-4 antibodies[6].

Observational studies suggest that maintenance immunosuppression is associated with reduced relapses and better clinical outcomes. Given that para-infectious, monophasic-NMO syndromes are likely to be common in regions where infections are prevalent, whether all patients diagnosed with NMO should be prescribed long-term immunosuppression at first presentation needs consideration. Patient B did not experience any relapses. However, relapses in NMO can happen decades after the index case[5] and a benign form of NMO cannot be clearly defined. Seropositivity of NMO-IgG is a useful marker to predict a higher risk of relapse[5,7] and to commence maintenance immunosuppression, but there are reports of relapsing seronegative-NMO. Currently maintenance immunosuppression is recommended when a diagnosis of NMO is established. Further studies on clinical, neuroimaging and serological predictors of outcome and randomized trials of long-term immunosuppression are required to develop discerning guidelines for long-term immunosuppression in NMO. Patient B understandably refuses long-term immunosuppression unless a relapse occurs given her good health since the presenting episode.

Acknowledgement

Professor Angela Vincent, Neurosciences Group, University of Oxford, United Kingdom for kindly performing the NMO-IgG assays.

References

1. Lennon VA, Wingerchuk DM, Kryzer TJ, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004; **364**: 2106-12.
2. Wingerchuk DM, Lennon VA, Pittock SJ, et al. Revised diagnostic criteria for neuromyelitis optica. *Neurology* 2006; 66: 1485-9.
3. Wingerchuk DM, Hogancamp WF, O'Brien PC, et al. The clinical course of neuromyelitis optica (Devic's syndrome). *Neurology* 1999; **53**: 1107-14.
4. Wingerchuk DM, Weinshenker BG. Neuromyelitis Optica. *Current Treatment Options in Neurology* 2005; **7**: 173-82.
5. Wingerchuk DM, Weinshenker BG. Neuromyelitis optica: clinical predictors of a relapsing course and survival. *Neurology* 2003; **60**: 848-53.
6. Sellner J, Hemmer B, Muhlau M. The clinical spectrum and immunobiology of parainfectious neuromyelitis optica syndromes. *Journal of Autoimmunity* 2010; **34**: 371-79.
7. Matiello M, Lennon VA, Jacob A, et al. NMO-IgG predicts the outcome of recurrent optic neuritis. *Neurology* 2008; **70**: 2197-200.