

CASE REPORT

Neuromyelitis optica (NMO) and autoimmune thyroiditis

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Abstract

Neuromyelitis optica (NMO or Devic's syndrome) is a rare demyelinating disease of the CNS that predominantly affects the spinal cord and optic nerves and shares many clinical and radiological features with multiple sclerosis (MS). The association of NMO with autoimmune thyroiditis has been reported very rarely. Early differentiation between NMO and MS is very important because they have different natural courses and treatment regimens. We report a case regarding a 53-year-old woman who was admitted initially with hiccups and paraesthesias, but was not evaluated during first two episodes and presented with severe progression of NMO. Patient was found to have autoimmune thyroiditis with lymphocytic infiltration of thyroid which progressed to hypothyroidism. NMO was diagnosed with seropositivity for NMO-IgG and longitudinally extensive spinal cord lesions (three or more spinal segments). Patient poorly responded to treatment due to the lack of early diagnosis and aggressive immunosuppressant therapy.

INTRODUCTION

Neuromyelitis optica (NMO; Devic's syndrome) is a demyelinating disease of the CNS that predominantly affects the spinal cord and optic nerves and shares many clinical and radiological features with multiple sclerosis (MS) [1–3]. NMO is considered as a disease entity after the discovery of a novel, pathogenic auto-antibody (NMO-IgG or AQP4-Ab) in 2004 [4, 5].

NMO is a rare syndrome constituting <1% of demyelinating disease [6, 7]. Clinical, MRI and spinal fluid features from several case series are illustrated in Table 1 (<http://www.medscape.com/view>

[article/446182_4](http://www.medscape.com/viewarticle/446182_4)). Prevalence estimates of prevalence of NMO in Japan is ~14 per 1 000 000 [8], and of northwest England is ~4 per 1 000 000 with a female-to-male ratio of 3 : 1. The Mayo Clinic proposed a revised set of criteria for diagnosis in 2006 (Table 2).

Hashimoto's thyroiditis (chronic lymphocytic thyroiditis) is an autoimmune disease characterized by cell- and antibody-mediated immune processes against thyroid gland. Diagnosis requires observations of lymphocyte infiltration of thyroid and autoantibodies against thyroid peroxidase, thyroglobulin and thyroid hormone-stimulating receptor.

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Table 1: Clinical, MRI and spinal fluid features from several case series

Features	Number (proportion)
Women/men	87/36 (2.3 : 1)
Average age at onset	37
Monophasic/polyphasic	72/40 (1.8 : 1)
Optic neuritis presentation	50 (45%)
Transverse myelitis presentation	43 (38%)
Combined optic neuritis/transverse myelitis presentation	19 (17%)
Autoimmune disease/antibodies	28/104 (27%)
Antecedent infection	22/91 (24%)
Normal brain (MRI)	48/63 (76%)
Abnormal spinal cord (MRI)	55/58 (95%)
Cerebrospinal fluid (CSF) pleocytosis	63/85 (74%)
>50 cells/mm ³	27/84 (32%)
CSF polymorphonucleocytes	34/67 (51%)
CSF oligoclonal bands	23/77 (30%)

Table 2: Mayo clinic criteria for NMO

Absolute criteria:	
1. Optic neuritis	
2. Acute myelitis	
Supportive criteria:	
1. Brain MRI not meeting criteria for MS at disease onset	
2. Spinal cord MRI with contiguous T ₂ -weighted signal abnormality extending over three or more vertebral segments, indicating a relatively large lesion in the spinal cord	
3. NMO-IgG-seropositive status (The NMO-IgG test checks the existence of antibodies against the aquaporin-4 antigen.)	

CASE REPORT

A 53-year-old woman was admitted in a local hospital on November 2013 with complaints of hiccups, vomiting and paraesthesias of left upper and lower limb from 5 days. Patient completely recovered in a period of 30 days. Only thyroid profile was abnormal, which was suggestive of hyperthyroidism for which she took no medication (Table 3). In July 2014, patient was admitted with complaints of weakness of bilateral lower limbs and left upper limb along with band-like sensation around the chest at the T4 level. Patient also complained of difficulty in seeing distant objects in right eye. An MRI scan of brain and spine revealed lesion in the spinal cord at the levels of C2–C5, enhancing signal was seen at the levels of C3–C5.

Patient was given injection methylprednisolone 1 g intravenous for a period of 5 days and oral steroids for 4 weeks. However, the thyroid function tests were normal during that episode (Table 3). In February 2015, patient was admitted with fever, cough with expectoration, breathlessness, paraesthesias and diminished vision. She was diagnosed with left lower lobe pneumonia and treated. In March 2015, patient was brought to emergency room with complaints of bilateral lower limb weakness, bilateral upper limb weakness (distal > proximal) and band-like sensation over the chest and hiccups. Mini-Mental Status Examination (MMSE) was 28/30 (Table 4). Vision was diminished to counting fingers in right eye. Other cranial nerves were normal.

Hypertonia was noted in all limbs. Power was 3/5 bilaterally proximally and 2/5 distally in upper limbs. Lower limb power was 0/5 on admission but improved to 1/5 in 15 days. Upper

Table 3: Thyroid profile

Investigation	November 2013	June 2014	March 2015	Normal range
T3 (ng/dl)	300	100	50	75–200
T4 (µg/dl)	20	7.1	1.3	4.5–11.5
TSH (µU/ml)	2	3.2	10.4	2.3–4.0

Table 4: MMSE of patient

Category	Possible points	Description
Orientation to time	5	From broadest to most narrow. Orientation to time has been correlated with future decline.
Orientation to place	5	From broadest to most narrow. This is sometimes narrowed down to streets and sometimes to floor.
Registration	3	Repeating named prompts
Attention and calculation	5	Serial sevens or spelling 'world' backwards. It has been suggested that serial sevens may be more appropriate in a population where English is not the first language.
Recall	3	Registration recall
Language	2	Naming a pencil and a watch
Repetition	1	Speaking back a phrase
Complex commands	4	Varies. Can involve drawing figure shown.

limb reflexes were 2+ and knee and ankle reflexes were 3+. Babinski's reflex was present bilaterally. Loss of joint position and vibration sense till bilateral anterior superior iliac spine was revealed. Abdominal reflex was absent.

Antibodies to HSV1, HSV2, CMV, EBV, HBV, VZV, HCV and HIV in serum and cerebrospinal fluid, as well as sarcoidosis and tumor markers in serum, revealed no abnormality. Polymerase chain reaction in CSF for HSV1 and HSV2 was negative. Cerebrospinal fluid analysis demonstrated no oligoclonal bands. Immunological tests for ANA titer were 1 : 320; tests for anti-extractable nuclear antigen, anti-dsDNA, anti-cardiolipin, anti-β2GPI, lupus cells and cryoglobulins were negative. A thyroid profile was suggestive of hypothyroidism (Table 3). Laboratory studies confirmed the presence of antithyroid antibodies (Table 5).

MRI brain and spine revealed (i) hyperintensity in the cervical cord at lower half of C6 and upper half of C7 vertebral body (Figs 1 and 2), (ii) hyperintensity in the thoracic cord at the level of T7, T8 and T9 (Figs 3 and 4) and (iii) hyperintensity in the right optic nerve head (Fig. 5). Fine needle aspiration of thyroid confirmed lymphocytic infiltration (Figs 6 and 7). Serology was positive for NMO-IgG. Patient was started on methylprednisolone 1 g/day for 5 days and azathioprine (2.5–3 mg/kg/daily). Patient showed marginal improvement in motor symptoms. Patient was started on thyroxine 25 µg and later increased to 75 µg.

DISCUSSION

Devic's disease is a severe idiopathic immune-mediated inflammatory demyelinating disease that predominantly involves the spinal cord and optic nerves. The cardinal clinical features are longitudinally extensive transverse myelitis and optic neuritis.

Table 5: Laboratory studies

Investigation	Values	Normal range
Hemoglobin (g/dl)	11	12–16
Leukocyte count (cells/ μ l)	7000	4500–10 000
Platelet count (cells/ μ l)	200 000	150 000–400 000
Aspartate aminotransferase (U/l)	30	0–37
Alanine aminotransferase (U/l)	40	0–34
Albumin (g/dl)	3.9	3.5–5.2
Globulin (g/dl)	3.0	2.5–3.0
Thyroid-stimulating hormone (μ U/ml)	10.4	2.3–4.0
Free thyroxine (T4)	0.5 ng/ml	0.8–2.8 ng/dl
Antithyroglobulin antibody (IU/ml)	155	<10.0
Antithyroid peroxidase (IU/ml)	805	<10.0

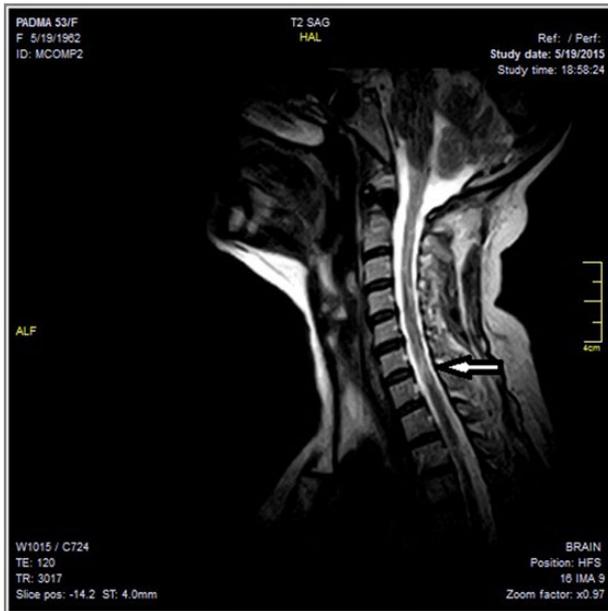


Figure 1: MRI cervical spine showing hyperintensity at the level of C6–C7.



Figure 2: MRI cervical spine showing hyperintensity at the level of C6–C7.

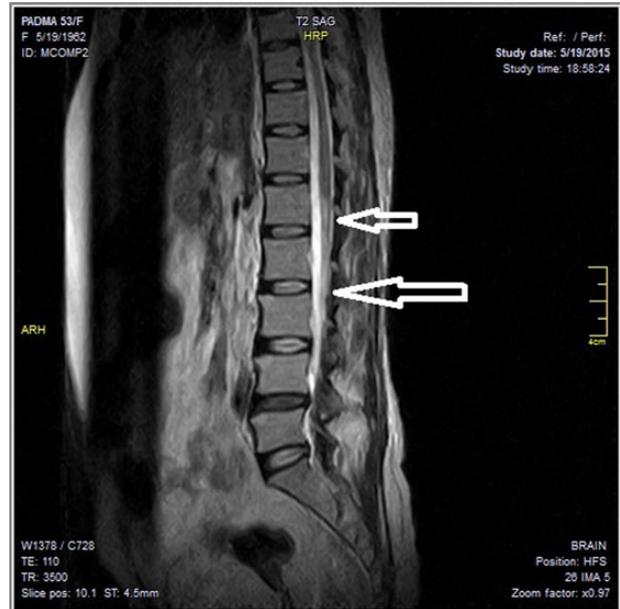


Figure 3: MRI spine showing hyperintensity at the level of T7, T8 and T9.

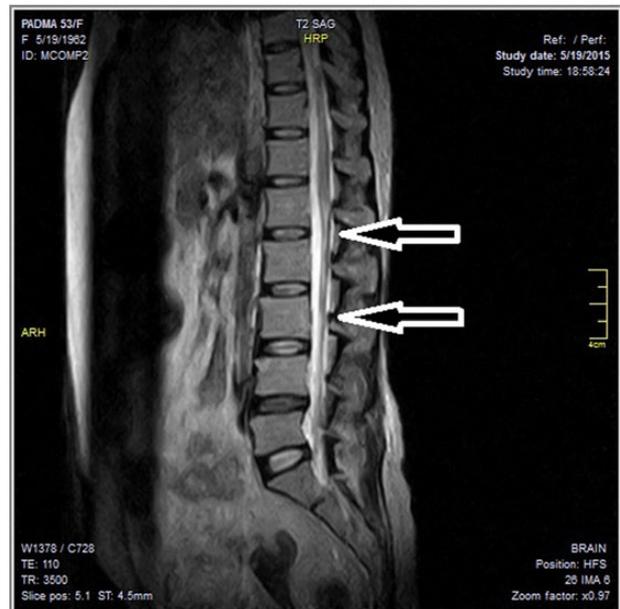


Figure 4: MRI spine showing hyperintensity at the level of T7, T8 and T9.

Several differences exist in the characteristics and outcomes of patients with the monophasic and relapsing forms (Table 6).

The NMO-IgG autoantibody is highly specific (91%; 85–99%) and sensitive (73%; 58–76%), and has less common occurrence in MS. Its target antigen is AQP4, a richly distributed water-pump channel in the central spinal cord, hypothalamus, periventricular area and periaqueductal area. Spinal cord histopathology in NMO found loss of AQP4 in acute inflammatory lesions surrounding immunoglobulin and complement-deposited hyalinized small vessels.

Intravenous methylprednisolone 1 g daily for 5 days is the first-line therapy. Nakamura et al. [9] suggested a neuroprotective effect of high-dose steroids when given within first 2–3 days after

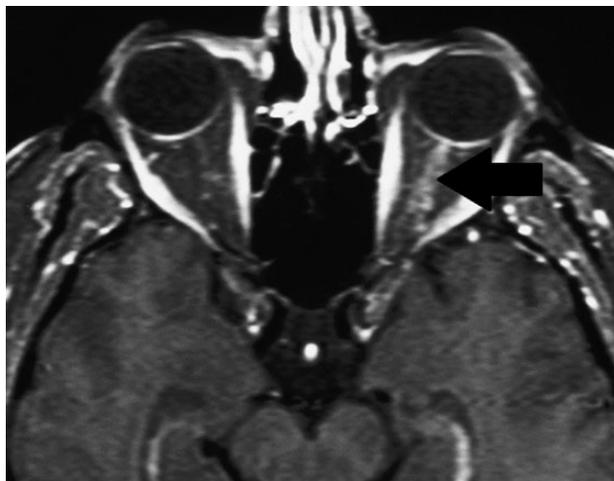


Figure 5: MRI brain showing hyperintensity in the right optic nerve head.

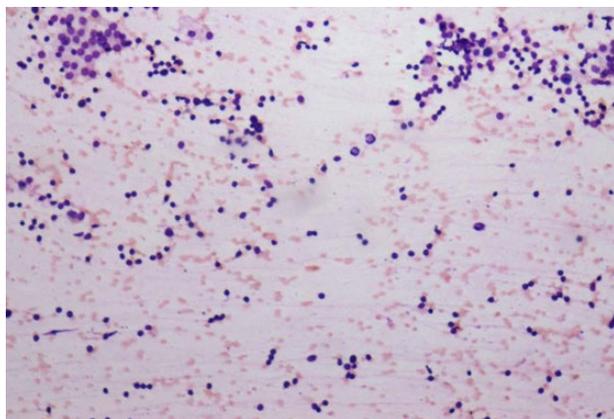


Figure 6: FNAC showing lymphocytic infiltration of thyroid.

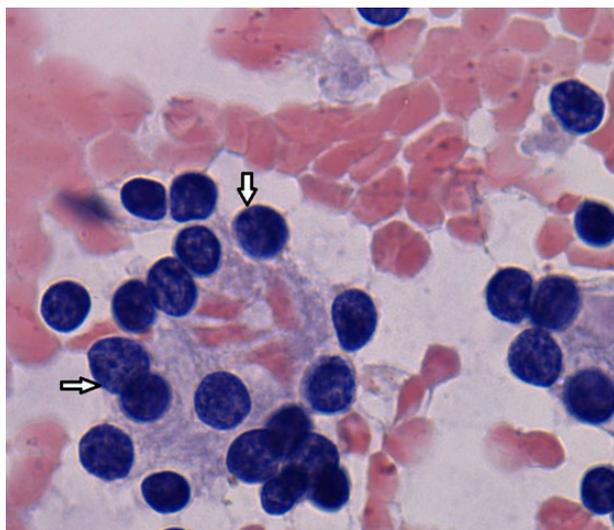


Figure 7: FNAC showing lymphocytic infiltration of thyroid.

onset of optic neuritis. Many severe NMO attacks respond inadequately to corticosteroid treatment. Plasma exchange and intravenous immunoglobulin were also tried for acute attacks.

Table 6: Characteristics of monophasic and relapsing NMO

Characteristics	Monophasic	Relapsing
Frequency (%)	Less common (20)	More common (80)
Age of onset (year; median)	29	39
Sex: ratio of females (%)	50	80–90
History of autoimmune disease	Uncommon	~50%
Optic neuritis/myelitis (%)	48	90
Bilateral optic neuritis (%)	17	8
Simultaneous optic neuritis + myelitis (%)	31	0
Severity at nadir	More severe	Less severe
Respiratory failure 5 years	Rare	Approximately one-third
Mortality rate (%)	10	32
Recovery	Good	Fair

Interferons and other MS therapies, such as natalizumab and fingolimod, may aggravate NMO as reported by some studies such as Min *et al.* [10] and Jacob *et al.* [11]. Current options are azathioprine, mycophenolate mofetil, rituximab, mitoxantrone, cyclophosphamide, methotrexate, intravenous immunoglobulin and prednisone. Rituximab (anti-CD20) has a rapid onset of action (full activity in 2 weeks) and less frequent dosing (two infusions every 6 months). In the absence of comparative controlled trials, no single drug is the best for every patient with NMO.

The association of NMO with autoimmune thyroiditis has been reported very rarely [12], even though autoimmune diseases occur frequently in patients with other autoimmune diseases. Steady progression of autoimmune thyroiditis from hyperthyroidism to hypothyroidism was noted over a period of 2 years. Early diagnosis and aggressive immunosuppressive treatment is of paramount importance in management of NMO. However, its role in autoimmune thyroiditis is not clearly known. IgG-NMO testing is very useful in diagnosis even if clinical and para-clinical autoimmune indices are available. Long-term immunosuppressive treatment is required to prevent relapses. Guarantor: S. Sreenivasa Rao.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

- Jarius S, Ruprecht K, Wildemann B, Kuempfel T, Ringelstein M, Geis C, *et al.* Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: a multi-centre study of 175 patients. *J Neuroinflammation* 2012;9:14.
- Wingerchuk DM, Hogancamp WF, O'Brien PC, Weinshenker BG. The clinical course of neuromyelitis optica (Devic's syndrome). *Neurology* 1999;53:1107–14.
- Kitley J, Leite MI, Nakashima I, Waters P, McNeillis B, Brown R, *et al.* Prognostic factors and disease course in aquaporin-4 antibody-positive patients with neuromyelitis optica spectrum disorder from the United Kingdom and Japan. *Brain* 2012;135:1834–49.
- Lennon VA, Kryzer TJ, Pittock SJ, Verkman AS, Hinson SR. IgG marker of optic-spinal multiple sclerosis binds to the aquaporin-4 water channel. *J Exp Med* 2005;202:473–7.

5. Lennon VA, Wingerchuk DM, Kryzer TJ, Pittock SJ, Lucchinetti CF, Fujihara K, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004;**364**:2106–12.
6. Shibasaki H, McDonald WI, Kuroiwa Y. Racial modification of clinical picture of multiple sclerosis: comparison between British and Japanese patients. *J Neurol Sci* 1981;**49**:253–71.
7. Pálffy G. Multiple sclerosis in Hungary, including the Gypsy. In: Kuroiwa Y, Kurland LT (eds). *Multiple Sclerosis, East and West*. Fukuoka: Kyushu University Press, 1982, 149–58.
8. Kira JI. Multiple sclerosis in the Japanese population. *Lancet Neurol* 2003;**2**:117–27.
9. Nakamura M, Nakazawa T, Doi H, Hariya T, Omodaka K, Misu T, et al. Early high-dose intravenous methylprednisolone is effective in preserving retinal nerve fiber layer thickness in patients with neuromyelitis optica. *Graefes Arch Clin Exp Ophthalmol* 2010;**248**:1777–85.
10. Min JH, Kim BJ, Lee KH. Development of extensive brain lesions following fingolimod (FTY720) treatment in a patient with neuromyelitis optica spectrum disorder. *Mult Scler* 2012;**18**:113–5.
11. Jacob A, Hutchinson M, Elson L, Kelly S, Ali R, Saukans I, et al. Does natalizumab therapy worsen neuromyelitis optica? *Neurology* 2012;**79**:1065–6.
12. Sergio P, Mariana B, Alberto O, Claudia U, Oscar R, Pablo M, et al. Association of neuromyelitis optic (NMO) with autoimmune disorders: report of two cases and review of the literature. *Clin Rheumatol* 2010;**29**:1335–8.