

The seroprevalence of NMO-IgG in Singapore: A pilot study

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Background: Multiple sclerosis (MS) among Asians is often characterised by severe and selective involvement of the optic nerve and spinal cord and is sometimes called “Asian” optic-spinal MS (OSMS). It is believed that “Asian” OSMS may be distinct from “Western” or classic MS. The frequency of NMO-IgG, a novel autoantibody which targets the water channel protein aquaporin-4, or anti-aquaporin-4 antibody in neuromyelitis optica (NMO) patients and Japanese OSMS patients is between 55.6 to 73% of cases.^{1,2} This raises the possibility that “Asian” OSMS may be a form of NMO and quite distinct from MS. The seroprevalence of NMO-IgG among Singapore patients is unknown.

Objective: To determine the frequency of NMO-IgG autoantibody in Singapore patients with MS, transverse myelitis or optic neuritis.

Methods: We recruited 35 patients with MS or syndromes at high risk of developing the disorder and 20 additional control patients. Patients were divided into 6 groups:

- 1) NMO or OSMS: relapsing (n = 11), monophasic (n = 1)
- 2) Classic MS, or clinically isolated syndrome with high risk for conversion to MS (n = 13)
- 3) Transverse myelitis, single or recurrent (n = 5)
- 4) Optic neuritis, single or recurrent (n = 5)
- 5) Patients with miscellaneous neurological or autoimmune disorders: stroke (n = 1), Tolosa-Hunt syndrome (n = 1), myasthenia gravis (n = 1), idiopathic generalised epilepsy (n = 1), primary autonomic failure (n = 1), hyperthyroidism (n = 1), Type 1 diabetes mellitus (n = 1), rheumatoid arthritis (n = 2), systemic lupus erythematosus (n = 1)
- 6) Healthy controls (n = 10)

We obtained demographic and clinical information, including race, sex, age at onset, neurological symptoms and signs, history of autoimmunity, and recorded laboratory and imaging data. Serum NMO-IgG was detected by identifying the distinctive staining pattern in mouse cerebellum by indirect immunohistochemistry.¹ The study was approved by the institutional review boards of the National Neuroscience Institute and Tan Tock Seng Hospital.

Results: One of 11 patients with relapsing NMO/OSMS was positive for NMO-IgG (Figure 1), corresponding to a frequency of 9.1% (95% CI 0.5 – 37.7). One control patient was positive for NMO-IgG (hyperthyroidism; TSH receptor antibody positive) (Figure 2). The patient has not developed signs of optic neuritis, myelitis or other neurological symptoms in 2 years following the detection of NMO-IgG. No patients with classic MS, transverse myelitis, optic neuritis, other autoimmune or neurological diseases or healthy controls were NMO-IgG seropositive.

Conclusions: In this pilot study, the frequency of NMO-IgG among Singapore patients with NMO/OSMS is much lower than in published literature. The presence of NMO-IgG in a neurologically asymptomatic patient with autoimmune thyroid disease may represent a false positive or a link between anti-thyroid autoimmunity and a subgroup of NMO patients.

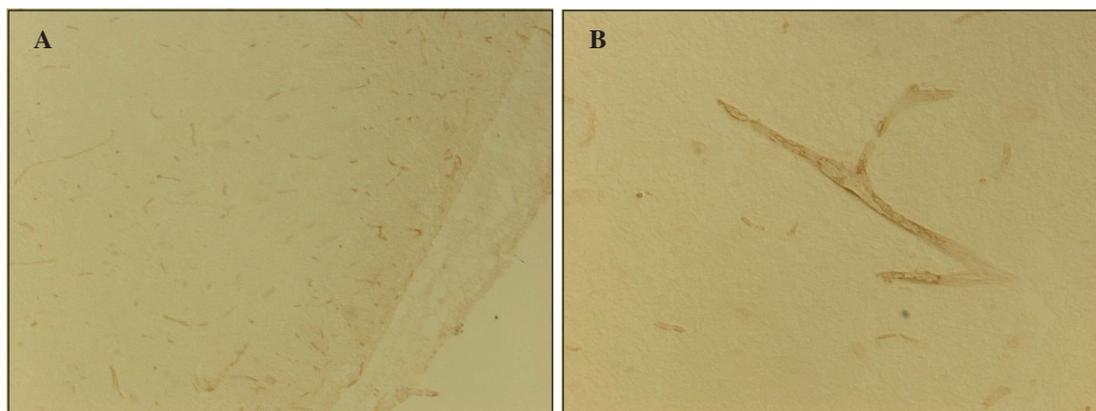


Figure 1. Immunoperoxidase pattern of bound NMO-IgG in mouse cerebellum showing linear staining of juxtaposed pial membranes of cerebellar cortex and their microvessels (A, mag 20x) and prominent microvessel staining in cerebellar molecular layer (B, mag 40x).

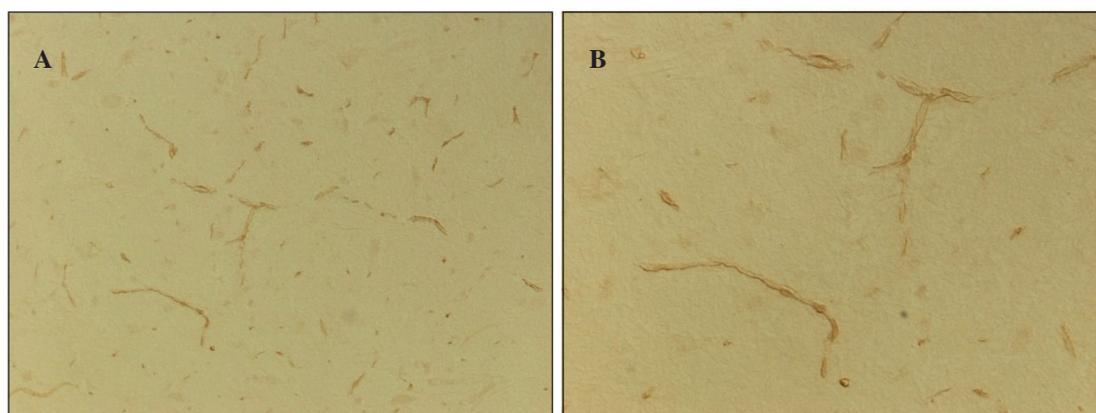


Figure 2. Immunoperoxidase pattern of bound NMO-IgG in mouse cerebellum of control patient with hyperthyroidism and was neurologically asymptomatic (A, mag 20x; B, mag 40x).

References

1. Lennon VA, Wingerchuk DM, Kryzer TJ, *et al.* A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004; 364(9451):2106-12.
2. Matsuoka T, Matsushita T, Kawano Y, *et al.* Heterogeneity of aquaporin-4 autoimmunity and spinal cord lesions in multiple sclerosis in Japanese. *Brain* 2007; 130(5):1206-23.