LETTER

Seroprevalence and clinical phenotype of MOG-IgG-associated disorders in Sri Lanka

INTRODUCTION

Antibodies targeting myelin oligodendrocyte glycoprotein immunoglobulin (MOG-IgG) detected by cell-based assays[1] are recognised biomarkers of a subgroup of central nervous system inflammatory demyelinating disorders (CNS IDDs) termed MOG-IgG-associated disorders (MOGAD).[2] Single episode and recurrent ON are the most common presentations of MOGAD followed by transverse myelitis (TM), acute disseminated encephalomyelitis (ADEM) and brainstem syndromes or combination of such manifestations.[1 3 4]

Population-based studies have demonstrated, in aquaporin-4 immunoglobulin (AQP4-IgG)-positive neuromyelitis optica spectrum disorders (NMOSD), that ethnicity plays an important role in determining risk for NMOSD. Afro-Carribeans from Martinique have a threefold higher prevalence of NMOSD compared with Caucasians in Olmsted County, Minnesota.[5]

It remains unclear whether ethnicity is a risk factor for the development of MOGAD. Sri Lanka located in South Asia has predominant Sinhalese ethnicity. The AQP4-IgG and MOG-IgG serostatus of CNS IDDs in these populations have not been previously determined.

PATIENTS AND METHODS

Serum samples of 726 consecutive Sri Lankan patients undergoing evaluation for suspected IDDs at the National Hospital of Sri Lanka, a tertiary care centre, between January 2013 and March 2018 were tested for AQP4-IgG and MOG-IgG by Clinical Laboratory Improvement Amendments approved flow cytometric assays. Infectious, granulomatous (eg, sarcoidosis) and neoplastic aetiologies were excluded.

MOG-IgG1 serostatus was defined as persistent when seropositivity confirmed at or more than 6 months after the onset attack. Clinical information was available for 550 patients (113 children and 437 adults).

STATISTICAL ANALYSIS

SAS V.9.4 and JMP V.13 were used. χ^2 or Fisher's exact tests were applied to compare categorical variables. Continuous data for two patient groups classified by serostatus were analysed by Student's t and rank sum tests. $P<0.05$ was deemed statistically significant.

RESULTS

Of sera from 726 consecutive patients undergoing evaluation for suspected IDDs at the National Hospital of Sri Lanka, 126 (17.4%) tested positive for MOG-IgG1. Ethnicities were 107 (85%) Sinhalese, 10 (8%) Muslim and 9 (7%) Tamil. For 550 patients with clinical data available, the frequency of MOG-IgG1 seropositivity was higher in paediatric (38.9%; 44 of 113) than adult (18.7%; 82 of 437). Only 36 (5%) tested positive for AQP4-IgG. None were positive for both. Overall, 24% of patients harboured a glial autoantibody biomarker.

Table 1 Demographic and clinical features of 126 MOG-IgG1-positive Sri Lankan patients

	MOG-IgG1-positive patients, N (%)		
Characteristics	Total N=126*	Paediatric N=44†	Adult N=82†
Age at onset, years, median (range)	26 (3–68)	9 (3–18)	33.5 (19–68)
Sex, female	70 (56)	22 (50)	48 (58)
Symptoms at onset			
Optic neuritis (alone)	64 (51)	17 (39)	47 (57)
Transverse myelitis	29 (23)	7 (16)	22 (28)
ADEM	11 (9)	11 (25)	0 (0)
Optic neuritis and transverse myelitis	8 (6)	2 (4)	6 (7)
Optic neuritis and ADEM	13 (10)	7 (16)	6 (7)
Optic neuritis and intractable hiccups	1 (1)	0 (0)	1 (1)
Clinical phenotype at last follow-up			
Optic neuritis (single or relapsing)	58 (46)	16 (36)	42 (52)
Transverse myelitis	24 (19)	4 (10)	20 (24)
ADEM	12 (10)	12 (27)	0 (0)
NMOSD	32 (25)	12 (27)	20 (24)
Duration of follow-up, years, median (range)	4 (0.12–20)	3 (0.5–18)	3 (0.25–20)
Number of patients with relapsing course	43 (34)	15 (34)	28 (34)
Median number of relapse (range)	1 (1–9)	1 (1–8)	1 (1–9)
Acute treatments‡	115 (100)	44 (100)	82 (100)
Long-term immunotherapy§	55 (50)	18 (45)	38 (53)

The final diagnoses for the 355 MOG-IgG1 seronegative adult cases were in decreasing order of frequency: optic neuritis (133), transverse myelitis (76), MS (45), AQP4-IgG-positive NMOSD (24), CRION (12), ADEM (4) and other (61).

*Available MRI spine data were available for 33 patients, who presented with transverse myelitis alone and optic neuritis with transverse myelitis. A total of 14 of the 126 patients were initially diagnosed as MS but subsequently tested positive for MOG-IgG.

†Clinical data were available for 550 patients: The final diagnoses for the 69 MOG-IgG1 seronegative paediatric cases were in decreasing order of frequency: transverse myelitis (24), optic neuritis (17), ADEM (8), MS (6), AQP4-IgG-positive NMOSD (4) CRION (1) and other (9).

‡Acute treatments included intravenous methylprednisolone, plasma exchange, immunoglobulin G and combination (data available for 115 patients).

§Long-term immunotherapy included azathioprine, prednisolone, mycophenolate mofetil and combination (data available for 110 patients).

ADEM, acute disseminated encephalomyelitis; CRION, chronic relapsing inflammatory optic neuropathy; MOG, myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorders.

The median age of onset for MOGAD was 26 years (range 3–68), younger compared with AQP4-IgG-positive NMOSD patients (median 38 years (range 15–73), p<0.001). MOGAD had a lower likelihood of relapsing disease compared with AQP4-IgG-positive NMOSD cases (34% vs 64%, p<0.001). Duration of follow-up of MOGAD was 3.6 years (range 0.12–20) and AQP4-IgG-positive NMOSD was 6.67 years (range 0.67–13.67), p=0.37. The preponderance of female sex was also less (56% vs 86%, p<0.01) (table 1).

ON at presentation was observed in 88 of 126 (62%) patients and occurred either in isolation (64, unilateral 17 and bilateral 47) or in combination with other demyelinating syndromes (22: ADEM 13; TM 8 and area postrema syndrome 1). About 19% had recurrent ON. For patients presenting with isolated ON, 90% had normal MRI brain outside of the optic nerve.

Of 126 MOGAD cases, only 32 (25%) fulfilled 2015 NMOSD criteria. The duration of disease of these patients was not different from those not fulfilling such criteria (p=0.36).

ADEM at presentation was observed in 24 of 126 (19%) patients and occurred either in isolation (13, 54%) or in combination with ON (ADEM/ON 11, 46%); 18 (75%) of these ADEM cases were children representing 46% (18/39) of all MOGAD children. The adult-onset ADEM cases represent only 6.9% of adult MOGAD patients (6/87).

Thirty-seven patients (29%) presented with TM: 29 (78%) in isolation and 8 (22%) in combination with ON. Just over half (57%) of all TM cases had longitudinally extensive TM on MRI: 6 of 9 (67%) paediatric and 15 of 28 (54%) adult cases.

A total of 43 out of the 121 (34%) had relapsing disease. The duration of follow-up was longer in the relapsers (8 years, range 0.5–20) compared with those monophasic (2 years, range 0.25–5) at last follow-up (p<0.001). The median time from the first to second attack was 1 year (range 0.25–13 years). Samples from >6 months postonset (considered evidence of persistent seropositivity) were available in 17 patients: 13 patients (76%) had greater than one attack after median follow-up of 7 years (range 3–17) while 4 patients (24%) remained monophasic after median follow-up of 1 year (range 1–2), p=0.011.

Visual outcome data were available for 59 of 86 MOG-IgG1-positive ON cases with median duration of follow-up of 4 years (range 0.12–20.0): 44 (74%) normal, 8 (14%) mild visual impairment and 7 (12%) severe visual impairment or blind in one eye. All attacks were treated with steroids or immunoglobulin G or plasma exchange. Maintenance immunosuppressant medications (prednisolone, azathioprine, mycophenolate mofetil or, combinations thereof) were used in half of the MOGAD cases (table 1). Mobility data were available for 118 patients with median duration of follow-up of 3 years (range 0.25–20 years): 111 (94%) expanded disability status scale (EDSS)<6, 6 (5%) EDSS 6–8.5 and 1 (1%) had EDSS 10.

DISCUSSION

In this clinic-based study of Sri Lankan patients presenting for evaluation for suspected IDDs, MOG-IgG was detected in one of six (17%) patients and was 3.5 times more common than AQP4-IgG (5%). The MOGAD demographics and phenotypic spectrum in Sri Lankan patients were similar to other reported cohorts.[1 3 4] Age of onset of MOGAD was not different from previous reports.[1 3 4] Only 25% of MOGAD fulfilled 2015 NMOSD criteria. Persistent MOG-IgG seropositivity predicted a relapsing course, though the findings in this study are limited by the shorter disease duration in the monophasic cases.

Most MOGAD patients (93%) were able to walk independently and 58% had normal vision at last follow-up. Only 8% were blind in one eye and none were blind in both. Such favourable visual outcomes are consistent with other reports.[1 3 4]

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Competing interests EPF is a principal investigator in a randomized placebo-controlled clinical trial of inebilizumab (a CD19 inhibitor) in neuromyelitis optica spectrum disorders funded by MedImmune/Viela Bio. SJP is a named inventor on filed patents that relate to functional AQP4/NMO-IgG assays and NMO-IgG as a cancer marker; consulted for Alexion and MedImmune; and received research support from Grifols, MedImmune and Alexion. All compensation for consulting activities is paid directly to Mayo Clinic.

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