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Neuromyelitis optica relapses: Race and rate, immunosuppression and impairment

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ABSTRACT

Objective: Neuromyelitis optica (NMO) is a rare antibody-mediated CNS disease characterised by disabling relapses leading to high morbidity and mortality. Understanding relapse activity and severity is important for treatment decisions and clinical trial design. We assessed (1) whether clinical and demographic factors associate with different relapse rates and (2) the relative impact of immunosuppressive treatments on relapse rates and on attack-related residual disability.

Methods: Clinical, demographic and treatment data were prospectively collected from 79 consecutive aquaporin 4 antibody positive patients seen in the nationally commissioned Oxford NMO service. The influence of clinical features on annualised relapse rates (using multiple regression) and the effect of immunosuppression on relapse-associated residual disability for transverse myelitis and optic neuritis attacks (using a mixed effect model) were analysed.

Results: The mean annualised relapse rate was 0.93. Relapse rates were significantly higher in Afro-Caribbeans, children and in those of shorter disease duration. Relapse rates reduced on treatment (from 0.87 to 0.42). Delay to first treatment did not influence eventual on-treatment relapse rate. Immunosuppressive treatment significantly reduced the residual disability from ON ($p < 0.01$), and TM ($p = 0.029$) attacks.

Conclusions: Relapse rates in NMO are influenced by multiple factors, including age, ethnicity and disease duration. Current immunosuppressive treatments reduce but do not abolish relapses, however, they appear to additionally lessen the chronic disabling effect of a relapse.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is a rare inflammatory condition with a predilection for the optic nerve and spinal cord, and is associated with specific antibodies to aquaporin-4 water channels (AQP4Abs) (Wingerchuk et al., 2006). Unlike multiple sclerosis, relapses are the sole cause of disability and, due to their severity, cause significant morbidity and mortality (Wingerchuk et al., 2007). Detailed published attack data is limited. The majority of patients are treated with long-term immunosuppression in the absence of randomised controlled trial data (Kimbrough et al., 2012). Designing new treatment trials requires accurate attack data and a better understanding of the factors influencing attacks.

The study population is Oxford's UK-wide nationally commissioned cohort. Because AQP4Ab negative NMOSD comprise a heterogeneous group of diseases (Bernard-Valnet et al., 2015), analysis was restricted to AQP4Ab positive patients only.

We sought to determine (a) whether clinical and demographic factors associate with different attack rates, and (b) the impact of immunosuppressant treatments (IST) on relapses.

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2. Methodology

2.1. Patients

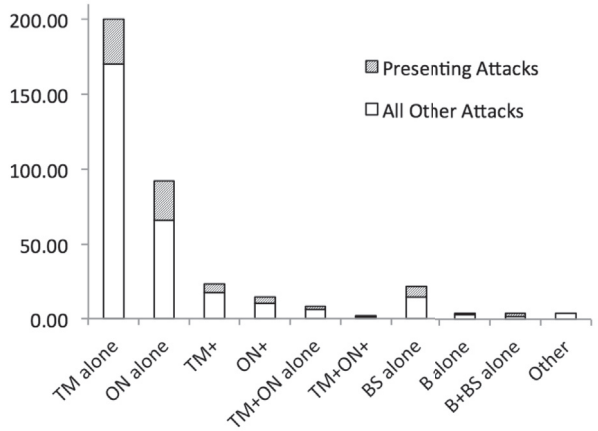
All 79 AQP4Ab positive NMOSD patients seen as part of the national NMO clinic up until April 2014 consented for their data to be prospectively collected and held on a database (NRES ref. 10/H0606/56). Data collected included gender, age of onset, ethnicity, onset attack phenotype (transverse myelitis (TM), Optic neuritis (ON), TM and ON, attacks with brain and or brainstem involvement), visual acuities and the EDMUS grading scale (a validated simplified EDSS measure using only whole integer scores (Amato et al., 2004)).

2.2. Statistical analysis

Comparisons of mean onset age, disease duration, time to diagnosis and time to treatment for different ethnic groups was performed using a one-way ANOVA. The proportion of females by ethnic group was compared using chi-squared.

Mean annualised relapse rates (ARRs) were calculated with onset attacks included. Contribution to the ARR was determined by multiple regression analysis with independent variables for gender, age of onset (< 18/adult), onset attack phenotype, ethnicity and disease duration, and interaction terms of the independent variables. The final model retained statistically significant factors for age of onset, ethnicity, disease duration and the ethnicity-by-age interaction.

	n	%
Total	**79**	
Female	68	86.1
Age <18 yrs at Onset	12	15.2
Ethnicity		
Caucasian	43	54.4
Afro-Caribbean	15	19.0
Asian	9	11.4
Mixed White/Asian	1	1.3
Mixed Other	1	1.3
Not Stated/Unknown	10	12.7
Attacks (onset)	372 (79)	
TM alone (onset)	200 (30)	53.8 (38.0)
ON alone (onset)	92 (26)	24.7 (32.9)
TM *plus** (onset)	23 (6)	6.2 (7.6)
ON *plus** (onset)	14 (4)	3.8 (5.1)
TM & ON alone (onset)	8 (2)	2.2 (2.5)
TM & ON *plus** (onset)	2 (1)	0.5 (1.3)
BS alone (onset)	21 (7)	5.6 (8.9)
Brain alone (onset)	4 (1)	1.1 (1.3)
Brain & BS alone (onset)	4 (2)	1.1 (2.5)
Other (onset)	4 (0)	1.1 (0)



TM, transverse myelitis; ON, optic neuritis (unilateral or bilateral); BS, brainstem; B, brain.

Fig. 1. Demographics and attack features. TM, transverse myelitis; ON, optic neuritis (unilateral or bilateral); BS, brainstem; B, brain. * '*plus*' indicates the listed attack-phenotype did not exist in isolation but included other relapse types as part of the disease *excepting* other phenotype combinations shown in the table. For example, 'TM *plus*' refers to TM with any combination of brain, BS or other attacks but does *not* include combinations with ON which are covered in the table by 'TM and ON alone' and 'TM and ON *plus*'.