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Psychiatric comorbidities and suicidality among patients with neuromyelitis optica spectrum disorders in Argentina

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ABSTRACT

Background: Neuromyelitis optica is a relapsing inflammatory, secondarily demyelinating astrocytopathy that most commonly affects the optic nerves and the spinal cord.

Objective: This study aimed to evaluate the psychopathological profile, presence of current depression, and suicidality in patients with neuromyelitis optica spectrum disorders (NMOSD) in an Argentinean cohort, and compare these parameters to those in patients with multiple sclerosis (MS) and in healthy controls (HCs).

Methods: Twenty patients with NMOSD, 18 with MS, and 20 healthy controls were included. The presence and grade of current depression were assessed using Beck's depression inventory (BDI), while psychiatric disease and suicidality were assessed using the Mini-International Neuropsychiatric Interview.

Results: The prevalence of psychiatric disease in the NMOSD group was 45%, significantly higher than in the MS group (16%, p = 0.06) and the HCs (5%, p = 0.008).

Recurrent major depressive disorder was the most frequent psychiatric disease and was diagnosed in four (20%) patients in the NMOSD group and in two (11%) patients in the MS group. In the NMOSD group, two (10%) patients were diagnosed with past manic episodes, one (5%) with current dysthymic disorder, one (5%) with lifetime psychotic disorder, and one (5%) with bulimia nervosa. One patient (5.5%) in the MS group and one in the HC (5%) were diagnosed with current generalized anxiety disorder.

Ten patients (50%) in the NMOSD group had current depressive symptoms versus five (28%) patients in the MS group (p = 0.16) and two (10%) in the HC group (p = 0.02). Six (30%) patients with NMOSD versus only one (5.5%) patient with MS had attempted suicide at least once, this difference was statistically significant (p = 0.05). Current suicide risk was high in patients with NMOSD (8, 40%) and moderate in patients with MS (4, 22%).

Conclusions: Our study shows that the prevalence of psychiatric comorbidities in patients with NMOSD is significantly higher than in patients with MS and healthy controls. Given the high frequency of suicidality, assessment of pertinent psychiatric disorders in such patients to optimize monitoring and comprehensive treatment is required.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is a unifying term for neuromyelitis optica (NMO) or Devic's disease and related syndromes. It is a relapsing inflammatory, secondarily demyelinating astrocytopathy that most commonly affects the optic nerves and the spinal cord. Discovery of the first antibody marker specific to NMO, and its reporting in 2004, was a major breakthrough and helped in the differential diagnosis with multiple sclerosis (MS); considering that, until a few years earlier, they were regarded as variants of the same disease (Lennon et al., 2004, 2005).

The 2015 international consensus diagnostic criteria for NMOSD by The International Panel for NMO Diagnosis (IPND) (Wingerchuk et al., 2015) emphasized the fact that this disease is not confined to the optic nerves or spinal cord, but includes broader phenotypes. To wit, the condition may target other parts of the central nervous system (CNS), and is now recognized that there are six “typical” CNS regions that may be compromised: the optic nerve, spinal cord, area postrema of the dorsal medulla, brainstem, diencephalon, and the cerebrum, causing signs and symptoms such as severe optic neuritis, extensive transverse myelitis, persistent and intractable vomiting and hiccups, and sleeping and eating disorders, among others (Wingerchuk et al., 2015; Pittock

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and Lucchinetti, 2016).

There is increased interest in studying the overlap between inflammatory neurological diseases, such as MS and NMOSD, and cognitive and psychiatric symptoms that are frequently present in these patients. It is now recognized that patients with MS frequently present with mood disorders, psychosis, and significant cognitive impairment, but this association has been poorly studied in patients with NMOSD (De Cerqueira et al., 2015; Marrie et al., 2015a). As clinicians, we frequently observe that patients with NMOSD present with psychiatric comorbidities, but little is known about this issue. Could it be a manifestation of inflammation/demyelination of certain CNS areas? Could it be immune mediated, as there is evidence of autoantibodies causing neuropsychiatric diseases, such as NMDA encephalitis? Could it be a clinical characteristic of the broader spectrum of NMOSD phenotypes?

There are few reports assessing psychopathology in individuals with NMOSD, although it is important given its impact on patients' quality of life, adherence to treatment, and prognosis (Moore et al., 2016; Vanotti et al., 2013; Meng et al., 2017). To our knowledge, this is the first pertinent study conducted in Latin America.

The objective of the present study was to evaluate the psychopathological profile and suicidality in patients with NMOSD in a hospital-based study in Buenos Aires, Argentina, and compare these parameters to those in patients with MS and in healthy controls (HCs).

2. Methods

Twenty consecutive patients with NMOSD attending follow-up medical visits at the Neuroimmunology Section, at Ramos Mejia Hospital, in Buenos Aires City, between august 2015 and September 2017, were recruited. Eighteen patients with MS matched for age, disability, and years of education were provided with information about the study and agreed to participate. Moreover, 20 healthy participants matched for age and education were included as the HC group.

The inclusion criteria were diagnosis of NMOSD according to the 2015 criteria for the NMOSD group (Wingerchuk et al., 2015) and diagnosis of MS according to Mc Donald 2010 criteria for the MS group (Polman et al., 2011), that had not experienced a relapse in the last 3 months. All participants in both patient groups and healthy controls were aged > 18 years. All participants provided informed consent. The study was reviewed and approved by the Hospital Ramos Mejia ethics committee. Demographic data including sex, age, and years of education were collected. All patients underwent detailed clinical assessment, including rating of disability on the expanded disability status scale (EDSS) (Kurtzke, 1983). Current depression status was assessed using the self-administered Beck's depression inventory (BDI) and suicidality and psychiatric illness (current or past) using the Mini-International Neuropsychiatric Interview (MINI), 5.0.0 Spanish version, administered by a psychiatrist.

The BDI is a self-administered survey that assesses and grades current depression and includes 21 questions, each one scored from 0 to 3. A result between 11 and 16 indicates mild mood disturbance, from 17 to 20 borderline clinical depression, from 21 to 30 moderate depression, from 31 to 40 severe depression, and over 40 extreme depression.

The MINI is a structured clinical interview designed to be used for both research and clinical purposes to investigate the possible presence of major psychiatric disorders. It is considered to be a reliable and valid tool for assessing the presence of Diagnostic and Statistics Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnoses and has a high level of concordance with the structured clinical interview of DSM-IV diagnoses (SCID-I) (Sheehan et al., 1998).

Statistical analyses were performed using SPSS statistics version 21 (IBM, Chicago, IL). The prevalence of different psychiatric disorders between the groups was examined using the chi-squared test.

Table 1
Demographic and disease characteristics of patients with NMOSD, MS, and HC.

	NMOSD (N = 20)	MS (N = 18)	HC (N = 20)
Gender (% Male: Female)	10:90	39:61	30:70
Mean age (range)	43.4 yo (19–69)	44.7 yo (27–61)	42 yo (25–65)
Mean years of education (range)	12.5 (6–18)	12.7 (7–18)	14 (7–18)
Mean EDSS (range)	5.0 (1.0–8.0)	3.0 (1.0–7.0)	NA
% IgG-NMO sero-status (pos: neg) over 16 patients	56:44	NA	NA
Mean Annualized relapse rate (range)	1 (0.1–3)	0,6 (0.1–1,2)	NA
Disease duration/years (range)	8.05 (1–18)	11.7 (1–35)	NA
Patients under psychoactive treatment (%)	9 (45%)	1 (5,5%)	0

NMOSD: neuromyelitis optica spectrum disorder, MS: multiple sclerosis, HC: healthy controls, EDSS: expanded disability status scale, NA: Not applicable.

3. Results

We collected data from 20 patients with NMOSD (NMOSD group), 18 patients with MS (MS group), and 20 healthy participants (HC group). In the NMOSD group, 90% were women, the mean age was 43.4 years (range 19–69 years), the mean EDSS score 5.0 (range 1.0–8.0), the mean years of education 12.5 (range 6–18 years). In 16 of the 20 patients, the test results for IgG-NMO were available, being positive in nine of them (56%). Disease duration ranged from 1 to 18 years, with a mean of 8.05 (SD = 4.4) years. Regarding treatment, eight (40%) patients were under azathioprine and prednisone administration, five (25%) under azathioprine, three (15%) under rituximab, and three (15%) under rituximab and prednisone. One patient was under no treatment because of personal choice. In the MS group mean age was 44.7, the mean EDSS score 3.0, and the mean years of education 12.7. There were no statistically significant demographic differences among groups. These characteristics are summarised in Table 1.

The first interesting finding was that nine (45%) of the 20 patients in the NMOSD group were diagnosed with a psychiatric disease, while this was only found in three of the 18 patients (16.6%) in the MS group ($p = 0.06$) and in one of the 20 participants in the HC group (5%, $p = 0.008$).

According to the MINI, in the NMOSD group, mood disorders were the most prevalent in this sample. Recurrent major depressive disorder (MDD) was diagnosed in four (20%) patients, and current dysthymia in one (5%). Two (10%) patients had past manic episodes and one (5%) had lifetime psychotic disorder. Bulimia nervosa was diagnosed in one (5%) patient. One of the patients who had experienced manic episodes also had history of alcohol abuse. Among the MS group, two patients were diagnosed with recurrent MDD (11%) and one with current generalized anxiety disorder (GAD) (5.5%). Among the HC group, one participant (5%) was diagnosed with current GAD.

In 10 (50%) patients in the NMOSD group, the presence of current depression was evident based on BDI scores; six (30%) patients had mild depression, one (5%) moderate depression, and three (15%) patients were severely depressed. In the MS group, the prevalence of current depression was 28%, the difference between groups was not statistically significant ($p = 0.16$). When compared to the HC, the NMOSD group had significantly higher rates of current depression ($p = 0.02$).

A relationship between severe depression and major disability was observed, as three of the four patients moderately or severely depressed had an EDSS score > 6.0, although this difference was not statistically significant ($p = 0.2$).

The most outstanding result was that six (30%) of the twenty patients with NMOSD had attempted to commit suicide at least once. In