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Clinical trial

Neuromyelitis optica spectrum disorders in Algeria: A preliminary study in the region of Tizi Ouzou

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ABSTRACT

Background: Neuromyelitis optica (NMO) is a disabling inflammatory condition that targets astrocytes in the optic nerves and spinal cord. Recent advances led to the individualization of a set of conditions now referred as NMO spectrum disorder (NMOSD).
Objective: To describe the prevalence and characteristics of NMO SD in north Algeria.
Patients and methods: The present study is a retrospective and descriptive work which took place in Nedir Mohamed teaching hospital, Tizi-Ouzou, Algeria. 938 Medical files of patients with CNS inflammatory demyelinating diseases were reviewed then patients with optic neuritis and/or myelitis were preselected. Patients who met the 2015 neuromyelitis optica spectrum disorders criteria were selected and analyzed
Results: 08 Patients (3.4%) met the 2015 criteria for neuromyelitis optica spectrum disorders, 3/8 (37.5%) were positive to AQ4-IgG and 5/8 (62.5%) were negative. Mean age of onset was 29 years, female to male ratio was 3:1, cerebral MRI was normal in 75% of cases and longitudinally extensive transverse myelitis was present in 75% of cases. 37/232 Patients (15.9%) were considered at high risk of neuromyelitis optica spectrum disorders
Conclusion: The present study suggests that the spectrum of NMO disorders is a rare entity among patients with optic nerve and spinal cord demyelinating lesions in north Algeria. However, the lack of accurate AQ4-IgG test certainly underestimates its real prevalence.

1. Introduction

Neuromyelitis optica (NMO) or Devic's disease is an AQP4 IgG antibody-mediated autoimmune disease targeting astrocytic foot processes which results in demyelination and global tissue destruction affecting selectively the optic nerve and the spinal cord (Wingerchuk et al., 2007, 1999; Jacob et al., 2007).

Clinical, radiological and immunological (Lennon et al., 2004; Wingerchuk et al., 2006) advances led to the individualization of a set of conditions now referred as neuromyelitis optica spectrum disorder (NMO SD).

These last 10 years have been marked by several changes in the NMO and NMO SD diagnosis criteria, recently the IPND have unified neuromyelitis optica and NMO SD under the term of NMO SD (Dean Wingerchuk and Banwell, 2014), a new classification based on the AQ4-IgG status which allows the diagnosis in patients with negative AQ4-IgG status and more interestingly in patients with unknown AQ4-IgG status.

2. Patients and methods

The present study took place in Nedir Mohamed Hospital in Tizi-Ouzou, Algeria.

We present a retrospective and descriptive study of NMO SD patients.

We reviewed 938 medical files of Algerian Caucasoid patients attending the neurology department for multiple sclerosis (877 patients with definite MS according to poser's criteria and 2010 McDonald criteria between 1998 and 2014), optic neuritis (ON) and/or myelitis from unknown origin (61patients).

Patients with main symptoms affecting the optic nerve and/or spinal cord were pre-selected (some brainstem symptoms were accepted i.e. nausea, vomiting, vertigo) then those with a clinical and radiological picture of NMO/NMOSD were selected. On the other hand patients with symptoms linked to a vasculitis, connectivitis, infections, ADEM were not included in the current study.

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The 2015 NMO SD criteria (Dean Wingerchuk and Banwell, 2014) were applied and cases meeting the criteria were reviewed, demographic, clinical, imaging and laboratory data were collected and analyzed.

2.1. Collected data

2.1.1. Demographic and clinical characteristics

Age of onset, gender ratio, acute visual loss, motor disorders, sensibility involvement, brainstem symptoms and clinical course.

2.1.2. MRI findings

2.1.2.1. Cerebral MRI

1. Lesions meeting Barkhof criteria.
2. Non-specific inflammatory white matter lesions.
3. Normal MRI.

2.1.2.2. Spinal cord MRI

1. Longitudinally extensive transverse myelitis (LETM) (≥ 3 vertebral segments).
2. Shorts spinal cord lesions (< 3 vertebral segments).
3. Normal MRI.

2.1.3. Laboratory and visual evoked potential findings

Oligoclonal bands in CSF analysis (OCB), CSF cell count, CSF protein level, visual evoked potential (VEP) and AQP4 IgG.

2.2. NMOSD diagnostic criteria for adult patients: IPND 2015 (6)

2.2.1. Diagnostic Criteria for NMOSD with AQP4-IgG

1. At least 1 core clinical characteristic.
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended).
3. Exclusion of alternative diagnoses.

2.2.2. Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status

1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. Atleast 1 core clinical characteristic must be optic neuritis, acute myelitis with LEM, or area postrema syndrome.
   b. Dissemination in space (2 or more different core clinical characteristics).
   c. Fulfillment of additional MRI requirements, as applicable.
2. Negative test(s) for AQP4-IgG using best available detection method, or testing unavailable.
3. Exclusion of alternative diagnoses.

Core clinical characteristics

1. Optic neuritis.
2. Acute myelitis.
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting.
4. Acute brain stem syndrome.
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions.
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions.

Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with

Unknown AQP4-IgG status.

1. Acute optic neuritis: requires brain MRI showing.

   a) normal findings or only nonspecific white matter lesions; or
   b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium enhancing.

   lesion extending over $> 1/2$ optic nerve length or involving optic chiasm.

2. Acute myelitis: requires associated intramedullary MRI lesion extending over > 3 contiguous.
   segments (LETM) or > 3 contiguous segments of focal spinal cord atrophy in patients with prior.
   history compatible with acute myelitis
3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions.
4. Acute brain stem syndrome: requires associated peri-ependymal brain stem lesions.

3. Results

With retrospective evaluation of 938 patients with CNS Inflammatory Demyelinating Diseases from the neurology department of Nedir Mohamed Hospital in Tizi-ouzou, Algeria, in which 877 patients have clinically definite MS and 61 patients have CNS Inflammatory Demyelinating Disorders from unknown origin involving selectively the optic nerve and/or the spinal cord, 232 (24.7%) patients have symptoms involving the optic nerve and/or the spinal cord, 45/232 have a clinical and radiological picture of NMO/NMOSD, half of this sub-group (22 cases) were found to be tested for AQP4-IgG. 08 patients met the criteria for NMOSD according to the 2015 IPND diagnosis criteria.

Patients with definite NMO SD have a mean age of onset of 29.4 years ranging from 16 to 44 years and a female to male ratio of 3:1. 3/8 (37.5%) was positive to AQ4-IgG, 02 patients have myelitis (recurrent in one case) and one patient had recurrent optic neuritis with monocular residual blindness. All of them respond to the definition of limited forms of NMO regarding the 2007 Wingerchuk criteria for NMOSD.5/8 (62.5%) have a negative AQ4-IgG status, all of them had both optic neuritis and myelitis, one patient had an area postrema syndrome associated. All the patients also met the 2006 criteria for NMO.

The cerebral MRI (Table 1) was normal in six patients (75%), in one case nonspecific white matter lesions were detected. A long T2-hyperintense lesion and T1-weighted gadolinium enhancing lesion of the optic nerve was detected in the orbital MRI of the patient with recurrent optic neuritis, an atrophy squeal of the optic nerve was found in a control MRI.

Spinal cord MRI (Table 1) showed a LETM in 6 patients (75%), longitudinally extensive sequelar atrophy in one patient (12.5%) and a normal spinal cord MRI in the case of recurrent ON (12.5%).

Table 1
Neuro-imaging characteristics of patients with NMOSD.

Brain MRI	Patients (n)	Spinal cord MRI	Patients (n)
Normal	75%(6)	Normal	12.5% (1)
Non-specific white matter lesions	12.5%(1)	LETM	87.5% (7)
Long ON lesion	12.5%(1)		