**Abstract:** Four French West Indian women complained of oscillopsia and were found to have an acquired eye movement disorder. In 3 of them, different types of nystagmus were found, including upbeat, downbeat, and central form of vestibular nystagmus. One developed opsinclonus-myoclonus syndrome. Two patients had definite NMO, while the other 2 were considered to be at high risk for developing NMO. Treatment with high-dose systemic corticosteroids, with plasma exchanges, or in combination led to resolution of oscillopsia. We propose that eye movement disorders be added to the neurological manifestations of NMO.

**Case Reports**

**Case 1**

A 46-year-old Chinese woman who was previously healthy presented with acute bilateral visual loss. The patient could only see hand movements in each eye; pupils were sluggishly reactive to light, and the left optic disc was swollen. Visual evoked responses showed delayed latencies and amplitudes bilaterally. Cerebrospinal fluid (CSF) analysis showed 15 cells per cubic millimeter and a protein level of 53 mg/dL (normal, 20–40 mg/dL) without oligoclonal bands. Serum NMO antibodies were not detected. Brain MRI revealed areas of increased signal in the hypothalamus and both the optic tracts (Fig. 1). MRI of the spinal cord was normal. The patient partially improved following a 5-day course of intravenous (IV) high-dose corticosteroids.

Fifteen months later, she developed gait disturbance and oscillopsia. Neurological examination revealed tetraparesis, dysarthria, dysphagia, and tongue deviation to the right. Sensitivity to light touch on the left side of the face was decreased. Visual acuity was 20/200 in each eye. The patient had UBN in both eyes in primary position, which became more marked on upward gaze (see Video, Supplemental Digital Content 1, http://links.lww.com/WNO/A18). Range of eye movements was full. Fundus examination showed left optic atrophy.

Brain MRI now demonstrated a lesion in the dorsal area of the caudal medulla (Fig. 2), while MRI of the spine showed a gadolinium ring-enhancing lesion in the upper cervical cord. Despite high-dose IV corticosteroids, UBN persisted. Amplitude increased in upgaze and decreased in downgaze and with convergence. Neither ocular fixation nor head position modified the direction or amplitude of UBN. On videonystagmography, the nystagmus had an exponentially decreasing slow phase. Five treatments of plasma exchange led to complete resolution of oscillopsia within 2 weeks.
The patient was felt to have NMO. Following plasma exchange, the patient was given 4 infusions of IV rituximab (dose, 375 mg/m²), administered once per week. She has not experienced new neurological symptoms during 1 year of follow-up.

**Case 2**

A 37-year-old Afro-Caribbean woman had a 10-year history of NMO. During the course of her disease, she experienced bilateral ON twice, each time treated with corticosteroid therapy. Her visual acuity was counting fingers in the right eye and no light perception in the left eye. Several forms of therapy, including mitoxantrone, cyclophosphamide, and rituximab, had failed to prevent relapses. NMO antibody was found in her serum on several determinations. Weekly plasma exchange had been instituted but was suspended due to a presumed infectious spondylitis. Two months later, she complained of acute vertigo, unsteadiness of gait, and bilateral upper limb weakness. Neurological examination revealed DBN in primary position. Electronystagmography showed that the nystagmus increased in amplitude in lateral gaze and remained unchanged during convergence. Eye movements were full. Following plasma exchange, vertigo disappeared but the DBN persisted. Brain MRI performed 2 years later was unremarkable.

**Case 3**

A 49-year-old Afro-Caribbean woman without significant medical history noticed decreased sensation in her left arm, leg, and left side of her face. Within a few days, she experienced urinary hesitancy and she complained of oscillopsia in right gaze. Examination showed a right-beating horizontal–rotatory nystagmus in right gaze, which did not change with head position or convergence. Brain MRI disclosed a presumed inflammatory lesion in the left pons (Fig. 3). MRI of the spinal cord demonstrated extensive longitudinal myelitis. NMO antibodies were found in her serum. The nystagmus was considered to be a central vestibular form of vestibular nystagmus since it was not associated with symptoms such as tinnitus, hyperacusis, or vertigo. High-dose IV corticosteroids led to disappearance of nystagmus. The patient was felt to be at high risk for NMO, and treatment was begun with mitoxantrone at a dose of 12 mg/m² administrated once per month.

**Case 4**

A 22-year-old Afro-Caribbean woman with a history of systemic lupus erythematosus was referred for quadraparesis, slowly worsening for more than 1 week. Symptoms then rapidly progressed over a few hours to flaccid paraplegia associated with severe multimodal hypoesthesia of lower limbs, sphincter disturbances, hypovigilance, and oscillopsia. Examination revealed opsoclonus consisting of multidirectional rapid involuntary eye movements. She also had myoclonus of right arms during voluntary movements. CSF contained 300 cells per cubic millimeter and a protein level of 155 mg/dL (normal, 20–40 mg/dL). There were no oligoclonal bands. Brain MRI showed involvement of the hypothalamus and increased signal in the medulla, pons, and cerebral peduncles in the periaqueductal area (Fig. 4A). MRI of the spine showed longitudinally extensive myelitis involving the entire spinal cord (Fig. 4B).

The patient received pulse IV methylprednisolone (2 g/day for 5 days), followed by a series of plasma exchange treatments with resolution of OMS, upper limb weakness,
and somnolence. She remained paraplegic, and neurological examination showed that pinprick, vibratory, and touch sensation were still abolished below T10 level bilaterally. Since she had NMO antibodies, the patient was felt to be at high risk for NMO. Mitoxantrone given at 12 mg/m², administrated once per month, was begun. Two months after the onset of symptoms, brain MRI showed disappearance of all brain lesions. Spinal cord MRI showed a significant reduction in high-signal lesions on T2 sequences, with a moderate decrease in edema of the thoracolumbar cord. The patient remained unchanged during the subsequent 4 months.

**DISCUSSION**

With established diagnostic criteria (2) and a specific serum biomarker (3), recognition of the clinical manifestations of NMO continues to expand. This has given rise to the concept of NMO spectrum disorders (Table 1). It is the brainstem involvement that led to our patients’ eye movement abnormalities and symptom of oscillopsia. Although these involuntary eye movements have not been previously described in the NMO spectrum, they do not appear to be exceptional in our French West Indian cohort of 50 NMO patients.

Our first patient experienced bilateral ON and subsequently developed UBN. While the amplitude of nystagmus increased in upgaze, it resolved in lateral gaze and with ocular fixation. Videooculography showed an exponential decreasing slow-phase velocity suggestive of neural integrator dysfunction. UBN may be due to lesions of the ventral tegmental tract (VTT) of the pons as well as the medulla. In our patient, MRI demonstrated a lesion involving part of the perihypoglossal nuclei, including the nucleus of Roller and nucleus intercalatus, 2 areas felt to be involved in the pathophysiology of UBN. A lesion of these nuclei results in loss of inhibition of flocculovestibular neurons leading to overinhibition of the VTT. This creates a slow downward drift of the eyes and corrective upward saccades (4).

Our second patient developed DBN without any other ocular motor abnormalities. Unlike cerebellar degeneration, inflammatory diseases of the central nervous system are seldom implicated in DBN (5). While the pathophysiology of DBN is not well understood, it may be due to impairment of cerebellovestibular inhibitory pathways between the

![FIG. 2. Case 1. T2 sagittal (A) and T1 axial (B) MRI demonstrates an area of increased signal in the caudal medulla. Accompanying schematic diagrams show extent of involvement (hatched area). Line with arrows on sagittal schematic drawing indicates level of axial scan (B). Structures affected include the nucleus intercalatus (red) located between nucleus prepositus hypoglossi (green) and medial vestibular nucleus (yellow). The nucleus of Roller (blue) is also involved.](image-url)
flocculus and superior vestibular nucleus. Such a lesion would lead to disinhibition of elevator motoneurons eliciting an upward slow-phase deviation, followed by corrective downward saccades (4). Unfortunately, we were not able to document a lesion in the lower brainstem at the nadir of attack producing DBN. We speculate that the signal of the lesion gradually disappeared over time in the same manner that is observed for some spinal cord lesions of NMO (6).

Binocular horizontal nystagmus with a right-beating fast phase characterized the eye movement disorder in our third patient. The nystagmus persisted despite ocular fixation, and MRI demonstrated a left pontine lesion with an involvement of the vestibular nucleus. This nystagmus was considered to be a central form of vestibular nystagmus.

Our fourth patient presented with OMS. The pathogenesis of opsoclonus is not completely understood, but it is believed to be either a cerebellar or brainstem disorder. Functional MRI studies suggest that fastigial nucleus activation leads to inhibition of omnipause neurons (OPN) in turn causing disinhibition of saccadic burst neurons and opsoclonus (7). The extensive pontine lesions on MRI in our patient included involvement of the pontine paramedian reticular formation where OPN are located.

NMO is a severe demyelinating disease that was initially thought to affect only optic nerves and spinal cord. Other neurological symptoms attributable to lesions outside these locations do not exclude a diagnosis of NMO according to recently revised diagnostic criteria (2). The NMO antibody that was present in 3 of our patients targets the water channel...
aquaporin-4 (AQP-4). In addition to the optic nerves and spinal cord regions that are enriched in AQP-4 include the hypothalamus, corpus callosum, periventricular region, and brainstem (8). Two of our patients had hypothalamic lesions, and 3 had an involvement of the brainstem.

We propose that the eye movement abnormalities in our patients with NMO or at high risk for NMO are due to inflammatory lesions in the brainstem. Fortunately, treatment with corticosteroids and plasma exchange led to clinical improvement in all our patients.

REFERENCES


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<tr>
<th>TABLE 1. NMO spectrum disorders</th>
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<tr>
<td><strong>NMO</strong></td>
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<tr>
<td>Limited forms of NMO</td>
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<tr>
<td>Idiopathic single or recurrent longitudinally extensive myelitis (≥3 vertebral segment spinal cord lesion on MRI)</td>
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<td>ON: recurrent or simultaneous bilateral</td>
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<td>Asian optic-spinal multiple sclerosis</td>
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<td>ON or longitudinally extensive myelitis associated with systemic autoimmune disease</td>
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<td>ON or myelitis associated with brain lesions typical of NMO (hypothalamus, corpus callosum, periventricular, brainstem)</td>
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From Wingerchuk et al (1). NMO, neuromyelitis optica; ON, optic neuritis.