Bilateral Internuclear Ophthalmoplegia as a Presenting Sign of Multiple Sclerosis: An Interdisciplinary Approach to Diagnosis and Management

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ABSTRACT
Abstract: Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system with various neurological and ocular manifestations. Ocular involvement occurs in approximately 80% of patients sometime during the course of the illness, and may be the presenting sign in about 50% of the patients with this disease. Bilateral internuclear ophthalmoplegia (BINO) is a common ocular complication of MS, occurring in up to one third of all MS patients. BINO is an ocular motility impairment characterized by a total or partial inability to adduct each eye accompanied by a concomitant nystagmus of the abducting eye on lateral gaze and a vertical gaze-evoked nystagmus. The importance of using an interdisciplinary approach to properly diagnose and manage MS will be discussed with a case review of a 57 year-old patient with BINO.

INTRODUCTION
There is no specific test for Multiple sclerosis (MS). However, the ophthalmic features of this disease may contribute to its correct diagnosis. Bilateral internuclear ophthalmoplegia (BINO) (see video at http://ijahsp.nova.edu/articles/Vol2number3/BINOweb5.mpg) is one of the most common oculomotor complications of MS and one of the most frequent ways that the disease is manifested. Smith and Cogan found that out of 29 cases of BINO, 96% were ultimately diagnosed with MS. BINO has been considered to be “pathognomonic” for this disease. MS can cause other visual, neurological, and psychiatric impairments that can have a significant impact on the patient’s quality of life. Therefore, it is essential that an interdisciplinary team of health professionals be involved in the diagnosis and management of this disease.

CASE REPORT
A 57 year-old Caucasian female presented with a complaint of decreased near vision in both eyes. She also reported a long-standing history of headaches that were relieved by Tylenol. Her past medical history was positive for severe chronic obstructive pulmonary disease and prior hospitalization for pneumonia and chronic bronchitis. Her social history was positive for smoking one pack of cigarettes per day for approximately forty years. She presented with a slight left head tilt. In addition, the patient’s gait appeared to be unsteady and she was significantly underweight. She reported weighting only 75-pounds, with a gradual weight loss over the past ten years.

Best-corrected visual acuity was 20/40 right eye and 20/40 left eye. Pupils were equal and reactive with no afferent defect. Ocular motility testing revealed bilateral adduction lag with an associated abduction nystagmus in the fellow eye. Slowed abduction saccades and a right hypertropia were also observed. Confrontation visual field testing and anterior segment
evaluation were unremarkable. Dilated fundoscopy revealed grade I nuclear sclerotic cataracts in each eye. Examination of the right optic nerve revealed mild temporal pallor (Figure I). The temporal aspect of the left optic nerve exhibited a greater degree of pallor (Figure II). The macule and retinal vasculature were normal in each eye.

Additional in office neurological testing revealed a positive bilateral Babinsky (upward toe sign, see video clip at http://ijahsp.nova.edu/articles/Vol2number3/Babinski%20Toe%20Sign.mpg). Threshold visual field testing revealed no central scotomas or marked neurological field defects. Color vision screening using Ishihara pseudoisochromatic plates revealed asymmetric color vision deficiency that was greater in the left eye. BINO and bilateral optic nerve pallor were diagnosed.

The patient was referred to her primary care physician for a complete physical examination and additional ancillary testing. Laboratory testing, including CBC, SMA-12, B12, folate and thyroid profile yielded unremarkable findings. A neurology consult was also requested. Neurological evaluation revealed a broad-based ataxic gait and abnormal visual evoked and brain stem auditory evoked potentials. Magnetic resonance imaging (MRI) of the brain revealed numerous areas of punctate signal intensity consistent with demyelinating plaques involving the pons, mid-brain, cerebellum, and cerebral hemispheres (Figure III). The neuro-ophthalmic findings of BINO and optic nerve pallor, coupled with the ataxic gait, abnormal visual and brain stem auditory evoked potentials, and MRI plaques supported a diagnosis of multiple sclerosis. Due to her age of onset of the neurological symptoms from this disease, she was given a poor neurological prognosis.
Bilateral Internuclear Ophthalmoplegia (BINO) is caused by demyelinating lesions within the medial longitudinal fasciculus (MLF) in the region between the third and sixth nerve nuclei.3-4, 6, 26 The MLF consists of fibers that carry conjugate horizontal eye movement signals from the sixth nerve nuclei to the contralateral third nerve nuclei. The MLF also consists of fibers for maintaining steady vertical position. Areas of demyelination compromise the neurological signal in the MLF, which leads to the clinical features of BINO: bilateral palsy of adduction on attempted horizontal gaze, bilateral horizontal nystagmus of the abducting eye, and a vertical gaze-evoked nystagmus (Figure IV).4, 20 The impaired adduction on attempted horizontal gaze may be complete, where the eye does not move past the mid-point, or partial, where the eye either incompletely adducts or adducts slower than normal in speed.

BINO is considered pathognomonic for MS because there is a strong predilection for the demyelinating lesions of MS to affect the MLF.3-6 However, it remains unsatisfactorily explained in the literature why this predilection for the MLF occurs. While BINO is considered pathognomonic for MS, other etiologies are possible and should be considered in cases not consistent with a diagnosis of MS. Common causes of BINO are listed in Table I.23-25
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Table I: Causes of BINO

<table>
<thead>
<tr>
<th>Causes of BINO</th>
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<tbody>
<tr>
<td>Multiple Sclerosis</td>
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<tr>
<td>Arnold-Chiari Malformation</td>
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<tr>
<td>Wernicke's encephalopathy</td>
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<tr>
<td>Syphilis</td>
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<tr>
<td>Tumors</td>
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<tr>
<td>Head Trauma</td>
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<tr>
<td>Occlusive Vascular Disease</td>
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<tr>
<td>Myasthenia Gravis</td>
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BINO can occur as an isolated finding or coincidentally with other ocular manifestations of MS. Various ocular findings possible in MS patients are listed in Table II.

Other neurological and psychiatric complications may precede, occur concurrently with, or follow the development of BINO. A positive Babinski reflex is a common neurological sign that occurs with BINO. Smith and Cogan found that 45% of patients with BINO had a positive Babinski’s reflex, which reveals upper motor neuron lesions in these patients. Other symptoms of MS, including paraesthesia of the extremities, weakness of the limbs and face, vertigo, ataxia, disturbance of micturation, fatigue and depression, may occur with BINO.

Table II: Ocular Manifestations of Multiple Sclerosis

<table>
<thead>
<tr>
<th>Ocular Manifestations of MS</th>
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<tr>
<td>Bilateral Internuclear Ophthalmoplegia (BINO)</td>
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<tr>
<td>Optic Neuritis</td>
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<tr>
<td>Optic Atrophy (Pallor)</td>
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<tr>
<td>Cranial Nerve Palsy</td>
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<td>Nystagmus</td>
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<td>Retinal Lesions</td>
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<td>Afferent Pupillary Defect</td>
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<td>Homonymous visual field defects</td>
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<tr>
<td>Posterior Uveitis</td>
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Prognosis

BINO occurs equally in men and women, and at any age in MS patients. Patients with BINO have an ocular prognosis that is as unpredictable as the MS disease itself. In some cases, BINO may resolve in a matter of days to weeks, while in others it can become recurrent and even permanent. The majority of BINO patients have no symptoms, but for those with double vision, prismatic spectacle correction may be beneficial. Patients who are older at the onset of BINO and exhibit multiple symptoms of MS generally have a worse neurological prognosis due to the deterioration of motor function.

Multiple Sclerosis Association

MS is a slowly progressive disease of unknown etiology. The disease occurs more commonly in women than men by a ratio of 2:1. There are three types of MS: the benign, relapsing-remitting, and progressive types. Patients with the benign type have complete or nearly complete resolution of symptoms. The majority of patients have the relapsing-remitting type. It is characterized by an unpredictable period of exacerbation and remission of neurological symptoms. The progressive type occurs in the later stage of the disease and is characterized by a gradual development of neurological problems. Patients with this type of MS generally have a poor prognosis due to the accumulating degree of disability.

There is no specific treatment that halts the progression of MS. Therapeutic management known as disease-modifying therapies (DMT) are used during different aspects of MS. The three main classes of drugs used to treat MS are immunosuppressives, steroids, and interferons. Each has significant side effects that limit their use. The only drug class that has been shown to reduce the frequency and severity of relapses over time in MS patients, while having limited side effects, is the Interferon-beta drugs. The only medications proven effective for the ocular manifestations of MS are intravenous methylprednisolone with a tapering course of oral prednisone, which is used specifically for the demyelinating optic neuritis.

MS is one of the most common causes of visual, neurological, and psychiatric impairment in North America. The disabling symptoms of this complex disease can prevent the patient from performing various daily activities and responsibilities. The
disease can interfere with the patient's cognitive abilities, family life, social life, emotional outlook, occupation or a combination of these. A few of these symptoms may be improved with pharmacological therapy. However, effective management of the many and varied complications of MS requires an interdisciplinary team approach. The primary care physician, neurologist, eye care physician, physician assistant, pharmacist, nurse, physical therapist, occupational therapist, and mental health specialist should all be involved in the management team.

CONCLUSION
BINO and other neuro-ophthalmic complications are important clinical findings that may help establish a diagnosis of MS. In some cases, patients may overlook other neurological signs, until a visual symptom develops. Therefore, all health care providers should be aware of the ocular signs of this disease.

The allied health professional plays an important role in the diagnosis and management of MS. The many and varied disabling complications of MS can have a significant effect on the quality of life for patients with this disease. It is essential that an interdisciplinary team of health care professionals be involved in the comprehensive care of patients living with MS.

REFERENCES
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