The National MS Society’s Professional Resource Center provides:

- Easy access to comprehensive information about MS management in a variety of formats;
- Dynamic, engaging tools and resources for clinicians and their patients;
- Clinical information to support high quality care; and
- Literature search services to support high quality clinical care.

FOR FURTHER INFORMATION:

VISIT OUR WEBSITE:
nationalMSsociety.org/PRC

To receive periodic research and clinical updates and/or e-news for healthcare professionals,

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Introduction

Disturbances of the visual system are among the most common manifestations of MS, affecting up to 80% of patients at some time in the disease course and serving as the initial symptom in many patients. The presence of monosymptomatic optic neuritis, in fact, heralds clinically definite MS within 5 years in over 50% of patients who also have three or more lesions on MRI, but in only 16% of patients with normal MRI findings. MS can affect any portion of the visual sensory system in ways that can result in significant disability, culminating in the inability to work and compromising the patient’s activities of daily living.

Optic Neuritis

Optic neuritis, or inflammation of the optic nerve, is the initial presenting symptom in nearly half of persons diagnosed with MS. It can be acute or chronic, and is characterized by any of the following:

- Unilateral vision loss progressing over hours or days
- Sequential involvement of the opposite eye
- Visual field defects, especially central visual field loss
- Diminished color perception and difficulty seeing in dim light
- Pain in or around the eye
- Visual phenomena

Asymptomatic optic neuropathy is also common in MS, as are abnormalities in color vision and contrast sensitivity, consistent with subclinical demyelination. Optic neuropathy also occurs in the form of chronic visual disturbances (often progressive) without an identifiable episode of acute optic neuritis.

Clinical Assessment and Disease Course

Numerous infectious or inflammatory disorders other than demyelinating disease may cause optic neuritis, but these conditions can usually be distinguished on clinical grounds without the need for ancillary tests. Central acuity is usually reduced, and most patients have a relative afferent pupillary defect or Marcus Gunn pupil (a relative lack of constriction during illumination when compared to responses in the opposite eye). The optic disc may appear normal or swollen. Retrobulbar involvement occurs in two-thirds of patients with acute optic neuritis.

The diagnosis can be confirmed with visual evoked potentials (VEP) and T-1 weighted MRI with gadolinium infusion. The VEP is particularly useful in establishing optic neuropathy in patients with clinically silent lesions.

The natural course of acute optic neuritis is variable, but vision typically worsens over several days to 2 weeks after onset. Patients then recover rapidly and achieve most of their improvement by 5 weeks (up to 1 year). Despite recovery of vision normal or near-normal, most
patients are aware of differences in the quality of their vision. Persistent deficits in contrast sensitivity, color vision, and depth perception are common.

Even though the natural history of acute optic neuritis is generally benign, over half of patients who recover visual acuity will still have deficits on the more sensitive measures of visual outcome. In the office, we use these tests to both quantify the new baseline, characterize deficits, and guide treatment and future management. We supplement bedside tools such as low-contrast visual acuity and color vision testing with Ishihara color plates with other metrics such as optical coherence tomography (OCT), which can quantify thinning of the nerve fiber layer and loss of cells after an optic neuritis, VEP, and visual field testing. These additional investigations provide a more sensitive description of the long-term impact of optic neuritis and chronic optic neuropathy in MS.

**Treatment**

Corticosteroids are the cornerstone of therapy for optic neuritis, based on their immunosuppressive and immunomodulatory effects. In patients presenting with optic neuritis as a first neurologic episode, treatment with a 3-day course of high-dose IV methylprednisolone, followed by a short course of prednisone, has been shown to reduce the rate of development of clinically defined MS over a 2-year period. The recommended treatment is 1 gm/day of methylprednisolone as a single daily IV infusion over 3–7 days, followed by a tapering dose of oral prednisone over 2–4 weeks.

Six randomized controlled trials have shown efficacy in starting an MS disease-modifying therapy in patients who present with optic neuritis and a brain MRI with lesions characteristic for MS. In these patients, who do not yet meet criteria to establish a diagnosis of MS but who are at high risk of developing MS in the future, these trials have shown that prompt initiation of treatment with interferons, glatiramer acetate, or terifluonomide reduce the risk of developing MS by 28-45% over the following 2-3 years. The decision to start an MS treatment in a patient with optic neuritis who does not meet criteria for MS is done on a case-by-case basis and is dependent on an individual’s background affecting their clinical risk of developing MS, comorbid health conditions, and personal preference of the treating physician and patient.

**Eye Movement Abnormalities**

- **Nystagmus:** Nystagmus is a repetitive, to-and-fro movement of the eyes that can reflect abnormalities in the mechanisms that hold images on the retina. In patients with MS, pendular nystagmus can produce oscillopsia (rotating, circular eye movement with the illusion of environmental movement), poor visual acuity, nausea, and disorientation. Treatment of nystagmus is challenging, as most pharmacologic agents are only moderately effective. Baclofen, clonazepam, gabapentin, and scopolamine provide some benefit in selected patients.
• **Internuclear Ophthalmoplegia**: Internuclear ophthalmoplegia, another neuro-ophthalmologic hallmark of MS is present in one-third of patients. The principal symptoms are diplopia, blurred vision, and oscillopsia, although many patients are without symptoms. Bilateral disease is most commonly associated with demyelination.

• **Internuclear ophthalmoparesis (INO)**: is seen in one third of patients and is the most common saccadic eye movement disorder in MS. INO in patients with MS is most commonly due to a demyelinating lesion in the medial longitudinal fasciculus (MLF), which connects the pairs of ocular motor nuclei is the final common pathway for all classes of conjugate eye movements. It is characterized as the slowing of the adducting eye during horizontal movements. Since the medial rectus of one eye and the lateral rectus of the other eye are a yoked pair, the increased innervation attempting to overcome the medial rectus adduction slowing leads to excess innervation to the lateral rectus in the other eye and exaggerated abduction followed by a drift backward and ultimately abduction nystagmus. The principal symptoms patients experience are diplopia, blurred vision, and oscillopsia, although many patients are without symptoms. Depending on the location of the lesion (more caudal or rostral within the MLF), and the extent of the lesion (bilateral MLF lesions, involvement of the ocular motor nuclei), patients can present with a variety of additional abnormalities in addition to the INO such as skew deviation, abnormal vertical pursuit, and bilateral exotropia (wall eyed) bilateral INO. The deficits of an INO usually resolve over weeks to months. However, in our experience (unpublished observations), if an INO persists for longer than 6 months it is likely to never fully resolve.

Internuclear ophthalmoparesis is not just a neurological sign to be documented. Depending on the severity, it can be a cause of significant disability. Because it is a dynamic deficit, it can lead to falling while walking or turning due to sudden loss of binocular fusion. Some patients are unable to drive safely and are at higher risk of car accidents as they can’t turn their head without developing double vision. In addition, patients who have an INO are at much higher risk of bladder dysfunction, as the pontine micturition center is located in the dorsal pons.

• **Cranial Nerve and Gaze Palsies**: In addition to the INO, MS patients can also develop cranial nerve palsies from lesions of the cranial nerve nuclei and fascicles. The most common cranial nerve palsy is a sixth nerve palsy, followed by third and fourth nerve palsies, which are much less common. These may occur in isolation, or, if the lesion involves another structure, such as the MLF, patients may have a combined deficit. For example, a patient may have a gaze palsy and an INO (named the one and one-half syndrome) due to a sixth nucleus or paramedian pontine reticular formation (PPRF) and an MLF lesion. Unlike the INO, which is a dynamic lesion and rarely causes misalignment in primary gaze, a cranial nerve palsy can often be treated with prisms in the patient’s spectacles.

• **Other eye movement abnormalities**: MS patients can have a variety of other eye
movement abnormalities that can not only cause significant symptoms, but their presence on examination can also clue the physician into the identification and localization of an MS lesion. Some examples of these other abnormalities include skew deviation, a vertical misalignment of the eyes due to a lesion in the otolith pathways, saccadic intrusions, retinal slip when attempting to hold visual fixation, and cerebellar-related eye movement abnormalities such as hypermetric or hypometric saccades, abnormal smooth pursuit, and gaze-evoked nystagmus.

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