A Practical Approach to Diagnosing and Treating Optic Neuritis

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Special Studies

A Practical Approach To Diagnosing and Treating Optic Neuritis

As defined in Kanski, optic neuritis is "an inflammatory or demylinating disorder of the optic nerve". It is typically categorized into three types:

1) **papillitis**

2) **neuroretinitis**

3) **retrobulbar neuritis**

The appearance of papillitis includes disc swelling, vitreous cells, and possible hemorrhages around the disc. Typically this occurs in children. Neuroretinitis has all the possible signs of papillitis with a macular star in addition. This is the least common of all three cases. It is typically present in end stage syphilis, and rarely associated with demylination. Retrobulbar neuritis is the classic senario of "patient sees nothing, doctor sees nothing" where the nerve head and retinal fiber layer appear normal. This form is most frequently associated with demylinating disease such as multiple sclerosis. (Kanski)

The focus of discussion will be: what ideally should happen in the exam room to diagnose and treat optic neuritis, educate the patient on their prognosis, and the chances of conversion to multiple sclerosis. Results of the Optic Neuritis Treatment Trial will also be summarized.

HISTORY OF THE OPTIC NEURITIS TREATMENT TRIAL

How to treat optic neuritis has been a controversial topic within the past decade. Mass doses of oral corticosteroids were the mainstay of treatment until after the Optic Neuritis Treatment Trial Study Group (ONTT) published it's results in 1991.
The ONTT was developed by Roy W. Beck, MD, Ph.D. and Jonathan D. Trobe, MD along with several others, to evaluate the value of oral corticosteroid treatment for acute

optic neuritis. A secondary plan of the study was to investigate the relationship between optic neuritis and multiple sclerosis. (Beck)

The ONTT utilized 15 clinical centers in the U.S. between 1988 and 1991 to enroll 457 patients in a National Eye Institute-sponsored randomized clinical trial. To be included in the study, the patient had to be between the age of 18 and 24, with acute unilateral optic neuritis with visual loss, an afferent pupillary defect (APD), and visual field deficit that had not been present for more than eight days. The patient could not have experienced any previous episodes of optic neuritis or received corticosteroid treatment for optic neuritis or multiple sclerosis. Systemic diagnoses other than multiple sclerosis that may have caused the optic neuritis were ruled out.

Four tests were used to assess visual function: (Beck)

Visual function	**Method**
▪ Visual Acuity	Snellen retroilluminated Bailey-Lovie Chart at 4 meters
▪ Color Vision	Farnsworth-Munsell 100-hue Test
▪ Contrast Sensitivity	Pelli-Robson Chart
▪ Visual Fields	30-2 Humphrey and Goldmann Perimeter

The three randomized treatment modalities used were: (Beck)

1) **Oral prednisone** (1mg/kg daily) X 14 days
2) **IV methylprenisolone sodium succinate** (250 mg qid X 3 days, followed by oral prednisone [1mg/kg daily] X 11 days)
3) **Oral placebo**

Important results of the treatment study were: (Beck)

- The IV group experienced a faster recovery of vision after the episode of optic neuritis but had no long-term visual benefit. Also, there was a reduced rate of

development of clinically definite multiple sclerosis (CDMS) during the first two years in patients with abnormal MRI consistent with demylination disease.

- The oral prednisone treatment did not improve visual outcome and had a higher rate of new optic neuritis attacks.

As a result, the treatment approach to optic neuritis was changed not only to produce a faster recovery from optic neuritis, but also to decrease the odds of developing multiple sclerosis.

DURING THE EXAM

The patient will most likely present with an unexplained, rapid onset of unilateral visual loss measured with Snellen acuity if possible. The patient may also complain of pain upon eye movement. (Kanski)

This visual loss typically reaches it's worst within one to seven days, and then gradually improves with time. Even when visual acuity recovers to 20/20 contrast sensitivity and color vision may still be abnormal. (Beck) This can leave the patient with imperfect vision.

Contrast sensitivity function should not be overlooked during this type of exam. (ON Study Group) At one time contrast sensitivity testing was thought to be too time consuming for use in the exam room. Because it is now simple and reliable, it has become a valuable diagnostic tool as well as an excellent way to assess the patient's quality of vision. This test is the most often abnormal in both first time and also recovered optic neuritis patients. Investigators hypothesize that there is target damage to channels carrying low-contrast visual information during an episode of optic neuritis.

Snellen acuity measures high contrast discrimination, where contrast sensitivity, color vision, visual field, and VEP may demonstrate a low-contrast loss. This could explain the continued complaints of patients whose visual acuity has returned to normal according to the Snellen chart. (Trobe)

During the ONTT, at the six-month follow-up visits, contrast sensitivity was 2.2 times more often abnormal than visual acuity, 1.8 times more often than visual field mean deviation, and 1.5 times more often that color vision. As reported by the ONTT, five years after an episode of optic neuritis, contrast sensitivity was the test most often abnormal compared with visual acuity, visual field, or color vision.

As mentioned previously, assessment of color vision should also be performed during the examination. The ONTT found 94% of patients had color vision deficits at entry and 40% still had residual deficiencies after six months. Although the color vision abnormalities were obvious, the type of abnormality (R/G or B/Y) was not well defined. Many of the defects in the ONTT at entry level and during the follow-ups could not be categorized into just one single type of color deficiency. They were predominately R/G or B/Y with a small amount of the other type mixed in. (Schneck)

The visual field defects present in optic neuritis are variable. The typical patterns and percentage of occurrence are listed in the table below: (Beck)

Pattern of Visual Field Defect	% of patients with defect
Diffuse	48
Altitudinal, arcuate, nasal step	20
Central, centrocecal	8
Other types	24

TESTS TO BE ORDERED OUTSIDE OF THE EXAM ROOM

How important and cost effective it is to have the patient obtain and MRI is always raised in the clinician's mind. MRI is used to reveal lesions associated with multiple sclerosis or any other abnormalities to explain the origin of the optic neuritis. The periventricular and brain-stem plaques diagnostic of multiple sclerosis are more evident in MRI compared to computed tomography. (Kanski) Thirty-five percent of patients who had no signs of multiple sclerosis at the time of entry had one or more visible plaques typical of multiple sclerosis on their baseline MRI scan. (Beck) The results of the MRI can dictate the patient's future treatment plan.

Researchers are still considering the role that cerebral spinal fluid (CSF) testing plays in the diagnosis of multiple sclerosis. CSF contains chemicals released by cells in the nervous system. Certain proteins that are present in MS can be detected by a process called oligoclonal banding. A negative test for oligoclonal banding is no more than one band found in the CSF that is not found in the blood serum. A positive test is two or more bands found. It is estimated from 48-61% of optic neuritis patients have this pattern of banding, suggesting a higher risk of conversion. (Clanet) In order to confirm MS, clinical symptoms must also be present. (drkoop.com) Although, CSF testing's predicative accuracy remains low, it can be used to rule out other systemic diseases. (Clanet)

At entrance level of the ONTT, patients were asked to give CSF samples on a voluntary basis. Of the 457 patients, 133 did so. The final report was restricted to only 83 patients who had a lumbar puncture with in 24 hours of being enrolled, had their MRI read at an ONTT MRI reading center, and had not been diagnosed with probable or

CDMS at enrollment. Within the group the treatment regimens were fairly evenly distributed with 22 placebo, 34 IV methylprednisolone, and 27 oral prednisone. The study attempted to analyze: (Rolak)

1) CSF changes in optic neuritis

2) Any relationship between MRI and CSF abnormalities

3) Efficacy of performing lumbar puncture in patients with optic neuritis

In the end, studies on CSF testing resulted in inconclusive findings and lumbar puncture results would not have altered the diagnosis or treatment of any patient. Therefore, lumbar puncture may not be necessary in the typical presentation of acute optic neuritis. There was no substantial correlation between MRI and CSF testing. Inconclusive results were found for chest X-rays and blood testing also. As time goes on and the ONTT continues to follow these patients the importance will remain to be seen. (Rolak)

EDUCATING THE PATIENT

After the assessment and explanation of optic neuritis is complete, the patient will undoubtedly have questions about the future of their vision, as well as the possibility of developing multiple sclerosis.

The best predictor of visual recovery is the initial visual acuity loss. Slowly within the first two weeks the visual recovery begins and by one month the majority is regained. An even slower continued recovery extending for several months restores nearly the entire remaining deficit. (Beck)

During the ONTT, by day five 88% of patients had improved at least one Snellen line and by day 30, 96% had improved one line. When the patients whose visual acuity

was 20/50 or less was compared to those whose visual acuity was 20/40 or better, the previous patients had a poorer visual outcome and more often had recurrent attacks of optic neuritis in the first six months. After twelve months of follow-up visual acuities were 20/40 or better in 93%, better than 20/20 in 69%, and 20/200 or worse in only 3%. Of those patents who had only light perception or no light perception (30 patients), 67% recovered to 20/40 or better. (Beck)

As for differences between treatment groups, the patients in the IV group started to recover their vision sooner than the other two groups. After 30 days into the study, the difference between the groups was small. (Beck)

DIFFERENTIAL DIAGNOSIS OF OPTIC NEURITIS

Pathology other than optic neuritis to consider would include:

- ✓ Ischemic Optic Neuropathy
- ✓ Acute Papilledema
- ✓ Severe Systemic Hypertension
- ✓ Orbital Tumor Compressing the Optic Nerve
- ✓ Intracranial Tumor Compressing the Afferent Visual Pathway
- ✓ Leber's Optic Neuropathy
- ✓ Toxic/Metabolic Optic Neuropathy
- ✓ Granulaomatous Optic Neuropathy

*adapted from Will's Eye Manual

The patient deserves a good case history to rule out the above possibilities. It is considered atypical if the patient does not improve at least one line of acuity within the first three weeks after onset of symptoms. The practitioner should also investigate further if a reduction of vision is evident after a course of corticosteroid treatment is completed. (Beck)

REOCCURANCES

According to results from the treatment trial, the chance of having a new episode of optic neuritis within five years was 19% for the affected eye, 17% for the fellow eye and 30% for either eye. (ON Study Group) As mentioned before, there was a greater chance for having another episode in the oral treatments group than in the other two. (Beck)

CHANCE OF MULTIPLE SCLEROSIS

An even more important question is the chance of developing multiple sclerosis. Patients who are youngest when optic neuritis develops have the highest risk of conversion to MS. Males also have a more frequent chance of multiple sclerosis than females. (Clanet)

When a brain MRI was performed at the time of ON, the presence of signal abnormalities was the most important predictor of CDMS by five years. Within these five years, CDMS developed in 27% and probable MS in an additional 9%. In the group of patients with optic neuritis in one eye with no brain MRI lesions and no prior neurologic episodes, there were three clinical features associated with a low risk of CDMS: (ON Study Group)

1) Lack of pain
2) Presence of optic disc swelling
3) Mild VA loss

When considering treatment groups, the IV treatment group developed CDMS at a slower rate compared to the other two within the first two years of follow-up. After two years, there was insignificant differences between the two groups. (Beck)

TREATMENT OF OPTIC NEURITIS

The next step in the exam is to develop a plan for the patient. The treatment options are aimed at not only curing the optic neuritis, but also lowering the odds of converting to multiple sclerosis. Based on recommendations from the ONTT oral prednisone is no longer a treatment option. Further treatments for multiple sclerosis specifically are mention later. Among patients in the study who had two or more signal abnormalities, CDMS developed in the following percentage of patients within two years: (Beck)

- Placebo (n=39) – 35.9%
- Oral (n=32) – 32.4%
- IV (n=37) – 16.2%

This beneficial effect was not evident after two years. By the end of the third year percentages were as follows: (Beck)

- Placebo- 21.3%
- Oral- 24.7%
- IV- 17.3%

As for side effects of the treatment options, they are few. Only transient mood changes, sleep disturbances, dyspepsia, and weight gain was reported in the two steroid groups more commonly than the placebo. (Beck)

In today's environment of costly medical treatment, obtaining a brain MRI is costly and doesn't provide any long-term protection. (Tanaka) The eye care professional along with the patient's primary care physician will have to weigh the cost/benefit ratio. Patients whose symptoms qualify for a brain MRI (i.e. severe vision loss, other clinical

symptoms, optic neuritis reoccurrence), and reveal two or more signal abnormalities should undergo an IV corticosteroid regimen. (Beck)

NEW TREATMENTS IN MULTIPLE SCLEROSIS

Of neurological disabilities in young adults not caused by trauma, multiple sclerosis is the most common. Studies show that early treatment of MS can be more effective. Eye care professionals are in the position to aid in this early diagnosis. A list of the most frequent symptoms associated with MS are listed on the following page. (Comi)

Symptom	% associated with MS
Motor disturbance	36
Sensory symptoms	24
Vestibulo-cerebellar dysfunction	17
Optic neuritis	12
Diplopia	17

The suspected mechanism of multiple sclerosis is an autoimmune response by the host. Interferon beta (IFN-B) is currently being studied as a treatment for multiple sclerosis because it has antiviral, antiproliferative and immunoregulatory properties and is produced naturally in the body. It was originally utilized because of it's antiviral properties, but now there is now evidence of it's effect on the immune system. (Comi) Findings of the IFN-B MS Study Group in April of

1993 showed a significant reduction in the number and size of new brain lesions in patients treated with INF-B. To date, two FDA-approved B-IFN's in the United States are Betaseron and Avonex. (Cross)

CONCLUSION

Practicing full-scope optometry includes not only preserving the patient's vision, but being concerned about the systemic systems as well. Optic neuritis had been proven to be linked to multiple sclerosis, a potentially life altering condition. It is imperative that the eye care professional fully educates the patient on the nature of optic neuritis and MS along with the risk/benefit ratio of laboratory tests and treatments. For a patient that has mild vision loss secondary to optic neuritis and no other symptoms, the optometrist and patient may agree no treatment is the most logical solution. In another situation, a patient with severe vision loss and numbness in the left arm that has reoccurred, may be motivated to investigate their health status further. Together the practitioner and patient may decide on a plan of attack that fits their unique situation.

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