Demyelinating optic neuropathy

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Introduction

Optic neuritis (ON) is an inflammatory process affecting the optic nerve. After glaucoma, it is the most common optic neuropathy affecting patients under the age of 50. The usual presentation of typical ON is unilateral subacute loss of vision preceded with some retrobulbar pain especially on eye movement. It most commonly affects young, otherwise healthy, females.

Although many autoimmune conditions such as sarcoidosis and systemic lupus erythematosus (SLE) can cause ON along with many infectious and para infectious and post vaccination causes have been recognised, the majority of ON can are secondary to demyelinating conditions. In adult patients, these include multiple sclerosis (MS), neuro myelitis optica (NMO) and myelin oligodendrocyte glycoprotein (MOG) related disease (MOGAD).

There have been many papers on optic neuritis, its aetiology, presentation and management. In this short article I will briefly discuss demyelinating optic neuritis presentation, its typical features and management plans.

Aetiology

Demyelinating conditions can affect the myelin sheath of the optic nerve leading to ON episode. This can be an isolated episode as in clinically isolated syndrome (CIS), MS related (MS-ON), NMO related (NMO-ON) or MOGAD. There are other rarer associations as well.

Presentation

Table 1 summarises features of typical ON presentation [1]. The more deviation from the typical presentation, the more atypical the ON is with increased need for more in depth investigations.

Features of typical optic neuritis
Female gender
Age between 15 and 45
Periocular pain especially on eye movement few days prior to vision deterioration
Subacute unilateral loss of vision
Visual acuity usually better than HM in majority of cases
Features of optic neuropathy (RAPD, reduced colour vision, reduced contrast sensitivity, field defects (usually central scotoma or general reduction of sensitivity but can be anything))
Normal looking optic nerve or very mild swelling
Worsening of vision for up to two weeks before spontaneous improvement in 90% of patients
Near full recovery in more than 90% of patients

Table 1: Features of typical optic neuritis, adapted from Hoorbakht, et al [1].

Differential diagnosis

1. Any other cause of inflammatory optic neuropathy
2. Non-arteritic anterior ischaemic optic neuropathy (NAION)
3. Compressive optic neuropathy
4. Leber's hereditary optic neuropathy (LHON).

Diagnosis criteria

There is no consensus on the criteria to diagnose ON. Majority of the diagnoses depends on clinical features as well as some laboratory and imaging investigations. A recent paper published in 2022 suggested some criteria to reduce misdiagnosis of ON based of the opinion of more than 100 experts in neuro ophthalmology [2].

Table 2 summarises clinical and investigation features needed to reach a diagnosis of ON.

Diagnosis criteria for ON
Clinical criteria: • A: Monocular, subacute loss of vision with orbital pain worsening on eye movements, reduced contrast and colour vision, and RAPD • B: Painless with all other features of (A) • C: Binocular loss of vision with all features of (A) or (B)
Investigation criteria: • OCT: optic disc swelling acutely or difference of 4% or four microns in the GCL or 5% or five microns between the eyes within three months of onset • MRI: Contrast enhancement of the symptomatic optic nerve and sheaths acutely or an intrinsic signal increase within three months • Biomarkers: Aquaporin 4 (AQP4), MOG, Collapsin response mediator protein 5 (CRMP5) antibodies in the blood or CSF IgG oligoclonal bands
Definite ON: • A with one investigation criteria • B with two investigation criteria • C with two investigation criteria one of which is MRI scan
Possible ON: • Any of the clinical criteria if seen acutely with fundus examination and natural history typical of ON in the absence of investigations • Positive investigations, with a medical history suggestive of optic neuritis

Table 2: Diagnosis criteria of optic neuritis, adapted from Petzold, et al [2].

Optic neuritis in MS, NMO and MOG conditions

Optic neuritis is usually part of the spectrum of presentations in these demyelinating conditions. It can be the first presenting feature which poses a dilemma and a challenge to the clinician on how to manage this ON case.

Dissemination in space (on MRI scan)	One or more T2-hyperintense lesions characteristic of multiple sclerosis in two or more of four areas of the CNS: periventricular, cortical or juxtacortical, and infratentorial brain regions, and the spinal cord
Dissemination in time (on MRI scan)	• Simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time • New T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI

Table 3: Dissemination criteria for MS diagnosis, adapted from Thompson, et al [3].

The 2017 McDonald criteria for diagnosis of MS in patients with an attack at onset		
Clinical attack	**Number of MRI lesions**	**Additional information needed to reach a diagnosis of MS**
Two or more	Two or more	None
Two or more	One (as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location)	None
Two or more	One	Dissemination in space: an additional clinical attack implicating a different CNS site or by MRI
One	Two or more	Dissemination in time: an additional clinical attack or by MRI or positive CSF oligoclonal bands
One	One	Dissemination in space AND Dissemination in time

Table 4: McDonald criteria for MS diagnosis, adapted from Thompson, et al [3].

Suggested diagnosis criteria for MOGAD (A, B, C needed)
A: Clinical demyelinating episode: • Optic neuritis • Myelitis • Acute disseminated encephalomyelitis (ADEM) • Cerebral monofocal or polyfocal deficits • Brainstem or cerebellar deficits • Cerebral cortical encephalitis
B: Positive MOG-IgG test Cell-based assay in serum: • Clear positive: no need for other supportive features • Low positive, negative with positive CSF: requires negative AQP4 and supportive clinical or MRI feature(s)
Supportive clinical or MRI features: • Optic neuritis: - Bilateral simultaneous clinical involvement - Longitudinal optic nerve involvement - Perineural optic sheath enhancement - Optic disc oedema • Myelitis: - Longitudinally extensive myelitis - Central cord lesion - Conus lesion • Brain, brainstem, or cerebral syndrome: - Multiple ill-defined T2 hyperintense lesions in supratentorial and often infratentorial white matter - Deep grey matter involvement - Ill-defined T2-hyperintensity (pons, middle cerebellar peduncle, or medulla) - Cortical lesion
C: Exclusion of better diagnoses including multiple sclerosis

Table 5: Diagnosis criteria for MOGAD, adapted from Banwell, et al [4].

Diagnosis criteria for NMO spectrum disorder (NMOSD)
Absolute clinical criteria: • Acute optic neuritis • Acute myelitis
Supportive investigation criteria: • Brain MRI not meeting diagnosis criteria for MS • Spine MRI showing T2 signal change over 3 or more vertebral segments • Seropositive AQP4 antibodies

Table 6: Diagnosis criteria for NMOSD, adapted from Hoorbakht, et al [1].

Common features of ON in MS, NMOSD and MOGAD (helping to guide clinical decision on diagnosis and course of treatment)			
Feature	**MS**	**NMOSD**	**MOGAD**
Paediatric presentation	Uncommon	Rare	Common
Gender	F>M	F>M	F=M
Course	Relapsing or progressive	Relapsing	Monophasic or relapsing
Visual acuity impairment	Mild to moderate	Severe	Severe
Bilateral presentation	Rare	Common	Common
Steroid response	Very good if needed	Sometimes refractory	Steroid responsive
Recovery	Very good	Risk of poor recovery	Good
ON swelling / OCT	Mild or none	Swollen but less common than MOGAD	Commonly swollen
MRI brain	Multifocal T2-hyperintense white matter lesions	May be normal	May be normal
MRI spine	Multiple focal lesions	Longitudinally extensive lesion (conus rarely involved)	Longitudinally extensive lesion (H-sign and conus lesions)
CSF oligoclonal bands	Very common	Uncommon	Uncommon

Table 7: Diagnosis criteria for NMOSD, adapted from Hoorbakht, et al [1] and Banwell, et al [4].

Treatment [1,2]

The optic nerve treatment trial (ONTT) is used as the gold standard guidance for treatment of optic neuritis. Most MS-related ON recover spontaneously, with recovery starting two to three weeks after onset and continuing for a year. The ONTT showed that intravenous methylprednisolone (IVMP) helped speed up the recovery of ON, but the final visual acuity was similar in treated and placebo given patients, although treatment group had better contrast sensitivity, colour vision and field tests than the placebo group. The ONTT also showed that the oral prednisolone group had a larger relapse rate compared to the IVMP group and the placebo group.

The current practice for treating suspected demyelinating optic neuritis varies between centres – the usual approach is to discuss with the patient the benefits and risks of steroid treatment and treat cases with severe visual loss with IVMP followed by oral prednisolone 60mg OD for 11 days and a short taper, based on the recommendations of the ONTT study. There are many discussions in the neuro ophthalmology societies about the limitations and the age of the ONTT study and the need for a new study to guide treatment, especially with more accurate assessments of visual functions and optic nerve structure via OCT scans. It is important to emphasise that MOGAD and NMO related ON are steroid responsive and early intervention with IVMP is crucial to preserve or improve visual functions.

There are many studies on the benefits of early treatment with immunosuppression for patients who are at high risk of developing MS. These include controlled high-risk subjects Avonex multiple sclerosis prevention study (CHAMPS), early treatment of MS study (ETOMS) and Betaferon in newly emerging multiple sclerosis for initial treatment (BENEFIT). They showed reduction of risk of developing MS with early treatment with disease modifying drugs (DMDs).

Conclusion

Optic neuritis is one of the most common optic neuropathies in young adults. In its most common form, it is caused by demyelination. It can be a feature of multiple sclerosis, neuro myelitis optica spectrum disorder or MOG-related disease. Early and accurate diagnosis is important, then depends on various clinical criteria as well as many investigations such as antibodies titres and neuro imaging. Treatment depends on the initial process and is currently guided by the ONTT study although there is a need for an up-to-date guidance.

References

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