



Acute Demyelinating Optic Neuropathy

Acute demyelinating optic neuropathy in adults not known to have multiple sclerosis is a common entity that frequently presents to ophthalmic casualty departments. It is a clinical diagnosis but various uncommon entities that pose serious threat to vision and life must be excluded. Prognosis for vision is good but there is a high risk of subsequent development of multiple sclerosis. The most appropriate acute and long-term treatments continue to be debated. Ophthalmologists are in a good position to diagnose and possibly treat acute demyelinating optic neuropathy but subsequent management, particularly assessment of risk of multiple sclerosis, requires neurological expertise.

Terminology

Optic neuritis means inflammatory optic neuropathy of whatever aetiology. Although acute demyelinating optic neuropathy is the most common cause, using the terms optic neuritis and acute demyelinating optic neuropathy interchangeably leads to a failure to consider the other potential aetiologies, of which some have more serious consequences for vision and life.

Epidemiology

The annual incidence of acute demyelinating optic neuropathy ranges from 1.5 per 100,000 in Stockholm, Sweden to 5.1 per 100,000 in Minnesota, USA. Age at presentation is usually 20-50 years, the mean age in the Optic Neuritis Treatment Trial (ONTT) being 32 years. 75-80% of patients are female and in the ONTT 85% of patients were Caucasians.

Clinical features

Acute demyelinating optic neuropathy typically causes unilateral visual loss, progressing over a number of days. In over 90% of cases there is periocular pain often exacerbated by eye movements. Visual acuity at presentation ranges from normal to no perception of light. Colour vision is particularly impaired. Humphrey central visual field perimetry most commonly shows diffuse loss. Visual field testing by confrontation, tangent screen or Goldmann perimetry usually reveals a central scotoma. There is a relative afferent pupillary defect. The optic disc is usually normal. In 20-40% of eyes there is optic disc swelling that is usually mild but may be associated with haemorrhages. Retinal exudates and vitreous cells are occasionally seen but not cotton-wool spots. Optic disc pallor does not occur in the acute stage of a first episode of acute demyelinating optic neuropathy.

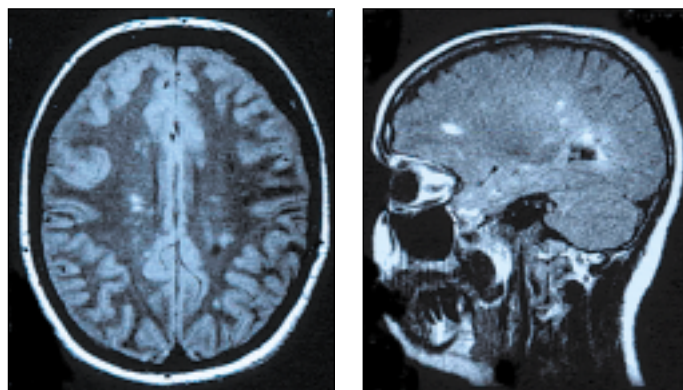


Figure a (Left) Axial and Figure b (Right) sagittal brain MRI showing periventricular cerebral white matter lesions typical of demyelinating disease.

Investigation

Acute demyelinating optic neuropathy can be diagnosed reliably on clinical grounds as long as atypical features are heeded (Table). In the ONTT only 4 out of 450 patients (0.9%) were misdiagnosed. If the clinical features and clinical course are typical, no investigations are required to confirm the diagnosis.

Differential diagnosis

Optic disc pallor, temporal visual field loss in the contralateral eye indicative of a lesion at the anterior chiasm, progressive visual loss or failure of vision to recover necessitates imaging to exclude a compressive lesion. Protracted severe pain particularly localised to the vertex, history of sinus disease, and systemic illness or pyrexia, are suggestive of sphenoid sinus mucocoele requiring urgent sinus drainage and systemic antibiotic therapy. Fungal infection of the sphenoid sinus should be considered in the immunosuppressed. Thin slice contrast-enhanced CT of brain and orbits is generally adequate for excluding a compressive optic neuropathy but MRI is more sensitive and identifies intrinsic disease.

Known sarcoidosis or systemic vasculitis should be assumed to be causative and treatment instituted urgently with systemic steroids. They should also be considered if there is progressive visual loss or failure of vision to recover. Intraocular inflammation is present in up to 28% of patients presenting with acute demyelinating optic neuropathy, but particularly when it is marked it should raise the possibility of sarcoidosis or infectious disease. The possibility of syphilis should be borne in mind, especially in HIV-positive patients.

In anterior ischaemic optic neuropathy visual field loss is usually altitudinal and pain is uncommon. The optic disc is always swollen in the acute stage. Non-arteritic disease generally occurs after the age of 50. Giant cell arteritis must always be considered in patients over age 55. Ischaemic optic neuropathy without optic disc swelling (posterior ischaemic optic neuropathy) is a diagnosis of exclusion necessitating investigation.

Vitamin B12 deficiency, tobacco-alcohol amblyopia, drug-induced optic neuropathy (e.g. ethambutol), and toxic optic neuropathy are usually present with symmetrical subacute bilateral optic neuropathy, characteristically with small central scotomas. Amiodarone may cause optic neuropathy with disc swelling. Leber's hereditary optic neuropathy usually presents in young males with painless sequential or simultaneous severe bilateral visual loss that develops over weeks or months.

Acute demyelinating optic neuropathy, often bilateral, may occur after immunisations or viral illnesses, when in both instances there is no risk of subsequent multiple sclerosis, in acute disseminated encephalomyelitis or in Guillain-Barré syndrome. Inflammatory disease limited to the anterior visual pathway and spinal cord may be a manifestation of multiple sclerosis, sarcoidosis, systemic vasculitis, or Devic's disease.

Visual outcome and treatment of the acute episode

Without treatment, in 93% of cases visual acuity improves by 5 weeks from onset of visual loss. Only 5% of eyes have visual acuity worse than 6/12 at 6 months. Even among eyes that lose all perception of light visual acuity at 6 months is 6/12 or better in 64%. Long optic nerve lesions on MRI, particularly those involving the intracranial segment, are associated with poor visual recovery.

Steroid treatment accelerates visual recovery but does not improve final visual outcome. At 15 days after institution of treatment in the ONTT, median visual acuity after steroid treatment was 6/6 compared to 6/7.5 in the placebo group. Surprisingly in the ONTT oral steroid therapy alone was associated with an increased risk of subsequent episodes of acute demyelinating optic neuropathy. Whether oral therapy alone should be avoided remains uncertain.

Development of multiple sclerosis

The risk of developing multiple sclerosis following a first episode of acute demyelinating optic neuropathy is approximately 30% at 5 years rising to 60% at 40 years. The major risk factors are female gender, multiple white matter lesions on brain MRI (Figure) and CSF oligoclonal bands. In the ONTT, the 5-year risk of development of multiple sclerosis rose from 16% if there were no white matter lesions to 51% if there were 3 or more. Steroid therapy reduced the risk of development of multiple sclerosis but only at 2 years.

Long-term beta interferon in patients with multiple white matter

lesions on brain MRI, reduces the risk of development of multiple sclerosis at 2-3 years by 24%. One interpretation of these results, prevalent in the USA, is that beta interferon reduces the risk of conversion to multiple sclerosis and that beta interferon should be offered to all such patients. The alternative interpretation, common in the UK, is that beta interferon delays the development of the next relapse in those patients destined in any case to develop multiple sclerosis. Thus beta interferon is recommended according to the same criteria as in relapsing-remitting disease, i.e. at least 2 clinically significant relapses in the last 2 years, which means that it is not considered until at least a second neurological event has occurred.

What should the patient with a first episode of acute demyelinating optic neuropathy be advised?

It is reasonable to state that the patient has suffered an episode of optic nerve inflammation, that no investigations are necessary (as long as the clinical features are typical), and that whatever the level of visual loss there is a very high chance of good recovery of vision. Steroid treatment can be offered, particularly to those with poor vision in the fellow eye, severe pain, or a particular reason for rapid recovery of vision but it must be stressed that the benefit is modest and final visual outcome will not be improved. The patient should be informed that there is a risk of further episodes of central nervous system inflammation. The possibility of multiple sclerosis may be discussed, particularly if the patient raises the topic. Information from the Internet often needs to be put into context. Although it may be reasonable to arrange brain MRI, it is outside the remit of ophthalmologists to provide any further assessment of the patient's risk of developing multiple sclerosis and advice on the role of interferon therapy. These require referral to a neurologist.

Table. Clinical features atypical for acute demyelinating optic neuropathy

- Age over 50 years
- Bilateral visual loss
- Absence of pain
- Severe pain localised to the vertex
- Systemic illness or pyrexia
- History of systemic disease associated with optic neuropathy
- Immunocompromise or immunosuppression
- No relative afferent pupillary defect
- Temporal field defect in the contralateral eye
- Marked intraocular inflammation
- Optic atrophy in the acute stage
- Progressive visual loss or lack of visual improvement

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