Optic neuritis - many hats

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Abstract

Demyelinating optic neuritis is the most common cause of optic neuropathy typically presenting with acute or subacute painful loss of vision. In 20% of patients with multiple sclerosis, optic neuritis is the presenting symptom and half of the patients with isolated optic neuritis develop multiple sclerosis within 15 years. A correct and early diagnosis is necessary to ensure optimal further investigations and treatment. It is imperative to rule out other causes of optic neuropathies such as connective tissue disorders,ischaemic neuropathies, infectious diseases ortumours, which are less common but clinical and therapeutic management can differ significantly. We present two patients admitted to our hospital with optic neuropathy. Differential diagnosis of optic neuritis and clinical red signs that require careful diagnostic assessment for other diseases have been discussed.A flow chart for the diagnosis of optic neuropathies is presented.

Keywords: Multiple sclerosis, Optic neuritis, NAION, AAION, NMO

Abbreviations: ON-Optic neuritis, MS- multiple sclerosis, RAPD- relative afferent pupillary defect, ONTT- Optic Neuritis Treatment Trial, SLE-systemic lupus erythematosus, SS- Sjögren's syndrome, NMO- Neuromyelitis optica, NAION- Non arteriticischaemic optic neuropathy, AAION- arteritic anterior ischaemic optic neuropathy, PION- Posterior ischaemic optic neuropathy, GCA- giant cell arteritis, VFA- Visual fields anlysis, FFA- Fundus fluorescein angiography, VEP- Visually evoked potential, MRI- Magnetic resonance imaging, DMD-disease-modifying drugs, RNFL- retinal nerve fiber layer

Optic neuritis (ON) is the most common cause of acute unilateral visual loss in young adults with an incidence of 1–5 in 100,000 per year. Caucasians and women are more often affected, with a peak manifestation between the ages of 15 and 49[1,2]. Patients with Optic neuritis typically present with the triad of subacute unilateral loss of vision, periocular pain on eye movement and impaired colour vision. The symptoms usually worsen over the course of a few days to 2 weeks but spontaneously recover in >90% of cases after 2–3 weeks regardless of treatment occurs. In most patients a relative afferent pupillary defect (RAPD) is obvious, although this is not specific to Optic neuritisand is present in most optic neuropathies[2]. An atypical clinical presentation, e.g. no pain, bilateral vision loss or absence of spontaneous recovery after 2–3 weeks should prompt careful diagnostic search for other differential diagnoses.

In most individuals, Optic neuritis is caused by idiopathic inflammatory demyelination. This may occur as an isolated syndrome or in association with multiple sclerosis (MS). Approximately 50% of patients with isolated ON develop MS within 15 years[1]. The most predictive factor for the development of MS after ON is the presence of asymptomatic demyelinating lesions in the central nervous system. In the Optic Neuritis Treatment Trial (ONTT) the 5-year risk for definite MS was 52% in those patients with one or more asymptomatic white matter lesions on brain MRI compared with a 5-year risk of only 16% in patients with normal brain MRI[3].

CASE 1:

42 year old female presented with complaints of sudden onset diminution of vision in both eyes noticed 2 months back. There was no associated pain on eye movement, headache, nausea, vomiting ortransient ischaemic attack.No history of systemic illness. Best corrected visual acuity in right eye(RE) FC 2mt and left eye (LE) 6/36, near vision in both eyes was N36. On examination, anterior segment was normal, pupil was circular reacting to light, no colour desaturation. Fundus examination of RE showed a pale, tilted disc with blurred superior disc margin. Hard exudates inferior to disc were seen.Macular star present. Left eye disc was tilted with superior blurring of disc margin. Inferior conus with disc pallor was seen.

Investigations: Hb – 8.3gm/dl, TLC– 11000cells/mm^3 ESR – 49mm/hr, RBS – 89mg/dl, Urine examination – normal.

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VFA showed generalized depressed fields. MRI – Bilateraloptic nerve shows hyperintense signal, with perineural fat stranding suggestive of bilateral optic neuropathy.

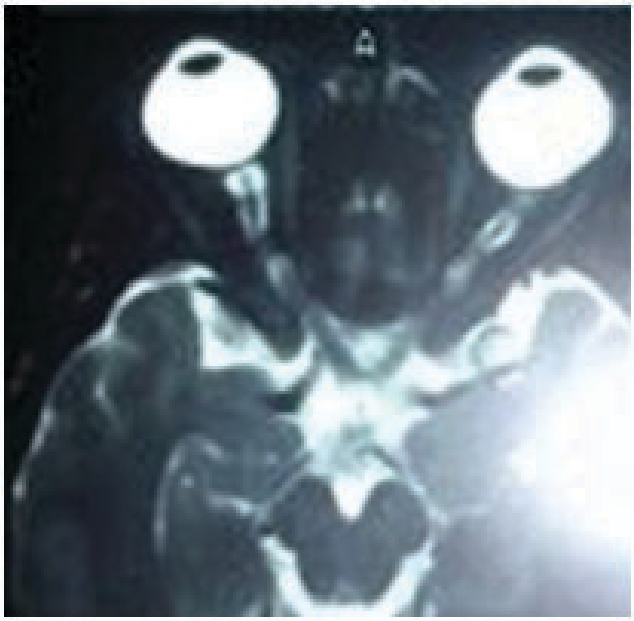

Fig 1.

Differential diagnosis of NAION was made in view of pallid disc oedema, but NAION is usually unilateral, and improvement of vision to 6/12 in RE and 6/9 in LE and near vision to N6, after a trial of iv methylprednisolone 1 gm x 3 doses,(tapered by oral prednisolone over 11 days) confirmed optic neuritis.

CASE 2:

54 year old male was operated for RE cataract. Preoperative vision RE is 6/60 and LE 6/9 with normal fundus in both eyes.Preoperative systemic investigations were normal. There was no history of hypertension, diabetes, sleep apnea. He was a smoker, used to smoke 10-12 cigarettes a day. Post op day 1 RE vision 6/18 with normal IOP. On 14th post op day, patient complained of diminution of vision in RE. Uncorrected visual acuity is 6/60, intraocular pressure was normal. Fundus of RE showed elevated disc with dilated veins with scattered hemorrhage with macular oedema. LE normal.

FFA showed disc leakage (Fig 2) and VFA altitudinal defect (Fig 3) in the right eye. Left eye was normal. Diagnosis of RE NAION was made.In view of disc oedema patient was started on 40mg oral prednisolone and tapered over 4 weeks. Visual acuity improved to 6/12.

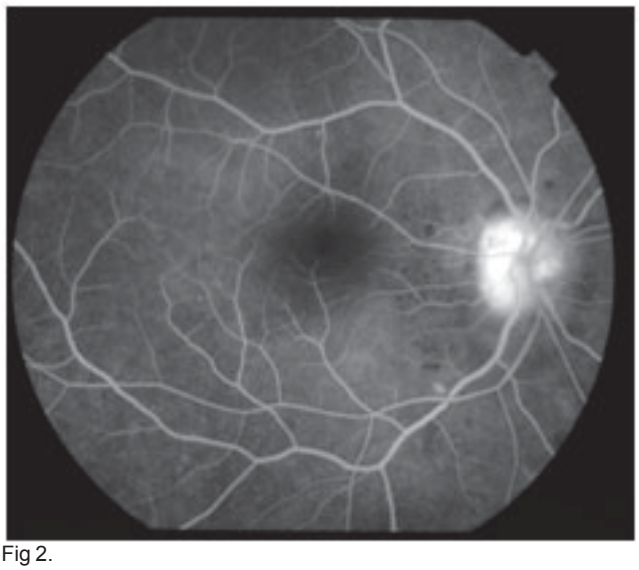

Fig 2.

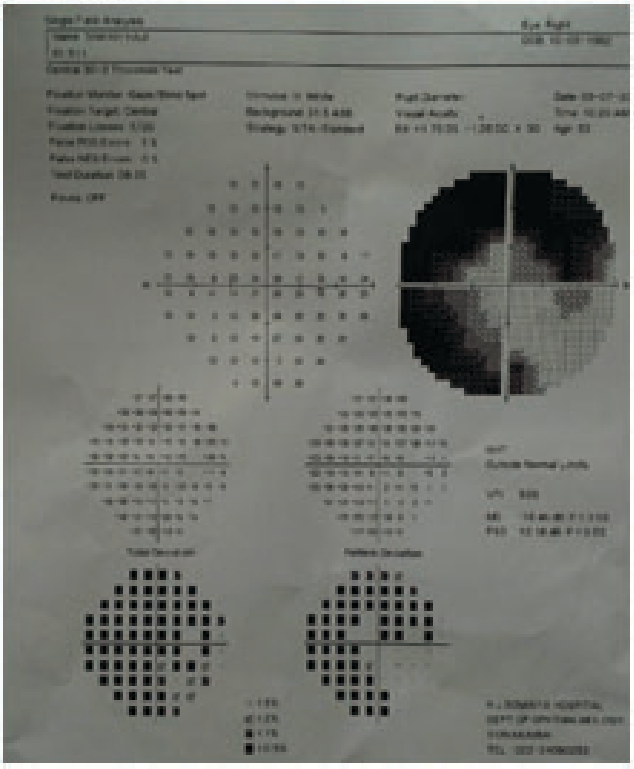

Fig 3.

Discussion:

ON is the most common cause of acute unilateral optic neuropathy in young adults (20-40years old). It is more common in Caucasian females. Typically a patient with ON presents with acute or subacute, unilateral vision loss which can be progressive up to 2 weeks. There may be

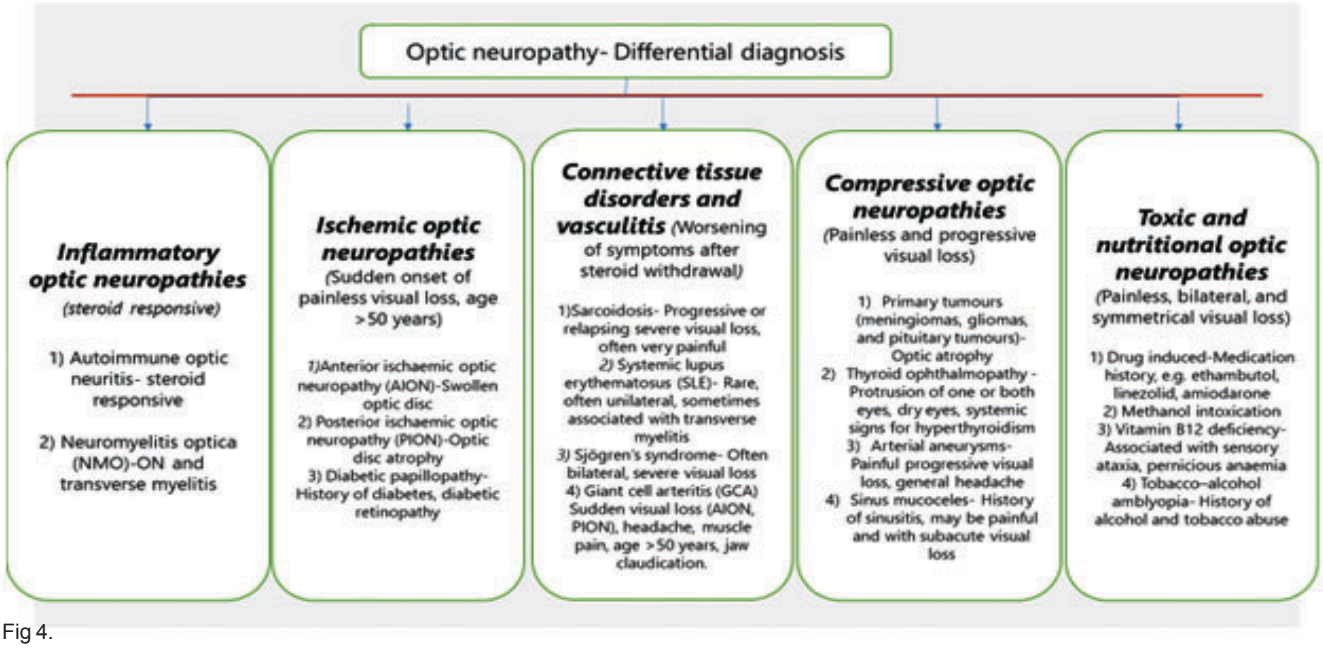

Fig 4.

periocular pain and painful eye movement. Previous history of ON or MS and neurological signs and symptoms suggestive of MS must be looked for. On examination, reduced colour and contrast vision and RAPD may be seen, optic disc may be normal or swollen, macula and peripheral retina are generally normal. Routine Blood tests including CBC, ESR, CRP, glucose, ANA should be done in all cases of suspected optic neuritis. MRI shows optic nerve enhancement and periventricular multifocal white matter lesions which may or may not enhance -Dawsons fingers. There may be spontaneous recovery after 2–3 weeks. Intravenous methylprednisolone (1g per day for 3–5 days) can be considered to speed the recovery of visual acuity, however, this does not affect the long-term visual outcome (Optic Neuritis Treatment Trial).In those patients with no or incomplete recovery after steroid treatment a plasma exchange therapy may facilitate an improvement of visual function. In patients with single episode of ON, the risk of developing MS is estimated to be low if the MRI remains negative for demyelinating white matter lesions over time[3,7]. In recurrent inflammatory optic neuropathy, patients typically suffer from severe, painful and subsequent bilateral visual loss that is ameliorated by corticosteroids but often relapses after withdrawal of steroids. These patients usually require long-term immunosuppression with DMDs[8].

If a patient with optic neuropathy, presents with atypical features likeatypical age, progressive visual loss for >2 weeks, no perceptions of light, bilateral visual loss, severe or persistent pain >2 weeks, optic disc haemorrhage, marked uveitis or retinal periphlebitis, deterioration after withdrawal of steroids; we should look for clinical symptoms suggestive of diseases other than MS (NMO, connective tissue disorders, tumors, ischaemia), the prognosis and treatment of which are completely different from ON associated with MS[4,5,6]. A flowchart for the diagnosis of ON is summarized in Fig 5.

Devics disease or NMO (Neuromyelitis optica),is a demyelinating autoimmune disease that in contrast to

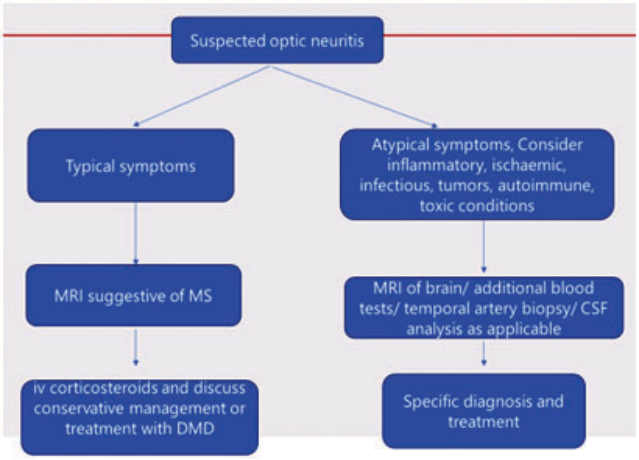

Fig 5.

MS,primarily affects the optic nerve and spinal cord. [9] The clinical presentation of ON in NMO is variable but is often bilateral and recurrent, and visual loss is more severe with less improvement when compared with ON seen in MS. If the patient is a <12 or >40 years of age, presents with severe pain, retrobulbar optic neuropathy or papillitis, no RAPD due to bilateral presentation, consider NMO. History of intractable hiccups, nausea vomiting, symptomatic narcolepsy must be sought. MRI with gadolinium may show longitudinally extensive enhancement or bilateral or chiasmal enhancement of the sheath. Serum NMO immunoglobulin G Ab (NMO-IgG), that bind to the water-channel protein aquaporin-4, has been established as a biomarker for NMO. These antibodies are highly specific (>90%) with a sensitivity of 65%)[9]. The differentiation of NMO from MS is of importance for the long-term treatment, as the disease-modifying drugs (DMDs) used for MS are usually ineffective in NMO.Immunosuppressive treatment with azathioprine or rituximab as a first-line or with mitoxantrone, cyclophosphamide or mycophenolate mofetil as a second-line therapy is recommended[10].

Patients with ischaemic optic neuropathy typically present with of a sudden onset monocular painless loss of vision. These patients are usually of older, >50 years of age and have a history of cardiovascular riskfactors[11]. It occurs due to inflammatory or thrombotic occlusion of posterior ciliary artery or due to blood loss following surgery. Ischaemia can occur anterior (anterior ischaemic optic neuropathy - AION) or posterior (posterior ischaemic optic neuropathy- PION) to lamina cribrosa. AION again could be of two types arteritic (AAION) and non arteritic (NAION).

NAION is seen in younger age groups, usually unilateral, optic disc in affected eye may be swollen. Pallor is less common. Visual acuity is> 20/200 in over 60% of cases. VFA shows altitudinal defect in the affected eye. Optic disc in other eye shows small crowded discwith small or absent cup.5 year risk of other eye is 14.7%.Risk factors for NAION are systemic hypertension, diabetes, smoking, hyperlipidemia, sleep apnea, phospho-diestrase inhibitors. There is no effective treatment for NAION,treat the vasculopathic risk factors, aspirin can be given if there are no contraindication. Steroids have been used to reduce the disc oedemae specially in the incipient form of NAION, but it is not considered as a standard of care.

In elderly patients, especially when visual loss is associated with eye pain, AAION associated giant cell arteritis (GCA) should always be considered as differential diagnosis and routine blood testing should include ESR, CRP, platelet count. Symptoms of GCA like headache, scalp tenderness, jaw claudication, TIA, transient diplopia, amaurosis fugax must be asked for. Severe visual loss, palid disc oedema may be seen. F.F.A shows delayed choroidal filling. Temporal artery biopsy confirms the diagnosis. Immediate therapy with IV prednisolone 1 g/ day for 3-5 days, tapered with oral prednisolone 100 mg/ day over 3-12 month or more.

Posterior ischaemic optic neuropathy (PION) is diagnosis of exclusion and is characterized by unilateral or bilateral sudden vision loss without disc oedema but subsequent optic disc atrophy. Most common risk factor for PION are GCA, history of cardiac, spine surgery (where ischaemia could be attributed to blood loss, hypotension).

Connective tissue disorders such as Systemic Lupus Erythematosus, Rheumaoid Arthriris, Sjogren's Syndrome or systemic vasculitis and granulomatous optic neuropathies like sarcoidosis or Wegener's granulomatosis can all be associated with optic neuropathy[12,13]. In most patients with connective tissue disorders, sarcoidosis or vasculitis, signs and symptoms of other systemic disorder can be found, although the inflammatory activity can be, at least initially, restricted to the optic nerve. Typically, these optic neuropathies come along with severe eye pain and progressive visual loss. The bilateral presentation, absence of spontaneous improvement and recurrence of symptoms after steroid withdrawalare red flags and are suggestive of other corticosteroid-responsive optic neuropathies. Immunological laboratory tests (e.g. ANA, ACE, RF, anti-dsDNA-Ab, p/c ANCA, anti-phospholipid Ab) may lead to the correct diagnosis[4]. However, in some cases these parameters may be negative and only a biopsy can reveal the correct diagnosis.

Infections such as syphilis, tuberculosis, Lyme disease, toxoplasmosis, cat-scratch disease or viruses (e.g. herpes, hepatitis A virus or enteroviruses) may also cause optic neuropathies that are characterized with a progressive visual loss and severe optic disc oedema on fundus examination[14]. In children postinfectious or postvaccination optic neuropathies and neuroretinitis

presenting with swollen optic disc and macular star should also be considered[15].

Different kinds of tumours can cause clinical signs suggestive of ON due to compression of the optic nerve. Patients with compressive optic neuropathies caused by primary tumours or metastases, complain of a slowly progressive, painless vision loss, and often atrophy of the optic nerve is evident[16]. However, painful eye movement can be reported in patients with mucoceles[17]. or arterial aneurysms. Thyroid eye disease should be kept in mind as a cause of compressive optic neuropathy. Conventional and gadolinium-enhanced orbital MRI are important diagnostic tool to ascertain an orbital or retro-orbital lesion. Biopsy may be required to differentiate between primary tumours and other inflammatory diseases when MRI is inconclusive.

In most cases a thorough ophthalmologic examination including visual acuity, pupillary reaction, colour vision, visual field and fundoscopy can detect ocular cause of visual loss. VEP can help to differentiate between a retinal disease and an optic nerve dysfunction. Even though VEP is not useful to distinguish between different causes of optic neuropathy in the acute phase, it can facilitate to evaluate recovery in follow-up examination or to identify subclinical optic nerve dysfunctions. Optical coherence tomography (OCT) RNFL can aid to estimate neurodegeneration in MS and to differentiate between ON in MS and ON in NMO[18].

Conclusion:

It is advisable that when a patient presents with typical clinical features of ON, an MRI scan with gadolinium should be performed to assess the risk for development of MS and treated accordingly.

In a patient with suspected ON presenting with atypical findings, a careful ophthalmologic examination, an orbital and brain MRI with gadolinium and specificlaboratory tests should be carried out to rule out other aetiologies such as tumours,connective tissue disorders or infections, that require specific management. VEP can help identify optic nerve dysfunction and assess recovery on followup.

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