Clinical spectrum of first episode of optic neuritis in a tertiary care hospital in Southern India – A retrospective analysis

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Abstract:

PURPOSE: The purpose of this study was to determine the demographic and clinical patterns of optic neuritis (ON) in patients presenting to a tertiary health-care institute and to study the incidence of multiple sclerosis (MS), magnetic resonance imaging features in varied ON, treatment outcome, and prognosis.

METHODS: A retrospective analysis of patients with first episode of ON presenting to a tertiary care center during the period from March 2013 to March 2021 was done. Details of ocular examination were retrieved from medical records and statistically analyzed.

RESULTS: Three hundred and fifty-four participants with ON were included in this study. The mean age was 40.25 ± 12.2 years. The male: female ratio was 1:1.35. 48.1% had visual acuity of <3/60. Based on clinical presentation, papillitis was seen in 31.5% of subjects, neuroretinitis in 24.1%, and retrobulbar neuritis in 44.4%. Based on etiology, 79.6% were idiopathic, 1.8% presented with infectious ON, and 9.26% were associated with demyelinating disease (MS).

CONCLUSION: Females were predominantly affected. Idiopathic ON formed the major subset etiologically. Sixty-six percent had visual recovery of 6/18 or better following corticosteroid therapy. 9.2% revealed multiple intracranial lesions on neuroimaging, suggesting high association with MS. Therefore, early diagnosis, vigilant monitoring of steroid therapy, and regular follow-up screening for MS remain the mainstay of management in ON.

Keywords:

Multiple sclerosis, Optic neuritis, Retrospective analysis, Southern India

Introduction

Optic neuritis (ON) is an inflammatory condition of optic nerve characterized by unilateral, subacute visual loss without systemic or neurological symptoms. Female gender is three times more predisposed than male. This disorder shows a predilection for young women in the age group of 14–45 years.[1,2] Optic nerve inflammation shows varied presentations such as papillitis manifesting with an edematous optic disc, retrobulbar ON featuring a normal fundus, and neuroretinitis characterized by optic disc edema with a macular star.[1-3] ON is commonly seen in association with demyelinating diseases such as multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSDs), and myelin oligodendrocyte glycoprotein (MOG) associated diseases.[1,4]

Idiopathic, infective, neoplastic, toxic, metabolic, and hereditary neuropathies may contribute as predisposing factors for optic neuropathy.[1,3] In MS, ON is often the premonitory manifestation or develops later in the disease course.[1,4]

Typical ON is a clinical synonym for idiopathic demyelinating optic neuropathy that is often associated with MS, whereas atypical ON is a group of disorders that can be infectious, noninfectious, or postvaccination (e.g., neuromyelitis optica [NMO], syphilis, herpes simplex virus, cytomegalovirus, systemic lupus erythematosus, influenza virus, sarcoidosis, hepatitis, yellow fever, and rubella vaccines).[1,2] Typical ON usually presents as an acute, unilateral,

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inflammatory demyelinating disorder with characteristic magnetic resonance imaging (MRI) findings. However, atypical ON may be bilateral with systemic involvement.[2] Atypical ON is usually seen as a case of NMO or NMOSD.[5] Atypical features include lack of pain, bilaterality, lack of response to treatment, optic nerve head hemorrhages, cotton wool spots, or relapse upon tapering steroids. Causes of atypical ON vary widely and require thorough examination and exhaustive laboratory testing when suspected. The presence of atypical features and systemic associations should raise the suspicion of an alternate etiology that might be treatable.[1,4,5]

In this study, we discuss the presentation of ON, etiology, neuroimaging features, and outcome of therapy in a retrospective analysis from March 2013 to March 2021 in a tertiary hospital.

Methods

In this retrospective observational study, data were retrieved from the medical records of the patients with ON, who attended the ophthalmology and neuromedicine services of a tertiary health-care hospital, from the period of March 2013 to March 2021. The patients clinically diagnosed with ON based on presenting symptoms and clinical examination comprising visual acuity, relative afferent pupillary defect (RAPD), color vision, and fundus examination were included. MRI with contrast was performed in all patients to detect demyelinating disorder. Patients with evidence of hereditary, vascular, toxic, metabolic, infiltrative, or compressive optic neuropathy were excluded from the study.

A detailed history was rendered regarding the onset of visual loss, duration, laterality, painful extraocular movements, color desaturation, similar episode in past, and history of neurological symptoms. Clinical examination included visual acuity by Snellen chart, pupillary reflexes, swinging-flashlight test, extraocular movements, color vision using Ishihara chart, slit-lamp biomicroscopy with +90D lens, and fundus examination using indirect ophthalmoscope. We analyzed the clinical presentation, treatment outcome, and association with MS.

Statistical analysis was carried out using the Statistical analysis was carried out using software SPSS version 19.0. Independent "*t*"-test was used to detect the correlation between age and gender. $P < 0.05$ was considered statistically significant.

Results

Three hundred and fifty-four patients were enrolled in this study, of which 167 were males and 187 were females. The mean age was 40.25 ± 12.2 years. The mean age of male and female patients was 42.5 ± 14.5 and 40.2 ± 15.2, respectively. The difference in mean age among the genders was not statistically significant ($P = 0.57$). The demographic data of patients are shown in Table 1. Majority (98.1%) of the sample experienced unilateral ON. Left eye (55.55%) involvement was marginally more than the right (44.4%). The visual acuity at presentation was 3/60 or worse in 170 patients (48.15%) and 4/60 or better in 184 (51.85%) [Table 2]. Painful ocular movements were documented in 210 patients (59.2%). No significant family history was noted in 341 (96.2%) cases. Defective color vision and relative afferent pupillary defect (RAPD) were noted in all patients. Clinically, papillitis was seen in 31.5%, neuroretinitis in 24.1%, and retrobulbar neuritis in 44.4%. Radiological and immunological workup was done in all patients to rule out other possible etiological factors. 9.2% demonstrated lesions of MS on MRI brain at presentation [Table 3 and Figures 1-3]. Methylprednisolone 250 mg every 6 h for 3 days followed by oral prednisolone 1 mg/kg/day for 11 days was administered

Table 1: Age-gender distribution of patients

Age (years)	Male	Female	Total (%)
<25	10	69	79 (22.2)
26–45	68	56	124 (35.1)
46–60	57	61	118 (33.3)
>60	16	17	33 (9.2)
Total (%)	151 (42.5)	203 (57.4)	354

Table 2: Examination findings of patients

Variables	Total ($n=354$), *n* (%)
Laterality	
Right	157 (44.4)
Left	197 (55.5)
Visual acuity at presentation	
<3/60	170 (48.15)
4/60–6/60	118 (33.33)
6/36	66 (18.52)
Color vision	
Decreased	354 (100)
Painful eye movement	
Absent	144 (40.7)
Present	210 (59.2)
Painful vision loss	
Present	27 (7.5)
Absent	327 (92.6)
Pupillary reaction	
Defective	534 (100)
Optic disc	
Blurred	242 (68.5)
Normal	112 (31. 4)
Vision poststeroid	
<6/24	26 (7.4)
6/18–6/12	151 (42.6)
6/9	177 (50)
Color vision poststeroid	
Defective	79 (22.22)
Normal	275 (77.77)
MRI – MS lesion	
Present	33 (9.26)
Absent	321 (90.74)
Family history	
Present	13 (3.7)
Absent	341 (96.2)

MRI: Magnetic resonance imaging, MS: Multiple sclerosis

Table 3: Descriptive features in magnetic resonance imaging of our subjects presenting with multiple sclerosis, idiopathic optic neuritis, and poor visual acuity poststeroid therapy

Characteristic features – MRI	Idiopathic ON (*n*=282), *n* (%)	Visual acuity <6/24 after ONTT therapy (*n*=26), *n* (%)	MS (*n*=33), *n* (%)
Presence of optic nerve enhancement	115 (40.7)	7 (26.9)	12 (36.3)
Presence of optic nerve thickening	1 (0.3)	6 (23.1)	11 (33.3)
Hyperintensity of optic nerve on FLAIR	2 (0.7)	8 (30.7)	8 (24.1)
Retrobulbar optic nerve enhancement	157 (55.6)	4 (15.3)	2 (6.1)
Bilateral disease on MRI	7 (2.4)	1 (3.9)	0

MRI: Magnetic resonance imaging, MS: Multiple sclerosis, ON: Optic neuritis, ONTT: ON treatment trial, FLAIR: Fluid-attenuated inversion recovery

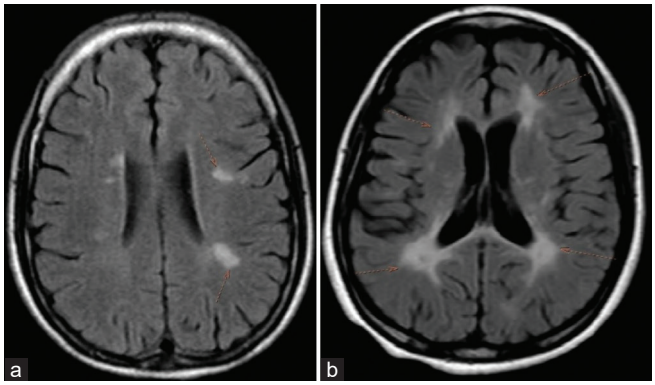

Figure 1: (a and b) Magnetic resonance imaging T2-weighted (fluid-attenuated inversion recovery) axial view showing multiple hyperintense lesions predominant in white matter, callosal, and pericallosal region in frontal, parietal, and temporal lobe

in all 354 subjects. The visual acuity improved in 328 (92.6%) patients equal to or better than 6/18, after a span of 2 weeks. In the other 26 patients (7.4%), it remained <6/24.

Discussion

ON is described as primary inflammation of the optic nerve associated with a variety of systemic disorders, acute demyelinating ON being the most common form. Based on the site of clinical involvement, ON is classified as retrobulbar neuritis which presents with normal fundus picture, papillitis manifesting as swollen disc, perineuritis characterized by optic nerve sheath inflammation, and neuroretinitis with optic disc edema and macular star.[1,2,4] It is primarily a clinical diagnosis based on history and examination findings. Funduscopic features aid in differentiating typical from atypical cases.[1,4]

Pathogenesis – Optic neuritis

The pathogenesis of ON depicts activated peripheral T-cells migrating and crossing blood–brain barrier, eventually releasing inflammatory mediators such as cytokines leading to axonal degeneration and cell death. ON most commonly affects healthy young adults between 20 and 45 years of age, female-to-male ratio being 3:1.[5,6] Infective etiology may occur due to direct neuronal entry by the virus leading to endothelial cell dysfunction causing ischemia and coagulopathy.[1] Neuronal involvement also occurs due to viremia traversing blood–brain barrier or through infected leukocytes.[2]

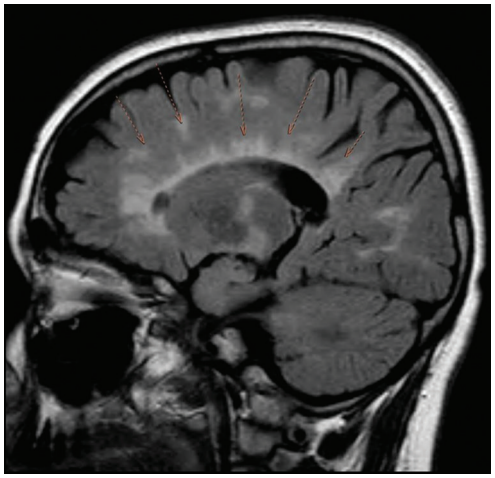

Figure 2: Magnetic resonance imaging T2-weighted (fluid-attenuated inversion recovery) sagittal view sequence revealing multiple hyperintense lesions suggesting periventricular demyelinating plaques perpendicular to the body of lateral ventricle, callosal, and pericallosal region – "Dawson fingers" characteristic of multiple sclerosis

Epidemiology

In our study, the mean age of presentation was 40.25 ± 12.2 years and the number of females (57.4%) affected by ON marginally outnumbered the males (42.5%). The age of presentation and female predilection noted in this study were similar to that reported by the ON Treatment Trial (ONTT) and other studies.[6-8]

The etiology of ON was noted to be idiopathic in the majority of the patients, following an exhaustive array of systemic investigations. Angiotensin-converting enzyme, chest X-ray, enzyme-linked immunoassay, venereal disease research laboratory for syphilis, immunofluorescence assay for *Bartonella henselae*, HIV, IgG for herpes, Lyme serology, anti nuclear antibody , antineutrophil cytoplasmic antibody, erythrocyte sedimentation rate, and C-reactive protein were done to rule out infectious and immune causes.[1,3]

Our study revealed six patients with infective etiology, namely 16.6% had herpes zoster, 16.6% had positive immunofluorescence assay for *Bartonella henselae,* and 33.3% had syphilis, whereas two patients (33.3%) were Mantoux positive suggestive of tuberculosis [Table 3]. In this study, retrobulbar ON was noted in 157 patients (44.4%), neuroretinitis in 85 (24.1%), and papillitis in 112 subjects (31.5%), which

correlate well with an Indian study.[6,8] Furthermore, 98.1% manifested unilateral ON which parallels other studies.[8]

Role of imaging – Optic neuritis

The involvement of the left eye was noted in 55.5%. No specific predilection for the right or left eye has been reported in the literature.[3] MRI brain is a valuable predictive tool in detecting patients at high risk of MS.[9-12] The potential use of immune-modulating therapy requires a multidisciplinary approach, collaborating ophthalmology, and neurology services.[10] 15%–20% of patients with MS feature ON at initial presentation and 50% develop the condition sometime during the course.[4]

All 354 patients in this study presented with sudden onset of defective vision which worsened subsequently over the next few days. MRI revealed demyelinating lesions suggestive of MS in 33 patients (9.2%). Optic nerve enhancement and thickening was the universal manifestation in our patients with MS. The risk of developing MS in ON was noted to be three times higher in women with positive lesions on baseline MRI when compared to those with normal neuroimaging.[11] Patients presenting with optic nerve head enhancement on imaging should promptly be worked up to rule out demyelinating etiology. 36.3% of our MS patients showed optic nerve head enhancement. A single MRI lesion doubled the 15-year risk to 50%, while three or more lesions increased it to 78%.[12] We found bilateral optic nerve head enhancement in 2.4% of patients, whereas Burman *et al*. found that simultaneous bilateral involvement was a rare occurrence of 0.42%[13,14] [Table 4].

Optic Neuritis Treatment Trial

The patients were treated with intravenous methylprednisolone 1 g/day for 3 days followed by oral prednisolone at a dose of 1 mg/kg/day in a tapering regimen for 2 weeks. Corticosteroid therapy was deferred in 5.56% due to systemic contraindications such as uncontrolled diabetes and hypertension.

In this study, painful ocular movements were present in 59.26% of cases in contrast to ONTT which reported the same in 92%.[8,10,12] Defective color vision at presentation was a unifying feature in all participants in the study. 22.2% showed persistent gross dyschromatopsia after corticosteroid therapy.

Visual outcome

Our study denoted that visual outcome was <6/24 in 33.33%, 6/18–6/12 in 42.592%, and <6/9 in 24.074%. Detailed evaluation to exclude NMOSD was done in patients with poor visual recovery. Although extensive differential diagnostic testing is warranted to detect the underlying cause, blood and neuroimaging revealed nothing noteworthy. An overall prognosis in terms of visual acuity and color vision was good. Detailed workups including aquaporin–four antibodies and anti-MOG antibodies for NMO were done in patients with poor visual recovery and were unremarkable.

In our patients, about 26.9% had optic nerve head enhancement with poor visual recovery post steroid therapy. In a study on Indian patients with ON, response to intravenous pulsed dexamethasone led to rapid recovery of vision in 81.4% with full visual outcome paralleling to our study.[8]

Table 4: Detailed investigative workup denoting infectious optic neuritis

Investigation	Infectious ON ($n=6$), n (%)
Chest X-ray, Mantoux (tuberculosis)	2 (33.3)
ELISA, VDRL (syphilis)	2 (33.3)
Immunofluorescence assay *Bartonella henselae*	1 (16.6)
IgG for herpes zoster	1 (16.6)
Blood culture – Positive	0

ON: Optic neuritis, VDRL: Venereal disease research laboratory

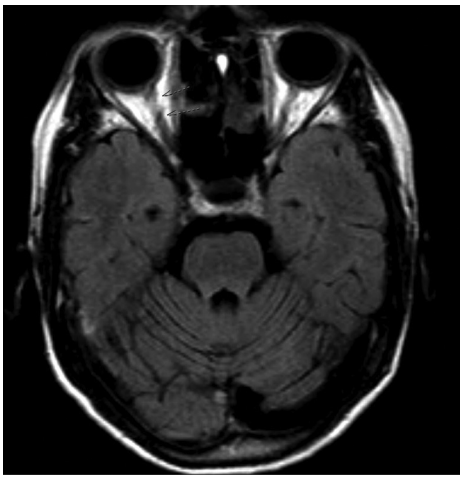

Figure 3: Magnetic resonance imaging T2 weighted (fluid- attenuated inversion recovery) Coronal view sequence revealing optic nerve head enhancement in a patient with optic neuritis

This retrospective comprehensive study of 354 patients with collaborative MRI imaging feature reveals infectious etiology in a minority. It is essential to do a comprehensive workup for every patient presenting with ON. The likelihood of development of acute ON in patients with MS needs to be considered and dealt with prudently.

A prospective study would better aid in evaluating visual outcome, prognosticate the risk of developing MS following first episode of ON, and assess long-term recurrence in all the study subjects. A retrospective study limits the above.

Conclusion

The clinical profile of ON in our patients was in concordance with multiple studies in the Asian subcontinent. Ruling out an infective, inflammatory, or autoimmune history is imperative in the management of ON. A judicious reference to an ophthalmologist helps in early diagnosis of the underlying etiology and enhances visual outcome.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Atkins EJ, Biousse V, Newman NJ. Optic neuritis. Semin Neurol 2007;27:211-20.
2. Balcer LJ. Optic neuritis. N Engl J Med 2006;354:1273-80.
3. Alamgir MJ, Ali SA, Hamdy NA, Khan MZ, Mohammad EE. Optic neuritis: Observation and experience at a tertiary care hospital in Qassim region, Saudi Arabia. Int J Health Sci (Qassim) 2017;11:30-4.
4. Gaier ED, Boudreault K, Rizzo JF 3rd, Falardeau J, Cestari DM. Atypical optic neuritis. Curr Neurol Neurosci Rep 2015;15:76.
5. Sarkar P, Mehtani A, Gandhi HC, Dubey V, Tembhurde PM, Gupta MK. Atypical optic neuritis: An overview. Indian J Ophthalmol 2021;69:27-35.
6. Pau D, Al Zubidi N, Yalamanchili S, Plant GT, Lee AG. Optic neuritis. Eye (Lond) 2011;25:833-42.
7. Zhang X, Wang W, Wei W, Wang Q, Wei Y, Kermode AG. Etiological profile of presumptive optic neuritis in China. J Clin Neurosci 2008;15:1346-9.
8. Suehiro S, Adachi-Usami E, Miyauchi O, Mizota A, Tsuyama Y, Fujimoto N, *et al.* Clinical profiles of patients with optic neuritis at the Ophthalmological Department of Chiba University. Neuro-Ophthalmol 2002;27:153-62.
9. Godar MS, Sharma AK, Thapa M, Sitaula S, Gurung S. Demographic pattern and clinical characteristics of optic neuritis in a tertiary eye care centre. Nepal J Ophthalmol 2017;9:51-5.
10. Rose N, Anoop TM, John AP, Jabbar PK, George KC. Acute optic neuritis following infection with chikungunya virus in southern rural India. Int J Infect Dis 2011;15:e147-50.
11. Optic Neuritis Study Group. Multiple sclerosis risk after optic neuritis: Final optic neuritis treatment trial follow-up. Arch Neurol 2008;65:727-32.
12. Menon V, Saxena R, Misra R, Phuljhele S. Management of optic neuritis. Indian J Ophthalmol 2011;59:117-22.
13. Burman J, Raininko R, Fagius J. Bilateral and recurrent optic neuritis in multiple sclerosis. Acta Neurol Scand 2011;123:207-10.
14. Kahloun R, Abroug N, Ksiaa I, Mahmoud A, Zeghidi H, Zaouali S, *et al.* Infectious optic neuropathies: A clinical update. Eye Brain 2015;7:59-81.