SCIENTIFIC REPORT

Clinical profile of simultaneous bilateral optic neuritis in adults

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Aim: To establish the clinical profile of simultaneous bilateral optic neuritis in adults, the efficacy of steroid therapy, extent of visual recovery, and neurological outcome.

Methods: The authors performed a retrospective review of records of patients referred to a neuro-ophthalmology service with acute bilateral optic neuritis from 2000–4. Exclusion criteria included previous multiple sclerosis or myelopathy, known systemic disorders or medications associated with optic neuropathy, uveitis, or neoplasm. Patients received intravenous methylprednisolone followed by oral prednisone. Visual acuity (logMAR conversion), mean deviation (dB) for visual fields, percentage of Ishihara plates seen, ophthalmoscopy, and neurological evaluation were recorded at baseline and at 6 months or 12 months. Owing to strong correlation for visual loss between eyes, the results for the worse eye in each patient were analysed.

Results: 11 men and four women, with an age range of 18–64 years, had bilateral decreased vision, 12 with pain on eye movement. Except for one patient, no aetiology was found. All patients had normal neurological evaluations, average visual acuity 1.71 (SD 0.55), colour vision 2.7% (SD 9.9%), and mean deviation −25.35 dB (SD −7.95 dB). Both optic nerves showed abnormal signal on magnetic resonance imaging. 14 patients improved and their last average visual acuity, colour vision, and mean deviation were 0.36 (SD 0.54), 69% (SD 46%), and −7.05 dB (SD 8.40 dB), respectively. No patient developed a neurological problem during the follow up with a mean of 11 months.

Conclusion: Idiopathic acute bilateral optic neuritis without myelopathy occasionally occurs in adults. Vision recovers with corticosteroid therapy and during the first year neurological dysfunction will frequently not occur.

Bilateral optic neuritis is usually thought to affect children, often follows a viral syndrome, and is not typically associated with subsequent multiple sclerosis.[1] In contrast, in adults simultaneous bilateral acute optic neuritis has been considered rare particularly in individuals without known systemic inflammatory or autoimmune disorders. Adult onset optic neuritis is typically unilateral and is commonly linked to multiple sclerosis. The natural course of the most unilateral acute optic neuritis is sudden onset of visual loss associated with pain on eye movement, which reaches its maximum deficit over 1–7 days. Vision recovery is significant regardless of the treatment.[2]

Although sporadic reports describe the presentation of bilateral optic neuritis, few papers have accumulated and described such a phenomenon is a case series of adults.[3] Few reports describe the course, recovery, and outcome after treatment with steroid therapy.[3 4]

Recently we noted an increase in the number of adult patients without known systemic autoimmune or neurological disease, who presented with acute bilateral optic neuritis and we documented the clinical profile. The effectiveness of corticosteroid therapy, time course of visual recovery, and visual and neurological outcome during a 6–12 months follow up were investigated.

Methods

We performed a retrospective review of patient charts and magnetic resonance imaging (MRI) of brain and orbits of patients who presented with acute bilateral optic neuritis to the New York Eye and Ear Infirmary neuro-ophthalmology service during a 4 year period from 2000 to 2004. Patients were included if they presented with new onset of acute bilateral visual loss diagnosed as caused by optic nerve disease, had complete clinical examination, laboratory analyses and MRI performed at presentation, and had follow up clinical examinations over at least 6 months. Exclusion criteria included known multiple sclerosis, previous optic neuritis or myelopathy, known systemic disorders associated with optic neuropathy, use of medications related to toxic optic neuropathy, known uveitis, or known systemic or intracranial neoplasm.

Visual function testing was performed for each eye at baseline and at follow up of 6 months, 12 months, or both. Visual acuity was assessed with wall projected Snellen letter charts and the results expressed in logMAR notation. Perimetry was performed on the Humphrey field analyser (Humphrey Instruments, San Leandro, CA, USA) (Program 24-2) with the mean deviation recorded in decibels (dB) as an outcome measure. Colour vision deficits were recorded using Ishihara colour plates as the percent of plates correctly identified. The presence or absence of pain with extraocular movement was documented. A neurological examination was performed at baseline and at a minimum of 6 months. All patients had MRI of the brain and orbits with coronal and axial view, fat suppression and T1 weighted images with and without intravenous gadolinium, T2 weighted images, and fluid attenuated inversion recovery images at time of initial presentation before therapy. Most patients had coronal view using short tau inversion recovery (STIR) sequence images of the optic nerves to the chiasm.

Each patient had laboratory investigations included haemogram, electrolyte and liver chemistries, angiotensin converting enzyme, antinuclear antibodies, fluorescent treponemal antibody absorption test (FTA-ABS), or microhaematoagglutination treponal test (MHA-TP), venereal disease research laboratory test (VDRL), purified protein derivative, or chest *x* ray if necessary. Cerebrospinal fluid was

Abbreviations: FTA-ABS, fluorescent treponemal antibody absorption test; MHA-TP, microhaematoagglutination treponal test; MRI, magnetic resonance imaging; NMO, neuromyelitis optica; STIR, short tau inversion recovery; VDRL, venereal disease research laboratory test

Table 1 Demographics and baseline evaluation

Case	Sex	Age	Right optic disc	Left optic disc	Pain with EOM*	RAPD†
1	F	38	normal	normal	yes	No
2	M	33	normal	normal	yes	No
3	F	28	oedema	oedema	yes	No
4	M	64	oedema	oedema	yes	Yes, LE
5	M	64	normal	normal	yes	Yes, LE
6	M	28	oedema	oedema	yes	Yes, RE
7	F	39	oedema	oedema	yes	Yes, LE
8	M	40	normal	normal	yes	Yes, RE
9	F	58	oedema	pale, oedema	unknown	No
10	M	46	oedema	oedema	yes	No
11	M	38	normal	normal	no	No
12	M	40	normal	normal	no	Yes, LE
13	M	39	normal	normal	yes	No
14	M	18	oedema	oedema	yes	No
15	M	39	oedema	oedema	yes	Non-reactive

*EOM, extraocular movement; †RAPD, relative afferent pupillary defect.

analysed for cells, protein, glucose, VDRL, and oligoclonal bands in all patients except for one who refused lumbar puncture.

Patients were hospitalised and received intravenous methylprednisolone 1000 mg per day in divided doses for 3–5 days, followed by oral prednisone 60 mg. for approximately 11 days followed by a gradual dose reduction depending on the clinical course.

We analysed the vision for the worse eye at baseline, determined by the visual acuity, followed by colour vision and mean deviation. We compared the baseline to the last examination results for one eye only, the worse eye, because the baseline visual acuity loss strongly correlated with the visual acuity in the opposite eye ($r = 0.60$, $p = 0.017$).

RESULTS

Demographics and presentation evaluation (tables 1 and 2)

There were 15 patients who met the study criteria in contrast with 220 patients with a first episode of idiopathic or demyelinating unilateral optic neuritis evaluated during the same period by the neuro-ophthalmology service. There were 11 men and four women with an age range of 18–64 years. Twelve patients with no previous relevant history were considered to have an unknown aetiology (80%), three patients (20.0%) had an immediate previous viral syndrome. Twelve patients had bilateral pain with eye movement. All 15 had blood evaluations that were normal except case 2 who had a positive MHA-TP with normal spinal fluid. Fourteen

Table 2 Visual performance at baseline and at follow up

logMAR visual acuity				Ishihara plates percentage identified			Mean deviation (dB)	
Case	Baseline	6 months	12 months	Baseline	6 months	12 months	Baseline	Last exam
1 RE	2.0	0		0	100		−30.17	−3.10
1 LE	2.0	0		0	100		−29.61	−1.68
2 RE	2.0	0.1		0	85		−19.56	−1.71
2 LE	2.0	1.3		0	35		−26.26	−20.96
3 RE	0	0		100	100		−8.40	−5.32
3 LE	2	0		0	100		−33.61	−3.40
4 RE	1.3		0.6	20	20		−17.28	−16.11
4 LE	1.3		1.3	0	0		−26.85	−26.36
5 RE	0.1	0.1		90	90		−15.60	−16.10
5 LE	1.3	.2		0	65		−16.96	−16.36
6 RE	1.2	0		0	100		−14.30	−5.02
6 LE	0	−0.1		100	100		−16.26	−4.89
7 RE	1.3	0.1		0	100		−30.00	−1.00
7 LE	2.0	0.1		0	100		−28.00	−4.00
8 RE	2.0	0	0	0	100	100	−27.00	−1.49
8 LE	2.0	0	0	0	100	100	−14.30	−0.046
9 RE	0.2		0.3	15		5	−7.66	−3.00
9 LE	1.0		0.9	5		15	−11.10	−3.00
10 RE	0.9	0	0	35	100	100	−18.52	−0.86
10 LE	2.0	0	0	35	100	100	−21.35	−1.48
11 RE	2.0		0	0		100	−35.00	−3.33
11 LE	2.0		0	0		100	−35.00	−6.99
12 RE	1.0	0.1		0	100		−35.00	−12.15
12 LE	1.0	0.1		0	100		−35.00	−11.68
13 RE	1.0	0.1	0.1	0	100	100	−16.00	−0.98
13 LE	1.0	0.1	0.1	0	100	100	−17.32	−0.35
14 RE	1.0	0.1	0.1	0	100	100	−19.49	−3.30
14 LE	0.4	0	0	0	100	100	−23.58	−2.23
15 RE	Blind	Blind	Blind	0	0	0	Blind	Blind
15 LE	2.0	2.0	2.0	0	0	0	−35.00	−35.00

patients had cerebrospinal fluid analysis (one patient refused), 12 of which were normal. Case 11 had 20 lymphocytes and a protein of 100 mg/dl and case 15 had 53 lymphocytes. All of the T1 weighted fat suppressed MRIs with gadolinium showed bilateral optic nerve enhancement. With T2 weighted imaging, only case 12 had two intracranial white matter bright signal 2 mm lesions, located in the left frontal and right atrial regions.

For the eye with worse vision at baseline, the average visual acuity before treatment was 1.71 (SD 0.55) and all but two eyes saw less than 0.0 (20/20). The average percentage of colour plates seen was 2.7% (SD 9.0%) and all eyes except for the two eyes with 20/20 had abnormal colour vision. All 15 patients demonstrated bilateral abnormal visual fields and the worse eye had an average mean deviation of −25.35 dB (SD −7.95). A relative afferent pupillary defect was present in six patients. Eight patients had ophthalmoscopic evidence of bilateral optic disc swelling, most mild. There was no cellular response in the vitreous and no patient developed a macula start. All patients had normal neurological examinations.

Follow up evaluations (table 2)

Follow up visual evaluations were performed at 6 months for seven patients and at 1 year for eight patients. Two patients experienced recurrence, one while on tapering oral prednisone therapy and one after stopping therapy at 2 weeks. Both recovered after restarting oral prednisone and neither deteriorated with a slower schedule of prednisone withdrawal. One patient, case 15, remained with severe permanent visual loss and no recovery in any parameter and is excluded from the following analysis. Nine patients experienced excellent visual acuity recovery (defined as $\geqslant$0.1, 20/25) bilaterally. For the 14 patients who had some improvement, their worse eye at baseline had a mean visual acuity of 0.36 (SD 0.54) (mean improvement was 1.3 (SD 0.85), $p = 0.001$). Two (cases 9 and 4) patients experienced limited recovery. One of the eyes in case 2 had previous cornea injury and 20/200 was his baseline before the acute vision loss. Nine patients experienced full recovery of colour vision (defined as seeing 100%) bilaterally. For the worse baseline eye the colour vision mean was 69% (SD 45.6%) (mean improvement 71.4% (SD 43%), $p = 0.001$). Three patients had normal visual fields (defined as >-3.50 dB) bilaterally. For the worse baseline eye, the average mean deviation was −7.05 dB (SD −8.40 dB) (mean improvement 16.8 dB (SD 11.0 dB), $p = 0.001$).

No patient had symptoms of subsequent neurological dysfunction and the clinical neurological examination was normal at the last evaluation, performed from 6–18 months.

DISCUSSION

Although the presentation and severity of visual loss in our cases of bilateral optic neuritis was dramatic, recovery was good to excellent in all but one patient. Marked asymmetrical visual loss occurred in four patients (a fifth had amblyopia in one eye before the optic neuritis). It is important to point out that although the age range was similar to the age of typical unilateral optic neuritis, we do not think that these patients had unilateral optic neuritis associated with multiple sclerosis. No eye had the mild visual field depression, typically mean deviation of −3.7 to −6.3 dB, reported for the fellow eye in 13.8% patients with unilateral optic neuritis on admission to the Optic Neuritis Treatment Trial.[5] Bilateral abnormal enhancement was seen in the intraorbital optic nerves in the MRI in contrast with the unilateral finding for affected optic nerves with typical demyelinating disease optic neuritis and no patient had enhancement of the intracranial optic nerves, chiasm, or optic tract.[6] Also, the frequency with which MRI demonstrated white matter lesions of the brain was less than with unilateral optic neuritis. The absence of a relative afferent pupil defect in some cases was probably because of bilateral afferent dysfunction. Cases in which a relative afferent defect was demonstrated more than likely reflected unequal dysfunction between affected optic nerves.

Only one patient had a definitive aetiology (sarcoidosis) identified. Infectious aetiologies, typically a viral prodrome, have been associated with bilateral optic neuritis in children and in unilateral demyelinating optic neuritis, but systemic processes were generally absent in our patients.[7 8] Although bilateral optic neuritis has been described in a patient known to have the immunodeficiency virus 1,[9] the association may be serendipitous and none of our patients developed symptoms of immunodeficiency during the follow up period. Neuromyelitis optica (NMO; also known as Devic's syndrome or Devic's disease) is an autoimmune disorder that affects both optic nerves and the spinal cord.[10] Acute transverse myelitis can be the initial or a later manifestation. None of our patients had a transverse myelitis by history or clinical findings on presentation or at follow up evaluations. It is important to note though that no spinal cord MRI was performed and subclinical disease cannot be excluded. One of the other cardinal features of NMO is a tendency for progressive or recurrent disease during the 6–18 month follow up of our patients. There were only two recurrences, both were associated with premature corticosteroid withdrawal. Except for these two patients, no patient had progressive or recurrent optic neuropathy typical of autoimmune optic neuropathy or chronic relapsing inflammatory optic neuropathy.[11 12]

This study was not a treatment trial and we do not know whether adults might spontaneously improve vision as in adults with idiopathic unilateral optic neuritis or as might occur in children. Given the severity of vision loss and the relative benign adverse effect profile for a limited course of corticosteroids, we opted to treat these patients with intravenous followed by oral corticosteroids. The two patients who experienced recurrent visual loss improved with reinstituting steroids and neither worsened again as the medication was slowly withdrawn. The improvement, whether steroid associated or not and the abnormal signal on STIR and abnormal enhancement on MRI are suggestive of optic neuritis. Our findings support previous reports that suggest that bilateral, presumably inflammatory, optic neuropathy, has a good prognosis in general[13] and could be responsive to high dose corticosteroid therapy.[14]

CONCLUSION

Acute bilateral optic neuritis without myelopathy occurs more often in adults than previously thought. The diagnosis and therapeutic approach to the patients with these symptoms and findings is applicable to patients who present without any previous neurological or associated systemic medical history. The bilateral vision loss typically improves with corticosteroid therapy without additional immunomodulatory therapy and good visual recovery is anticipated even after gradual withdrawal of therapy. Subsequent neurological disease or recurrent visual loss may not develop over the following year.

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