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Original Research Article

Contrast enhanced MRI in acute optic neuritis- length of enhancement a visual prognosis indicator?

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ABSTRACT

Background: To study the baseline length of optic nerve enhancement on contrast enhanced MRI in patients with acute optic neuritis and its correlation to visual acuity, color vision, visual field and contrast sensitivity.

Materials and Methods: The prospective cohort study was conducted on 30 patients attending Ophthalmology clinics with complaint of sudden painful loss of vision and clinical examination findings suggestive of acute optic neuritis. All patients underwent contrast enhanced MRI (1.5 Tesla) at presentation and then treated with intravenous and oral steroids with monthly follow up for 3 months. Visual acuity using Snellen's chart (in LogMAR), Color vision using Ishihara chart and contrast sensitivity by means of Pellie Robson chart were evaluated. The visual field was analyzed by Humphrey's Field Analyser, using a full threshold 30-2 programme.

Results: On contrast-enhanced MRI, all affected optic nerves showed enhancement. The length of portions enhanced for each affected optic nerve was measured. The optic nerves were divided into two categories of length ≤ 17mm and >17mm. At baseline, visual acuity worsened with an increasing length of optic nerve enhancement, color vision and visual field was better in subjects with enhancement <17mm while they do not correlate with the final visual outcome. On the contrary, Contrast sensitivity was found to be improved in subjects with <17mmm of enhancement on the last follow up.

Conclusion: Contrast- enhanced MRI plays a critical role as an adjunct to diagnosing acute optic neuritis especially in patients with retrobulbar neuritis. Initial length of enhancement does not correlate with the final visual outcome.

1. Introduction

Optic neuritis is an acute inflammatory condition of the optic nerve. It has been closely associated with the incidence of multiple sclerosis and is the very first presenting feature in nearly 20%[1–3] of the cases with multiple sclerosis as an isolated syndrome and 50%[4] chance during the course of disease. Typically, loss of vision in cases of acute optic neuritis is sudden and associated with pain in ocular movements. Usually, visual loss in optic neuritis reaches its maximum level within a week's time. Even in the absence of any treatment most patients gain vision over time and visual recovery is considerable. Even when visual acuity recovers to 20/20, mild deficits in other measures of visual function (e.g., contrast sensitivity, color vision and visual field) are common.[5]

Nowadays, MRI is a routine evaluation that is recommended in all patients with acute optic neuritis at the time of presentation. Several studies have been conducted to determine the role and importance of contrast-enhanced

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MRI in such cases. They have demonstrated that following intravenous gadolinium administration in fat suppressed MRI, there is an abnormal enhancement of the optic nerve when affected with optic neuritis[6] or vasculitis of the optic nerve.[7] This does not holds true in patients with nonarteritic anterior ischemic optic neuropathy.

Amongst the studies conducted, several studies support contrast -enhanced MRI as an effective tool to determine the extent of damage to the optic nerve both in terms of length and the segment involved in patients with acute optic neuritis and the effect of these two factors on the visual parameters such as visual acuity, color vision, visual field and contrast sensitivity. Few studies have suggested that the length of the optic nerve affected by optic neuritis on MRI without contrast is associated with the degree of visual loss and might predict visual outcome[8] while others debate that initial information on length and segment of optic nerve involvement are not always consistent with the results of visual recovery.[9–12]

Thus, typical Optic neuritis is an acute, severe visual disturbance without any clear diagnostic finding on ocular examination. It usually affects young otherwise healthy individuals. It may be the first manifestation of multiple sclerosis. Thus, in this study we attempt to establish if the length of the optic nerve measured using contrast -enhanced MRI involved in patients with acute optic neuritis correlates to the visual parameters.

2. Materials and Methods

After obtaining ethical clearance from the Institutional ethical committee a prospective cohort study was conducted on 30 patients in Central India between 2018-2020 who presented in Outpatient department with sudden painful diminution or loss of vision, presence of RAPD along with impairment of visual field and color vision,[13] were labeled as a case of acute optic neuritis. Informed consent was taken from the patients in agreement to participate in the study. Patients were excluded from the study if any of the following criteria were fulfilled; any episode of previous optic neuritis in the affected eye and vision did not return to 20/20; Non arteritic Anterior ischemic optic neuropathy and optic disc pallor of any cause; Visual field loss due to any other ophthalmic disorder; Given corticosteroid treatment for current episode of optic neuritis prior to clinical or MRI evaluation.

A thorough medical history and ophthalmic examination of all cases was conducted including baseline visual acuity, color vision, visual field analysis, contrast sensitivity, intraocular pressure, slit lamp biomicroscopy and fundus examination to rule out other causes of sudden vision loss. Visual acuity was recorded using a self-illuminated Snellen's vision chart situated at 6- meter distance from the subject. The readings were recorded on a LogMAR scale where 0.0 was considered normal vision (equivalent to 6/6 of Snellen's chart) and any vision >0.2 (equivalent to 6/9 of Snellen's chart) was considered a poor vision. Color vision was documented using an Ishihara chart in decimals (number of correct responses / total number of test plates) where normal color vision was ≥0.8 and <0.1 decimal equivalents was considered severe color vision loss. Contrast sensitivity by means of Pellie Robson chart was evaluated with a cut off value of >1.75 log units as normal. Visual field was analyzed by Humphrey's Field Analyser, using full threshold 30-2 program. A MD of ≥ -3dB was considered normal, a poor visual recovery was considered when MD was ≤-6.0dB at the last assessment and a value of -35 dB depicted severe visual field loss (when subject was not able to perform the test, this value was assigned). A gross torch light examination of all subjects was carried out. Swinging torch light test was performed to examine pupillary reaction and to identify RAPD.

Contrast- enhanced magnetic resonance imaging (CEMRI) following intravenous Gadolinium injection was performed at the presentation before systemic steroids were started to know the location of optic nerve involvement. Axial T1, T2 weighted and Fluid Attenuated Inversion Recovery (FLAIR) images; Sagittal T2 weighted images; coronal T2 weighted images were taken using 1.5 tesla superconducting unit with 3mm thick, 0.3mm spaced sections. Based on length of enhancement on CEMRI, the patients were divided into two groups of length >17mm and ≥ 17mm as per the data obtained.

Following CEMRI, blood investigations to rule out infectious etiology were performed. Patients were then treated with intravenous methylprednisolone 1gm daily for 3 days followed by systemic oral prednisolone (1mg/kg) for 10 days then fast tapering over 4 days. The regimen is based on ONTT trial.[14] Follow up examination was conducted at the end of 4, 8 and 12 weeks from the day of presentation and tests for visual improvement were repeated for individual patient at each visit.

2.1. Statistical analysis

Data was collected and stored in MS XL sheet format at the presentation, 1^{st}, 2^{nd} and 3^{rd} follow up. Data for each group was maintained in separate charts for the ease of analysis with SPSS software. Mann Whitney U test was used to determine the differences in the MRI based subcategories and the Fisher exact test for the strength of association between- length of lesion with individual visual parameters; P value of <5% was taken as statistically significant. Spearman rank correlation coefficient was applied to study correlations.

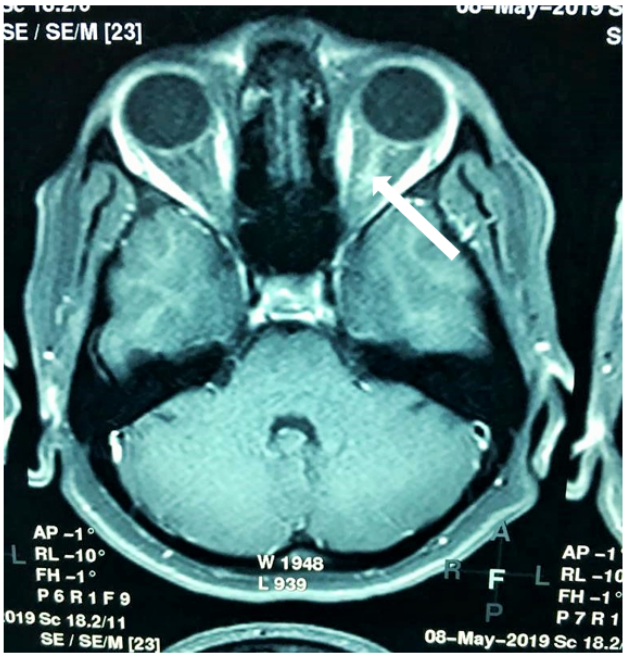

Fig. 1: Magnified image of an axial section of a subject with acute ON showing enhancement of left eye optic nerve sheath (white arrow)

3. Results

3.1. Demographic data

Maximum number of patients affected with acute optic neuritis belonged to an age group interval of ≥20-40 years (53%) and minimum in age group of <20 years (10%). Mean age of presentation was noted to be 37.26 ± 12.12 years. Female preponderance was noted (male: female - 3:7).

3.2. MRI data

In context to Table 1, on contrast enhanced MRI Orbit, 32 of the affected eyes showed contrast enhancement. 17 affected eyes (57%) had an enhancement of <17mm length of optic nerve and 15 (43%) eyes had an enhancement length of ≥17mm. None of the patients had any signs of demyelination on the MRI Brain and MRI spine was normal suggestive of an idiopathic etiology.[15] Overall Mean length of involvement was found to be 15.89 ± 4.56mm, while in the group with length <17mm involvement mean length was 12.41±2.21 and in group with ≥17mm enhancement 19.76 ± 2.34. The cut off value was taken to be 17mm because during the study it was found that lesions above 17mm of length had a poorer recovery as compared to those with <17mm of enhancement. The overall range of length involvement was 7.5 to 25mm. While the segments of the optic nerve involved in different cases have been compiled into Table 1.

3.3. Visual parameters

Most of the subjects attending the clinic had a duration of complaints between ≥7-12 days while the mean duration of complaints was found to be 9.63 ± 4.05 days.

At baseline (Table 2), When visual parameters were studied in relation to length of optic nerve involvement, subjects with <17mm of length had a mean visual acuity of 0.588±0.22, color vision 1.32±0.09, mean deviation on visual field analysis -8.024 ± 2.2 dB, contrast sensitivity 1.39±0.16 and with ≥17mm of length, mean visual acuity was noted to be 1.013±0.55, color vision 0.26±0.09, mean deviation -16.81±7.74 dB and mean contrast vision 1.29±0.12. A significant difference between the two groups categorized on the basis of length was noted when color vision and visual acuity were considered (P<0.0001 and P=0.01 respectively). A significant association was found between length of optic nerve involvement with color vision and visual field, where both the parameters were worse for patients with ≥17mm length than <17mm length of involvement.

At 1st month Follow up (Table 3), in subjects with length of involvement <17mm the mean visual acuity, color vision, mean deviation on perimetry and contrast sensitivity of the affected eye were recorded to be 0.22±0.27, 0.78 ±0.09, -5.2±2.97, 1.53±0.15 respectively whereas subjects with length ≥17mm had a mean visual acuity, color vision, mean deviation and contrast sensitivity of 0.51 ± 0.41, 0.73 ± 0.05, -11.56±3.9, 1.36±0.12 distinctly. A significant difference was observed when Visual acuity, Mean deviation and contrast sensitivity of the two groups were compared (P=0.04, P<0.0001 and P=0.006 in succession) though no significant association between the visual outcomes of the two groups was found.

At 2nd follow up (Table 4), two patients did not attend the clinics. The two groups significantly differed in terms of visual acuity, mean deviation and contrast sensitivity (P=0.01, P<0.0001 and P=0.01 in serial) along with this, a significant association was found only between the length of optic nerve involvement and visual acuity recorded on the second month follow up. In the group of subjects with the length of involvement of optic nerve <17mm, 11 eyes out of 30 affected eyes improved visual acuity to <0.2 LogMAR, a color vision of ≥0.8 decimal equivalents and 8 subjects improved to a good visual field of MD ≥-3dB and 9 subjects to a contrast sensitivity of ≥1.75. Amongst the group of subjects with the length of enhancement >17mm relatively lesser number of eyes improved to the cut off values for good visual prognosis as compared to the other group of shorter length. Mean visual acuity, color vision, Mean deviation and contrast sensitivity in the group of length <17mm was found to be 0.125±0.21, 0.82±0.07, -3.28±1.8dB and 1.65±0.14 respectively while in the group with length ≥17mm the mean values for above mentioned parameters were as follows: visual acuity 0.40±0.37, color

Table 1: Distribution of eyes according to segment of optic nerve involved on CEMRI

Segment of optic nerve involved	No. of eyes	Percentage
Intraorbital	16	50
Intraorbital+Canalicular	12	37
Canalicular+ Intracranial	04	13
Total no. of eyes	32	100

Table 2: Visual parameters at baseline

Length of optic nerve enhancement	Visual acuity		Color vision		Perimetry		Contrast sensitivity	
Cut off value	<0.2	≥0.2	≥0.4	<0.4	≥-8dB	<-8dB	>1.35	≤1.35
<17mm	1	16	7	10	9	8	7	10
≥17mm	0	15	0	15	0	15	3	12
Total number of nerves involved	1	31	7	25	9	23	10	22
			***P=0.007**		***P=0.0009**			

Visual Acuity in LogMar; Color vision in Decimal; Perimetric value from Mean Deviation in decibels (dB); Contrast sensitivity in Log units. Each column under different heads represent the number of eyes affected at baseline. The *represents significant differences between the two groups based on differences in length

Table 3: Visual parameters at 1^{st} follow up

Length of optic nerve enhancement	Visual acuity		Color vision		Perimetry		Contrast sensitivity	
Cut off value	**<0.2**	**≥0.2**	**≥0.8**	**<0.8**	**≥-3dB**	**<-3dB**	**>1.35**	**≤1.35**
<17mm	9	8	10	7	4	13	12	5
≥17mm	3	12	4	11	1	14	6	9
Total number of nerves involved	12	20	14	18	5	27	18	14

Visual Acuity in LogMAR; Color vision in Decimal; Perimetric values from Mean Deviation in decibels (dB) ; Contrast sensitivity in Log units. Each column under different heads represents the number of eyes affected at 1^{st} follow up. The * represents significant differences between the two groups based on differences in length.

vision 0.75±0.07, mean deviation -9.15±4.23 dB and contrast sensitivity 1.49±0.18.

At the last follow up (Table 5), a total of 30 eyes were followed up while 2 subjects failed to attend the clinics. Out of 30 eyes, a total of 15 eyes recovered to a visual acuity of <0.2 LogMAR and 15 eyes to a color vision of ≥0.8 while a total of 16 eyes had visual field with a mean deviation ≥-3dB and 19 eyes improved to a contrast sensitivity ≥1.75 log units. All visual parameters amongst the two groups differed significantly (for visual acuity P=0.005, color vision P=0.04, mean deviation P=0.01 and contrast sensitivity P=0.02). A note of significant association of length of involvement and contrast sensitivity was made. The mean values of visual parameters for visual acuity were 0.06±0.10, color vision 0.84±0.07, visual field -3.01±1.62 and contrast sensitivity 1.76±0.04 for lesion length <17mm and for enhancement ≥17mm mean visual acuity was 0.35±0.35, color vision 0.79±0.06, visual field -6.5±3.3 and contrast sensitivity was 1.66±0.12.

4. Discussion

Mean age of presentation in our study was 37.26±12.12 years with maximum subjects in the age group of >20-40 years. It is similar to the studies conducted by Dunker et al[8] between 1978 and 1992 (31 years), Tartaro et al[16] in 1995 at Chieti Italy (31.1±7.6 years), Kupersmith et al[17] in 2002 at New york (35.6±11.6years), Fatima et al[18] in 2013 at Yamanashi Japan (40.8 years), Cellina et al[19] in 2019 at Milan (33 years) while it was slightly different from mean age of group studied by DY Son et al[12] in 2017 at Goyang which was 44.03±13.77.

In our study we found predilection of optic neuritis for the female gender (Male: Female ratio 3:7), 70% were females and 30% were males. Results were comparable to studies conducted by Kapoor et al,[9] Hickmann et al,[10] Berg et al,[13] Kupersmith et al,[17] Fatima et al[18], Cellina et al[19] and Lu Ping et al[20] where the percentage of female subjects were 75%, 69%, 67.3%, 71%,71% 75%, and 72% respectively while the studies while in studies performed

Table 4: Visual parameters at 2^{nd} follow up

Length of optic nerve enhancement	Visual acuity		Color vision		Perimetry		Contrast sensitivity	
Cut off value	<0.2	≥0.2	≥0.8	<0.8	≥-3dB	<-3dB	≥1.75	<1.75
<17mm	11	5	11	5	8	8	9	7
≥17mm	3	11	4	10	2	12	4	10
Total number of nerves involved	14	16	15	15	10	20	13	17

*P=0.01

Visual Acuity in LogMAR; Color vision in Decimal; Perimetric values from Mean Deviation in decibels (dB); Contrast sensitivity in Log units. Each column under different heads represents the number of eyes affected AT 2^{nd} follow up. Two patients were lost to follow up. The * represents significant differences between the two groups based on differences in length.

Table 5: Visual parameters at 3^{rd} follow up

Length of optic nerve enhancement	Visual acuity		Color vision		Perimetry		Contrast sensitivity	
Cut off value	**<0.2**	**≥0.2**	**≥0.8**	**<0.8**	**≥-3dB**	**<-3dB**	**≥1.75**	**<1.75**
<17mm	11	5	10	6	11	5	14	2
≥17mm	4	10	5	9	5	9	5	9
Total number of nerves involved	15	15	15	15	16	14	19	11

*P=0.006

Visual Acuity in LogMAR; Color vision in Decimal; Perimetric values from Mean Deviation in decibels (dB); Contrast sensitivity in Log units. Each column under different heads represents the number of eyes affected at 3^{rd} follow up with two patients lost to follow up. The * represents significant differences between the two groups based on differences in length**.**

by Dunker et al[8] and Tartaro et al[16] observed a lower percentage of female subjects (59% and 65% precisely). DY Son et al[12] recorded a higher percentage (80%) of females in their study.

The mean duration of complaints in our study was observed to be 9.6±4.05 days where the earliest presentation was at 3 days and the most delayed presentation was 20 days from the day of onset of symptoms. The duration is quite comparable to the study done by DY Son et al[12] 6.31±4.16 days and Cellina et al[19] 7±6 days. The range of duration is similar to that observed by Hickmann et al[10] (range 7 to 24 days) and Kupersmith et al[17] where subjects presented within 20 days of onset of symptoms. Subjects that were included in the study by Zhang et al[11] presented within 14 days of complaints.

In studies carried by Dunker et al[8], Tartaro et al[16] and Fatima et al[18] the subjects presented much earlier i.e., within 1 to 5 days, 3 to 6 days and 2 days from the day of onset of complaint respectively while subjects who were studied by Kapoor et al[9] and Lu Ping et al[20] presented late during the course of disease with the) duration being 30 days and >14 days discretely.

ONH swelling was present in 50% of the subjects in our study. The disc swelling of the eyes affected with acute optic neuritis has been discussed in studies conducted by Kapoor et al[9] and Hickmann et al[10] where ONH swelling was found in 74% and 57.6% (comparable to our study) respectively. It was noted that optic disc swelling was always present when the anterior parts of the optic nerve such as the intraocular and intraorbital were affected which is similar to the observations made by Hickmann et al.[10]

5. CEMRI – Length and Visual Parameters

In our study, all subjects clinically diagnosed as cases of acute optic neuritis, the optic nerve enhancement of the affected portions was observed in 100% of patients. Thus, the sensitivity of CEMRI was considerable in detection of acute optic neuritis.[18] Alike this Hickmann et al[10] and Kupersmith et al[17] found that there was enhancement of inflamed optic nerve in 96.4% and 94.4% of all affected eyes. As per Berg et al[13] the sensitivity of CEMRI was high although they recorded contrast enhancement in 74% of the patients with acute optic neuritis. Normally the optic nerve is divided into 4 parts namely intraocular (1mm), Intraorbital (25mm), Intracanalicular(9mm), añd Intracranial (16mm). In our study, CEMRI revealed that intraorbital segment was the most commonly involved segment (50%) followed by combined intraorbital and canalicular (37%) segment and canalicular with intracranial segment (13%). The findings are comparable to the observations made by Dunker et al[8] {intraorbital (32%); Intraorbital and canalicular (36%); Canalicular and intracranial (9%)} and Berg et al[13] {Orbital (66.3%); Canalicular (29.8%); Intracranial (16.3%)}. Hence, intraorbital segment is most commonly affected.

The mean length of enhancement in our study was 15.5±4.02mm and range was recorded between 7.5 to

25mm. This is comparable to Kapoor et al[9] (15.5±9.5mm), Kupersmith et al[17] (14.6±9.3mm) and Cellina et al[19] (15mm). However, the mean length was noted to be shorter in studies performed by Zhang et al[11] (10.29mm), DY Son et al[12] (12.42±13.0mm) and Zou X et al[21](12.6mm). The range of length involvement is comparable to what was observed by Hickmann et al[10] (0 to 30mm) while it was much larger in observations made by Berg et al[13] (3 to 36mm).

The total length of enhancement at baseline correlated positively with baseline visual acuity(r=0.6, P<0.0001) while it correlated negatively with mean deviation(r=-0.8, p<0.05) and CV (r=-0.6, P<0.0001). The findings are comparable with the observations made by Dunker et al,[8] Tartaro et al[16] (r=-0.58, P<0.03) and Kupersmith et al[17] {Visual acuity (r= -0.24 P= 0.01), MD (r=-0.35 P=0.001)}. At baseline a significant association was found between the length of enhancement with color vision and mean deviation. In the subgroup with length <17mm the color vision and mean deviation were significantly better than the subgroup with a length of ≥17mm. This is akin to outcomes recorded by Kupersmith et al[17] where baseline lesions of >17mm in length, and visual parameters were worse (CV=0.21, P=0.01; MD=-26.1dB, P = 0.009).

Also, lesions <17mm at baseline were found to be positively correlated with visual acuity (r=0.5, P=0.03). Although the correlation is weak but it corresponds to the results obtained by Dunker et al[8] (at P<0.05 for lesion length <17mm).

In the present study, when length of lesion >17mm was analyzed for visual acuity at baseline a positive correlation was established (r=0.6, P=0.008). The correlation coordinated with the derivation made by Berg et al[13] and Kupersmith et al[17] (r=0.27, P=0.03) who reported that a short length of enhancement is associated with good visual outcomes than longer length of lesion.

Among studies conducted by Kapoor et al,[9] Hickmann et al,[10] Zhang et al[11] and DY Son et al,[12] no correlation was established between the initial length of enhancement and its effect on visual parameters.

At 2^{nd} month follow up no correlations were observed between length based MRI subcategories and visual parameters.

At 3^{rd} month follow up, a weak positive correlation was detected during data analysis between contrast sensitivity and length of optic nerve enhancement (r=0.5, P=0.03). DY Son et al[12] observed similar results where contrast sensitivity increased with an increase in lesion length.

One of the possible explanations for this unexpected finding could be the effect of segment involved over the length of enhancement.

6. Conclusion

The study is an addition to the attempts being made worldwide to assess the role of Magnetic Resonance Imaging and to correlate the information fetched by it with the visual outcomes in patients with acute optic neuritis. Few limitations of this study are the small sample size and attrition due to which it's not representative of normal population and hence results cannot be generalized. CEMRI is a sensitive tool to evaluate cases of acute optic neuritis with 100% sensitivity of detecting optic neuritis in this study and acts as an adjunct to supporting the clinical diagnosis in subjects presenting atypically. The cause of optic neuritis in our study was concluded to be idiopathic since no signs of demyelination were found and most cases were of isolated optic neuritis without systemic features of any other disease.[15] Correlations were noted between length of optic nerve involvement and visual acuity, color vision and visual field at baseline. Contrast sensitivity is affected by both length and segment of optic nerve involved. Thus, length and segment of optic nerve affected both need to be evaluated to establish their effect on visual prognosis.

7. Source of Funding

Nil.

8. Conflict of Interest

There are no conflict of interest.

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