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Longitudinally extensive optic neuritis in neuromyelitis optica spectrum disorder

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ABSTRACT

Background: Neuomyelitis optica, sarcoid, and multiple sclerosis can all cause optic neuritis. Further means of distinguishing the causes of optic neuritis among these etiologies would be valuable for the clinician.
Methods: This is a retrospective, cohort study from a single university based hospital and neuro-ophthalmology clinic. Blinded interpretation of orbit MRIs was performed on patients with acute optic neuritis from multiple sclerosis (n = 25), sarcoid (n = 5) and neuromyelitis optica spectrum disorder (n = 6).
Results: A length of >40 mm anterior visual pathway enhancement distinguished neuromyelitis optica spectrum disorder from multiple sclerosis ($p = 0.0376$). No statistically significant differences were found for presence of pain or papillitis, however there was a trend for bilateral involvement and chiasmal involvement in neuromyelitis optica spectrum disorder compared to multiple sclerosis.
Conclusions: In acute optic neuritis, enhancing anterior visual pathway lesion length >40 mm helps differentiate neuromyelitis optica spectrum disorder from multiple sclerosis. This degree of involvement can be considered longitudinally extensive optic neuritis. Further characterization is necessary as this degree of enhancement occurs in other clinical syndromes besides neuromyelitis optica.

1. Introduction

The anterior visual pathway (AVP) is morphologically and physiologically part of the central nervous system, with a similar response to injury. Demyelinating and inflammatory processes that affect the AVP are typically disruptive of the local blood brain barrier. In optic neuritis (ON), this phenomenon manifests as contrast enhancement on magnetic resonance imaging (MRI) [1]. The purpose of this study was to evaluate for longitudinal extension of radiographic AVP enhancement among different diseases causing optic neuritis. Research rationale was based upon the fact that the neurobiology of spinal cord and anterior visual pathways possesses similar clinical and pathologic characteristics. Eugene Devic noted this in the original descriptions of his eponymous disease [2,3]. Moreover, radiographic extensive involvement differentiates transverse myelitis (TM) in neuromyelitis optica spectrum disorders (NMOSD) from other etiologies such as multiple sclerosis (MS) [4]. Our major hypothesis was that AVP enhancement would more often be longitudinally extensive in NMOSD more often than in other causes of ON such as MS or sarcoidosis. Although AVP enhancement may involve the nerves, chiasm, or optic tracts, for simplicity we refer to this condition as longitudinally extensive optic neuritis (LEON).

2. Methods

This is a retrospective cohort study. A University Institutional Review Board approved the data review of patient records and imaging by the investigators.

The study setting was a single neuro-ophthalmology practice in a University hospital and clinic. A retrospective review of consecutive patients presenting with presumed inflammatory optic neuritis between 2009 and 2012 was performed. Patient selection was based on a clinical diagnosis of optic neuritis in the context of multiple sclerosis, sarcoidosis, or NMOSD. Sarcoidosis was diagnosed based on pathologic confirmation. NMOSD was defined as optic neuritis in the setting of aquaporin-4 seropositive status. Multiple sclerosis was diagnosed based on revised McDonald criteria. Inclusion criteria involved fat-suppression orbit MRI sequences confirming pathologic AVP enhancement, and neuro-ophthalmologic exam within four weeks of optic neuritis onset. Patients were excluded if they received corticosteroids or other immunosuppression for the acute optic neuritis episode prior to MRI. Thirty-six patients met study criteria. Digitized orbit MR images for these patients were coded and transferred to a review station. Fig. 1 displays representative orbit MRI image measurement technique.

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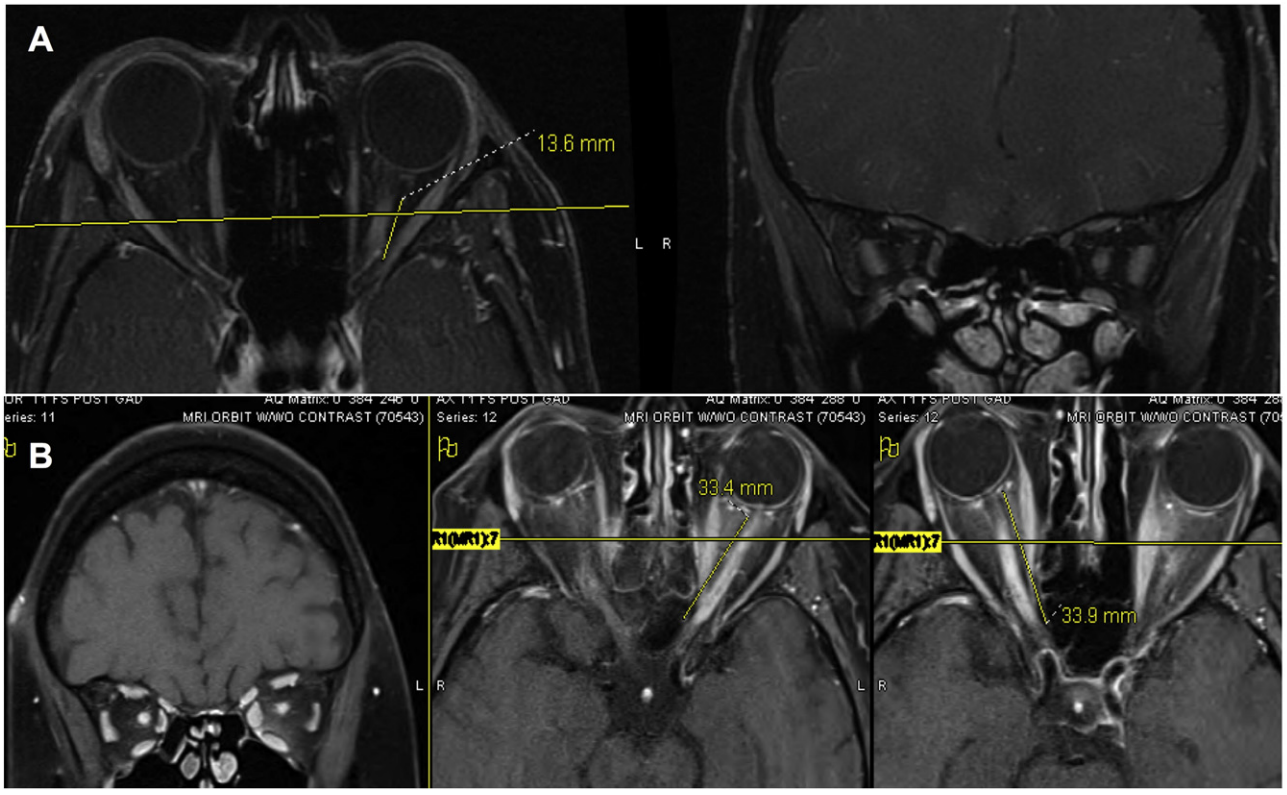

Fig. 1. Measurement technique of enhancement measurement for post-gadolinium orbit MRI. Fat saturation post-gadolinium orbit MRI sequences showing representative measurements for both MS (A) and NMOSD (B).

Blinded to etiology or clinical characteristics, one author (BK) determined 1) length of contiguous radiographic AVP enhancement, 2) presence or absence of bilateral optic nerve involvement, and 3) presence or absence of chiasmal involvement. Based on clinical records, 1) presence or absence of pain, and 2) presence or absence of papillitis were also recorded. 40 mm total AVP enhancement and 50 mm total AVP enhancement were chosen as lengths considered longitudinally extensive. The main outcome measure was the presence of longitudinal extension in NMOSD versus MS and sarcoid.

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3. Statistical analysis

Fisher's exact tests were used for categorical variable comparisons due to empty cells and smaller cell counts. For continuous variables, Wilcoxon two-sample test was conducted because of the small sample size. Statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC). Two-tailed p values were calculated for all tests and $p < 0.05$ was considered statistically significant.

4. Results

Patients with NMOSD, sarcoid, and MS were compared for the following outcome variables: >40 mm AVP enhancement length, >50 mm AVP enhancement length, bilateral optic nerve involvement, chiasm involvement, pain, and papillitis. The only statistically significant difference among any group was >40 mm AVP enhancement length in NMOSD versus MS ($p = 0.0376$), with the NMOSD group more likely to have a length of radiographic AVP enhancement greater than 40 mm as compared to MS. No statistically significant differences were found in other categories; however there was a trend for bilateral involvement (4% in MS, 33% in NMOSD) and chiasmal involvement (8% in MS, 33% in NMOSD). Table 1 details patient data and p values.

Lengths of AVP enhancement for NMOSD, MS, and sarcoid are depicted in the boxplot in Fig. 2. MS AVP mean involvement was 22.67 mm (range 4.39–42.0, sd 10.27). NMO AVP mean was 37.68 mm (range 22.6–54.0, sd 11.60). Sarcoid AVP mean was 27.05 mm (range 9.98–48.84, sd 17.49). The mean AVP difference did not reach statistical significance among the three groups.

5. Discussion

Although some reviews have described NMOSD optic neuritis as more extensive than MS [5], only rare reports have included radiographic

Table 1
Pairwise comparisons for the three groups: NMOSD, MS, and sarcoid.

		NMO	MS	Sarcoid	NMOSD vs MS	NMOSD vs sarcoid	MS vs sarcoid
		n	n	n	p	p	p
>40 mm	Y	3 (50)	2(8)	2(40)	**0.0376**	1.0	0.119
	N	3 (50)	23(92)	3(60)			
>50 mm	Y	1 (16.7)	0(0)	0(0)	0.194	1.0	N/A
	N	5 (83.3)	25(100)	5(100)			
Bilateral	Y	2 (33.3)	1(4)	1(20)	0.088	1.0	0.310
	N	4 (66.7)	24(96)	4(80)			
Chiasm	Y	2 (33.3)	2(8)	0(0)	0.160	0.454	1.0
	N	4 (66.7)	23(96)	5(100)			
Pain	Y	4 (66.7)	19(76)	4(80)	0.634	1.0	1.0
	N	2 (33.3)	6(24)	1(20)			
Papillitis	Y	2 (33.3)	10(40)	3(60)	1.0	0.567	0.628
	N	4 (66.7)	15(60)	2(40)			