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Optic Neuritis Incidence is Increased in Spring Months in Patients with Asymptomatic Demyelinating Lesions

Konstantin E. Balashov¹, Gian Pal¹, and Michael L. Rosenberg²

¹UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ

²New Jersey Neuroscience Institute, Edison, NJ

Abstract

Background—Optic neuritis (ON) patients can be divided based on the presence or absence of asymptomatic demyelinating lesions (ADL) on brain MRI. The presence of ADL is associated with an increased risk of progression to clinically-definite multiple sclerosis (CDMS).

Methods—The clinical data and brain MRI of 110 patients with acute unilateral ON were analyzed.

Results—Patients with ADL had a significantly higher incidence of ON in spring months as compared to patients with no ADL ($p=0.0024$). Increased incidence of ON in spring months was seen in patients with ADL whether or not they were diagnosed with CDMS on follow-up.

INTRODUCTION

Recent studies have elucidated the remarkable prognostic value of MRI in patients presenting with their first clinical neurological event. The risk of progression to clinically definite MS (CDMS) was increased from 11% in patients without asymptomatic demyelinating lesions (ADL) to more than 80% in patients with two or more ADL on brain MRI based on a 10-year follow-up study. [1]. This trend has been confirmed in other publications [2,3]. Even one ADL seen on brain MRI at the time of first clinical attack places the patient into a high risk group [3].

The etiology of MS remains unknown. Genetic markers as well as environmental factors, such as viral infection and exposure to sunlight/vitamin D, are suspected to be risk factors [4]. A seasonal pattern for both monosymptomatic ON and MS onset in the Northern hemisphere has been clearly established with the highest incidence of both in spring (March-May) and the lowest in winter (for review, see [5]). The opposite trend was reported in the Southern hemisphere [4].

We hypothesized that ON which results from a generalized demyelinating disease process is pathophysiologically different from isolated ON which has no tendency to cause demyelinating lesions in other parts of the central nervous system. As the presence of ADL on brain MRI at ON onset may serve as a marker of previous clinical or subclinical demyelinating events, we retrospectively evaluated a possible link between the presence of ADL in brain and the seasonal pattern of ON.

METHODS

Study population

We used all the electronic records available prior to May 2007 from the neuro-ophthalmology clinic of the New Jersey Neuroscience Institute to find patients with the new onset of mono-

symptomatic unilateral ON. The search revealed 132 patients. 22 patients were excluded from further study for the following reasons:

1. Prior history or clinical or laboratory evidence consistent with a disease which could cause ON, e.g., Lyme (n=5), Lupus (n=1), HIV (n=1).
2. The absence of brain MRI in clinical records (n=15).

The remaining population of 110 patients (81 females and 29 males) had an average age of 35.4 ± 0.9 (Mean $\pm$ SEM) years old. Their records were analyzed to compare brain MRI characteristics, clinical history and exam data. The patients were divided into four subgroups based on the season during which ON was diagnosed: winter (December to February), spring (March to May), summer (June to August) and fall (September to November).

Brain MRI

All 110 patients had a brain MRI study ordered at the time of their first visit. Most studies utilized 1.5 Tesla MRI machines and all had T1WI, T2WI sequences. The patients were divided into ADL-negative and ADL-positive based on the presence of ADLs reported by the neuro-radiologist.

Statistical methods

The figures and statistic analysis were done with a GraphPad package from GraphPad Software, Inc., La Jolla, CA. The Fisher's exact test using two-tailed P values was utilized.

RESULTS

Out of 110 ON patients, 72 patients were ADL-positive and 38 ON patients were ADL-negative. The incidence of ON was not evenly distributed throughout the year. A higher proportion of patients with ADL had the onset of symptoms in spring (41.7%) as compared with 13.2% ON patients with ADL-negative brain MRI, $p = 0.0024$ based on Fisher's exact test (Figure 1, Table 1) There was no statistical difference in ON incidence between those two groups in any other season. Neither the number of periventricular lesions nor the number of infratentorial lesions on initial MRI varied significantly with the season of presentation (not shown). The majority (81%) of brain MRIs performed with and without IV contrast had no active (contrast-enhancing) ADLs. Comparing ON patients with and without ADL, there was no significant difference in mean age at onset of symptoms (36.0 ± 1.1 vs. 34.1 ± 1.5 , $p = 0.3023$ based on *t*-test) or in the proportion of females to males (55 females and 17 males vs. 26 females and 12 males, $p = 0.3733$ based on Fisher's exact test). Prior to or at the time ON attack, CDMS, as per Poser's criteria [6], was diagnosed in 2 patients (1 ADL-positive and 1 ADL-negative). After the ON attack, the patients were followed for 22.8 ± 27.6 (mean $\pm$ SD) months and CDMS was diagnosed in 26 patients (24 ADL-positive and 2 ADL-negative). As expected, significantly more patients were diagnosed with CDMS among patients with ADL than among patients without ADL on brain MRI (24 of 72 vs. 2 of 38, $p = 0.0074$ based on Fisher's exact test). The increased ON incidence in spring months as compared to non-spring months was seen in both ADL-positive patients who were diagnosed with CDMS (not significant presumably due to a small number of patients in the group) and ADL-positive non-CDMS patients ($p = 0.0075$) as compared to ADL-negative patients (Table 1).

DISCUSSION

The published MRI studies to date have found no significant seasonal differences in MRI activity in CDMS [7–9]. This lack of variability could be partially due to the effect of treatment. A recent analysis of serial bi-weekly MRI involving a large group of more than 40 non-treated MS patients in New England revealed a statistically significant seasonal variation in the incidence

of new T2 lesions. The peak of disease activity shown on MRI was noted in spring-summer months with the minimal activity seen in September-February period (D. Meier, personal communication). None of these MRI studies included new lesions in the optic nerve due to technical limitations.

We report for the first time that patients with ADL have increased incidence of ON in spring months as compared to patients with no ADL. Our findings add to the mounting evidence suggesting that different environmental factors may trigger the demyelinating process in the optic nerve of patients with recurrent demyelinating disease as compared to patients with monophasic demyelinating attack of ON. Future studies may help to elucidate the exact nature of the above factors and lead to targets for new MS treatment.

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Seasonal Incidence of Optic Neuritis

Figure 1.

The seasonal incidence of optic neuritis (ON) was analyzed in 110 patients including 38 patients without asymptomatic demyelinating lesions (ADL-negative ON) and 72 patients with ADL (ADL-positive ON). ADL-positive patients had significantly increased ON incidence in spring months (March-May) as compared to patients ADL-negative patients, $p = 0.0024$. There was no significant statistical difference among above two groups in other seasons (winter, summer, fall).

Table 1
Increased incidence of optic neuritis in spring months in patients with asymptomatic demyelinating lesions

The incidence of optic neuritis (ON) is shown for patients with and without asymptomatic demyelinating lesions on brain MRI (ADL-positive and ADL-negative, respectively).

Patients	ON incidence: Spring months (March-May)/Non- spring months (June-February)		P value ** (ADL-positive vs. ADL- negative)
	ADL-positive	ADL-negative	
All ON patients (n=110)	30/42	5/33	0.0024
ON patients not diagnosed with CDMS (n=82)*	20/27	5/30	0.0075
ON patients diagnosed with CDMS (n=28)*	10/15	0/3	NS***

* Clinically definite MS (CDMS), as per Poser criteri, was diagnosed in 2 patients prior to or at the time of ON attack (1 ADL-positive and 1 ADL-negative) and in 26 patients after ON attack (24 ADL-positive and 2 ADL-negative).

** P-value was calculated based on Fisher's exact test.

*** NS - not significant.