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Neurological outcome and predictive factors of idiopathic optic neuritis in China

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ABSTRACT

Background: The neurological outcome and predictive factors of idiopathic optic neuritis (ION) in China are largely unknown.
Objective: The aim of this paper is to study the neurological outcome of Chinese ION and to investigate the early predictors for multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD).
Method: Retrospective medical record review and supplementary follow-up of 107 ION patients was performed. Statistical analysis of the baseline characteristics as risk factors for ION patients converting into MS or NMOSD was performed.
Results: With an average disease course of 9.5 years, 19 of the 107 (17.7%) ION patients developed either MS (9, 8.4%) or NMOSD (10, 9.3%). The estimated 5-year and 10-year combined accumulative risk rates were 14.1% and 26.0%, respectively. Significantly higher estimated accumulative conversion risk was found in female versus male ($P = 0.047$), adult versus children ($P = 0.032$), patients with brain MRI lesions versus patients without leasions ($P = 0.026$), patients with CSF positive oligoclonal bands and/or elevated IgG index versus without ($P = 0.003$) and patients with poor visual recovery versus patients with good recovery ($P = 0.007$). Furthermore, brain white matter lesions and good visual recovery were statistically more common typically in MS converters compared with the NMOSD converters ($P = 0.01$ and $P = 0.006$, respectively).
Conclusion: The combined conversion rate for ION to MS/NMO in Chinese population was lower than the reported rate for Western countries. In addition to some previously reported high risk factors, white matter lesions on the brain MRI at baseline and good visual recovery were found to be good predictors for Chinese ION converting into MS whereas poor visual recovery with a normal brain MRI suggested a higher likelihood of the ION converting into NMOSD.

1. Introduction

Acute idiopathic demyelinating optic neuritis (IDON) is a well-studied type of optic neuritis in Western countries. It usually occurs as an isolated phenomenon or is observed in patients with multiple sclerosis (MS) and hence is also known as MS-ON [1]. Cohort studies from Europe, Northern America and Australia reported the 10-year conversion rate from IDON to MS to be between 24% and 46%, which escalated up to 75% within 15 years of the first episode [2–5]. A few risk factors, including the presence of white matter lesion in the brain MRI, female gender and abnormal CSF IgG index, have been well-reported as the predictors for the conversion of IDON to MS. However, as with optic neuritis in Western countries, optic neuritis in Asia has been reported to have different clinical features and visual outcomes with typical IDON [6–11]. Even so, very few studies have investigated the neurological outcome of optic neuritis in Chinese population, especially in terms of the predictive factors [12–15]. Herein, we report a retrospective study of the visual and neurological outcomes of a group of idiopathic optic neuritis (ION) patients in Chinese population, with special attention to the conversion to MS or NMO and the related predictive factors.

2. Materials and methods

This study was approved by the Institutional Review Board, Beijing Tongren Hospital, Capital Medical University. Medical records of the patients hospitalized between January 2003 and December 2007 in the Department of Neurology, Beijing Tongren Hospital, with discharged diagnosis of "Optic Neuritis", "retrobulbar neuritis" or "papillitis" were reviewed. The patients who were unable to show up for the follow-up visits were subjected to a standard questionnaire via multiple phone calls made in January 2008, January 2011 and December 2013. Patients

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were identified to have idiopathic optic neuritis (ION) based on the following criteria: (1) acute loss of visual acuity and/or a acute onset of visual field defect; (2) presence relative afferent pupillary defect or abnormal visual evoked potential; (3) no evidence of causative diseases involving the retina, other ocular structure, optic chiasm or retrochiasmal visual pathways; and (4) no evidence of any compressive, vascular, toxic, nutritional, metabolic, infiltrative, hereditary optic neuropathy or infectious optic neuritis. Informed consent was acquired from all of the patients included in the study.

Clinical, imaging and cerebral spinal fluid data at baseline and patient neurological outcomes were collected. Severe visual loss was defined as visual acuity (VA) less than or equal to 20/200 in at least one eye. Good visual recovery in the affected eye was defined as an improvement in the VA to 20/40 or better. For the diagnosis of patient progression into MS or NMO during the follow-up period, the 2010 revised McDonald MS Criteria [16] and the 2006 revised NMO diagnostic criteria [17] were used.

Statistical Package for Social Sciences (SPSS for Windows, version 16.0) was used for statistical analysis. Kaplan–Meier Survival Analysis was used to calculate the estimated cumulative conversion rate from ION to MS and/or NMO. The log-rank test and logistic regression were used for the univariate and multivariate analysis of the baseline characteristics as risk factors for conversion. The converters were further classified into classic-MS and NMO spectrum disease (NMOSD) sub-groups, and the clinical features at baseline between these two groups were compared. The Chi-square test was used for categorical data. The visual acuity recovery was converted into Log MAR Score, followed by 1-way ANOVA for estimating the pairwise differences of the subgroups. We reported 2-tailed *P*-values. A $P < 0.05$ and 95% confidence intervals of odds rations (logistic regression) not including 1.0 were considered statistically significant.

3. Results

3.1. Patient information and clinical features at baseline

Out of the 185 patients who met the above criteria for ION, 78 cases were excluded due to the following reasons: 1) incomplete clinical or follow-up data (55 cases), 2) previous neurologic symptoms or signs suggesting demyelinating events (14 cases), and 3) preexisting history of other autoimmune diseases (nine cases) including two cases of systemic lupus erythematosus, four cases of Sjogren's disease, one case of rheumatoid arthritis and two cases of Behcet disease. The 107 cases included in the study were referred from 27 of 33 provinces or autonomous regions in Mainland China, with majority of the cases from the north and the east. There were 40 (37.4%) male and 67 (62.6%) female patients. Patient age ranged from 6 to 61 years, with a mean age of 25.3 years ± 14.0 years. Seventy (65.4%) cases had suffered only one attack of ON, while the other 37 (34.6%) cases had experienced recurrent attacks. Initial best corrected visual acuity in 179 affected eyes varied from 20/20 to no light perception, with 20/200 or worse in 119 eyes (66.5%), 20/199 to 20/41 in 32 eyes (17.9%) and 20/40 or better in 28 eyes (15.6%) (Fig. 1). All patients had undergone a brain MRI, with 103 patients MRIs (96.3%) performed within one month of the ON episode. One or more white matter lesions were found in 33 of these 103 cases (32.0%), but none of them met the criteria of "dissemination in Space" revised in 2010 [16]. The cerebral spinal fluid examination was performed in 87 (81.3%) patients, with positive oligoclonal bands in 19 of the cases (21.8%) and elevated IgG index in eight cases (9.2%).

3.2. Visual and neurological outcome

Follow-up data for 88 patients (82.7%) were acquired from their clinical visits, while the data for the remaining 19 cases (17.3%) were obtained via telephone questionnaires. Till the time of the last follow-up, the patients disease duration, as measured from the first-ever attack of ON, ranged from 5.1 years to 25 years with a mean of 9.5 years. The visual acuity of the 179 affected eyes improved to 20/40 or better in 148 eyes (82.7%), while 25 eyes (14.0%) remained 20/200 or worse (Fig. 1). During the follow-up period, 20 patients (18.7%) experienced at least one more ON episode. Seventeen (15.9%) patients experienced new clinical episodes affecting the cerebral hemisphere, brainstem and spinal cord in 5, 2 and 10 patients, respectively. From the remaining 90 cases that did not report any new clinical attacks, a follow-up brain MRI was performed in 18 cases, and a spinal cord MRI was performed in four cases. Six cases showed new cerebral white matter lesions, two of which met the dissemination in space criteria as defined by the McDonald criteria 2010. Five patients received the AQP4-Antibody test at the time of new clinical attacks, two of them were positive. Thus, during our follow-up time, total 19 patients (17.7%) progressed into either MS or NMO, with 13 (68.4%) of them developed within five years of the initial ON attack.

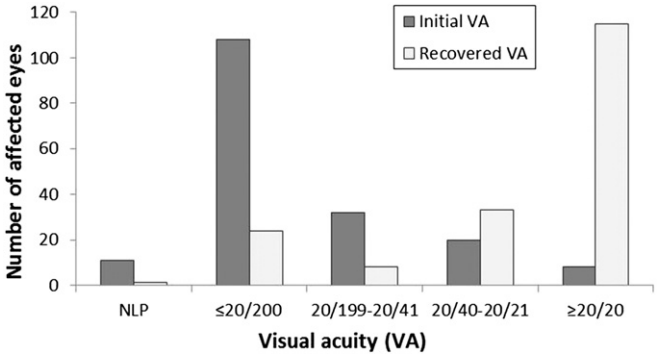

Fig. 1. Initial and recovered best corrected visual acuity of 107 ION patients.

The Kaplan–Meier Survival Analysis showed that the 1-, 3-, 5-, and 10-year combined cumulative conversion rates for progression into MS or NMO after the first ON event were 2.8% (95% confidence interval [CI], 0–5.9%), 8.1% (95% CI, 2.6%–13.6%), 14.1% (95% CI, 6.8%–21.4%) and 26.0% (95% CI, 14.4%–35.2%), respectively (Fig. 2). Table 1 shows the comparison of the combined cumulative conversion rates among patients with different baseline characteristics. The results of the multivariate analysis for these baseline risk factors are shown in Fig. 3. Table 2 shows the clinical and the ancillary data of the 19 progression cases. Seventeen cases met the 2010 revised McDonald criteria, with 8 of these 17 cases also meeting the diagnostic criteria of OSMS [18]. Two cases met the 2006 revised diagnostic criteria of NMO (Table 2). We combined the NMO and OSMS patients into the NMO-spectrum disorders (NMOSD) group [19]. The comparison of the baseline characteristics between the classic-MS and the NMOSD sub-groups is shown in Table 3.

4. Discussion

During the averaged follow-up time of 9.5 years, 19 of 107 (17.7%) patients developed CNS lesions in addition to their optic nerve lesions and progressed into either MS or NMO. The 5-year and 10-year estimated combined cumulative conversion risk for progressing into MS or NMO after the initial ON event was 14.1% and 26.0% (95% CI, 14.4%–35.2%), respectively. This result was similar to the 14.8% MS conversion rate reported for Chinese population in Taiwan [12]. Compared with the rates reported in Western countries (which ranged from 25% to 30% at five years and 34% to 42% at 10 years [1–5]), both the averaged and the estimated cumulative conversion risk in our ION patients were much lower. Furthermore, Pirko et al. have reported that the combined conversion rate for progression from ON to MS or NMO was 26.9% at 5 years and 42.3% at 10 years [20], which is nearly twice as high as that of our ION patients. There are a few possible explanations for this