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Magnetic resonance imaging findings at the first episode of acute optic neuritis

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ABSTRACT

Background: Optic neuritis (ON) is a focal demyelinating event, which may evolve into multiple sclerosis (MS).
Objective: To study MRI characteristics in the acute phase of the first ON episode.
Methods: A prospective population-based study was performed on 31 patients with a first episode of acute ON with a one year follow-up. MRI, clinical evaluation, and detection of aquaporin-4 (AQP4)-IgG and myelin oligodendrocyte glycoprotein (MOG)-IgG was undertaken. For lesion characterization on MRI the optic nerves were divided into three segments: intra-orbital (IO), canalicular (CAN) and chiasmal (CHI).
Results: Lesions of the optic nerve were observed in 80.6%(25/31), with IO location in 48%(12/25), CAN in 8% (2/25) and both IO and CAN in 44%(11/25). Patients who converted to MS had lesions located at IO in 77%(10/13), whereas the group with isolated ON had IO and CAN in 73% (8/11), $p = 0.003$. Brain lesions were observed in 84% (21/25) at onset of ON; 62%(13/25) progressed to MS with more frequent location in brainstem ($p = 0.030$) and lesions in periventricular areas ($p = 0.015$). Spinal cord lesions were detected only in patients who progressed to MS ($p = 0.002$). MOG-IgG was detected in one patient with an optic nerve lesion located at IO and CAN. Serum AQP4-IgG was detected in none. Follow-up MRI showed progression in optic nerve lesions in 55% (11/20) patients.
Conclusions: Specific location of optic nerve and brain lesions and the presence of spinal cord lesions in the acute phase of the first ON episode facilitated an MS diagnosis. The extension of optic nerve lesions following ON suggests a long-term progressive degeneration as an important element of ON pathology.

Abbreviations: AQP4, aquaporin-4; AQP4-IgG, AQP4 specific IgG antibody; CAN, Canalicular; CHI, Chiasmal; CNS, Central nervous system; CSF, Cerebrospinal fluid; DIR, Double inversion recovery sequence; DWI, diffusion-weighted imaging; FLAIR, Fluid-attenuated inversion recovery; Gd, gadolinium; IDD, inflammatory demyelinating disease; IO, intra-orbital; MOG-IgG, Myelin oligodendrocyte glycoprotein specific IgG antibody, MRI, Magnetic resonance imaging; MS, Multiple Sclerosis; NMOSD, Neuromyelitis optica spectrum disorder; ON, Optic neuritis; SPIR, Spectral presaturation with inversion recovery; STIR, Short tau inversion recovery; VA, Visual acuity; WHO, World Health Organization; WM, White matter

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1. Introduction

Optic neuritis (ON) is a common inflammatory demyelinating disorder (IDD) of the optic nerve that can be associated with multiple sclerosis (MS) (Petzold et al., 2014). ON causes acute, mostly monocular vision loss, often combined with retrobulbar pain (Petzold et al., 2014). It is normally a self-limiting event and recovery of visual acuity typically occurs within the first few weeks of symptom onset (Petzold et al., 2014). An initial rapid recovery is followed by a slow improvement that can continue for up to a year after onset (Kolappan et al., 2009), nonetheless some patients have persistent visual problems (Petzold et al., 2014). Magnetic resonance imaging (MRI) may facilitate diagnosis by helping detect optic nerve inflammation and exclude differential diagnoses (Petzold et al., 2014). Studies have investigated the predictive value of MRI for prognosis of visual impairment (Berg et al., 2015; Rocca et al., 2005), suggesting that long-segment inflammation of optic nerve is prognostic for loss of visual function (Kim et al., 2015). Differential MRI features of the optic nerve, including long lesions extending over half the optic nerve length, posterior nerve, and chiasmal involvement have been suggested to indicate antibody-mediated ON such as that occurring in neuromyelitis optica spectrum disorder (NMOSD) (Khanna et al., 2012; Ramanathan et al., 2016; Storoni et al., 2013). However, no significant differences have been observed distinguishing NMOSD from MS in the presence, degree or contrast enhancement of the optic nerve (Khanna et al., 2012; Storoni et al., 2013). Application of MRI to the assessment of optic nerve damage in a single episode of acute ON has been performed rarely. The aim of this study was to determine whether the specific location of optic nerve lesions was associated with risk of conversion to MS and acute or persistent visual impairment. Brain and spinal cord MRI were also examined, as simultaneous white-matter (WM) lesions (including the optic radiation), suggestive of demyelination, may contribute to visual outcome (Sinnecker et al., 2015) or risk for conversion to MS.

2. Methods

2.1. Study design

As part of a population-based study reported in detail elsewhere (Soelberg et al., 2017) a clinical database for patients diagnosed with ON in the time period 2014–2016 in the Region of Southern Denmark was established. The study was a population-based prospective case series with a one year of follow-up (Soelberg et al., 2017). All referred patients with acute or subacute onset of symptoms compatible with ON were offered a clinical examination within one week after referral and an MRI within two months (median 21 days (range 3–55)). After one year all patients had clinical follow-up and 20 patients underwent follow-up MRI (median 268 days (range 100–498)). The diagnosis of ON was obtained by independent neurological and ophthalmological examination according to previously described (The Clinical Profile of Optic Neuritis, 1991; Optic Neuritis Study, 2008). Exclusion criteria were ophthalmologic conditions not related to ON and patients were also excluded if they had been previously diagnosed with MS or NMOSD. Assignment of the MS diagnosis was based on the McDonald criteria 2010 (Polman et al., 2011; Soelberg et al., 2017).

2.2. Patient population

A total of 31 patients were obtained with the first episode of acute ON attack, who had complete MRI sequences for evaluation of the optic nerve sub-segments. All patients were Caucasian and the median age at onset was 40 years (range 17–66). The female:male ratio was 1.4:1. Twenty-nine patients had unilateral and two had bilateral ON symptoms (Table 1).

Table 1
Demographics and characteristics of patients.

Characteristics	
Subjects, n	31
Affected eyes (unilateral/bilateral)	29/2
Age [median (range)]	40 (17–66)
Gender, [F:M]	18:13
Ethnicity: Caucasian	31
Disease duration prior to acute MRI [days, median(range)]	21 (3–55)
Subjects follow-up MRI, n	20
Disease duration prior follow-up MRI [days, median (range)]	268 (100–498)

2.3. Standard protocol approvals, registrations, and patient

The study was approved by the Committee on Biomedical Research Ethics for the Region of Southern Denmark (ref. nos. S-20130137) and by the Danish Data Protection Agency (ref. no. 14/26345). All patients provided verbal as well as written informed consent.

2.4. MRI technique

All patients underwent MRI of the brain and orbit, performed on a 1.5 T scanner, in all but two cases in whom the follow-up MRI were performed using a 3.0 T scanner.

MRI of the brain included sequences as T2 weighted, fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI). Orbits were imaged on 1.5 T with 3D FLAIR, 2D FLAIR or 2D short tau inversion recovery (STIR). The two follow-up studies on 3.0 T substituted a 3D DIR and SPIR sequence for the FLAIR. Most patients had a 3D FLAIR sequence performed with 1-mm slice thickness in sagittal plane and were reformatted to coronal and axial planes (to visualize the entire length of the optic nerve). STIR and/or T2-weighted sequences were primarily analyzed in spinal cord imaging.

Brain MRIs were reported as normal, nonspecific, or MS-like, i.e. meeting the Barkhof criteria for dissemination in space used in the McDonald criteria (Barkhof et al., 1997; Polman et al., 2011).

The MRI protocol was standard MS protocol (1.5 T) for all initial investigations, despite two cases at follow-up (3.0 T). Therefore, no adjustment for different MRI protocols was performed.

For lesion characterization, the optic nerves were divided into the following three segments: Intra-orbital (IO), canalicular (optic foramen to chiasm) (CAN) and chiasmal (chiasm ± optic tracts) (CHI), as depicted in Fig. 1. One neuroradiologist (HPBS) re-evaluated all images, masked to the affected eye/eyes, clinical and serological information.

2.5. Vision test

Visual acuity (VA) was measured at disease onset and at six and 12 months follow-up. In patients with bilateral ON, VA was measured in both eyes. The results were recorded as decimal equivalent (e.g. 6/6 = 1.0, 6/9 = 0.67, 1/60 = 0.02, finger counting = 0.01, light perception = 0.001, no light perception = 0). Furthermore, the degree of visual loss was categorized semi-quantitatively into four groups; normal vision ($\geq$ 0.8), reduced vision loss ($\geq$ 0.25 to $<$ 0.8), severe vision loss ($\geq$ 0.05 to $<$ 0.25) and blindness ($<$ 0.05), as specified by the World Health Organization (WHO, 2014). Visual recovery at re-examination was divided into four groups: group 1 with complete visual recovery (VA better than 0.8); group 2 with partial recovery (VA remaining less than 0.8), group 3 unchanged, group 4 aggravation.

2.6. Autoantibodies

AQP4-IgG was determined with a immunofluorescence assay using transfected HEK293 cells as previously described (Asgari et al., 2011) and re-evaluated by means of an in-house cell based assay at the