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Case report

Eleven episodes of recurrent optic neuritis of the same eye for 22 years eventually diagnosed as neuromyelitis optica spectrum disorder

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ABSTRACT

It is difficult to predict whether a particular attack of neuromyelitis optica spectrum disorder (NMOSD) will affect the optic nerve [optic neuritis (ON): unilateral or bilateral], spinal cord (myelitis), brain or brainstem, or a combination of the above. We report an interesting case of recurrent ON of the same eye for a total of 11 episodes in a Chinese woman. Over a period of 22 years, the attacks only involved the left eye, and never the right eye and also no myelitis. For a prolonged duration, she was diagnosed as recurrent idiopathic ON. Only until she was tested positive for aquaporin 4 antibody that her diagnosis was revised to NMOSD. Optical coherence tomography revealed thinning of the retinal nerve fibre layer (RNFL) for the affected left eye, while the RNFL thickness was within normal range for the unaffected right eye. The disability accrual in NMOSD is generally considered to be attack-related – without a clinical attack of ON, there shall be no visual impairment, and no significant subclinical thinning of RNFL. Our case is in agreement with this notion. This is in contrast to multiple sclerosis where subclinical RNFL thinning does occur. This case highlights the importance of revisiting and questioning a diagnosis of recurrent idiopathic ON particularly when new diagnostic tools are available.

1. Introduction

Recurrent optic neuritis (ON) could be idiopathic, or as a manifestation of neurological disorders such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and relapsing acute disseminated encephalomyelitis (ADEM). We report an interesting case of recurrent ON (a total of 11 episodes) of the same eye for 22 years in a Chinese woman. For years, the aetiology of the recurrent ON in her was unable to be determined. Only until the discovery of aquaporin 4 (AQP4) antibody and with the availability of this antibody assay in our country, that finally a diagnosis of AQP4 seropositive NMOSD was made possible in her.

2. Case report

A 47-year-old Chinese woman presented in 1994 at the age of 25 years with a first episode of sudden blurring of vision of her left eye, associated with pain on movement of her same eye. Her visual acuity was 6/60 for left eye, and 6/9 for right eye. The left optic disc appeared normal, but a left relative afferent pupillary defect (RAPD) was present. Thus, a diagnosis of left retrobulbar neuritis was made. She was given oral prednisolone 40 mg daily and was slowly tapered off over two weeks. Her left eye vision eventually improved to 6/12.

Two years later in 1996, she had a recurrent ON of the same eye. Again, she had acute blurring of vision of her left eye with visual acuity reduced to hand movements. The eye was also painful during movement. Fundoscopy of her left eye showed pale optic disc, while her unaffected right eye showed a normal optic disc. She was diagnosed to have recurrent left retrobulbar neuritis and again was given oral prednisolone over 2 weeks. Her vision subsequently improved to 6/12.

From 1998 to 2006, she suffered further 9 episodes of recurrent retrobulbar neuritis of the same eye, and each time spared the opposite eye. For each episode, she presented with the same complaint of left eye sudden drop in visual acuity associated with pain on eye movement. Her left eye visual acuity on each presentation ranged from 6/36 to counting fingers. Each time,

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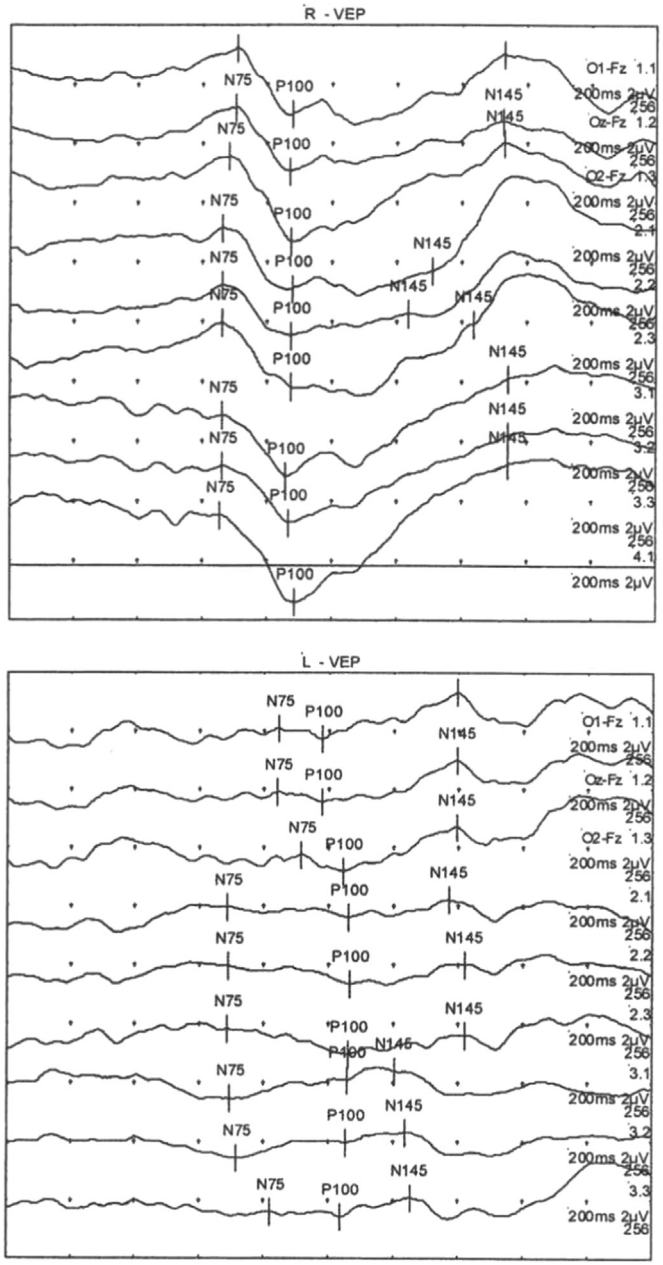

Fig. 1. Visual evoked potential (VEP) for this woman revealed a normal VEP for right eye (top panel), while for the left eye, P100 latency was delayed and the amplitude was reduced (bottom panel), providing neurophysiological evidence of left optic neuritis.

examination of her left eye revealed the presence of RAPD, with pale optic disc, while examination of her right eye was normal. During these episodes, she was either being given oral prednisolone, or being admitted to hospital (for a total of 5 episodes) for 3 days of intravenous methylprednisolone. Each time, her left eye vision improved to around 6/12 – 6/18. Her most recent visual acuity was 6/18 for left eye, and 6/9 for right eye.

Over the years, she was being extensively investigated for the aetiology of her recurrent ON. The following blood investigations were negative or unremarkable: anti-nuclear antibody (ANA), double stranded DNA (dsDNA), extractable nuclear antigens (ENA), erythrocyte sedimentation rate (ESR), Venereal Disease Research Laboratory (VDRL) test, rheumatoid factor (RF), and anti-neutrophil cytoplasmic antibody (ANCA).

Visual evoked potential (VEP) revealed a delayed P100 with reduced amplitude in the left eye suggestive of left ON. VEP of her right eye was normal (Fig. 1). Brain CT performed initially in 1994 was normal. A brain MRI performed in 2004, 10 years after her disease onset, was also normal, without any brain lesions, and this made a diagnosis of MS unlikely.

It was only until 2011, when the entity of NMOSD became better known among Asian neurologists, that her serum was sent for AQP4 antibody testing, and the result was positive. This led to her diagnosis being revised to NMOSD, and the aetiology of her recurrent retrobulbar neuritis was finally known. A repeat serum AQP4 antibody test in 2014 was still positive, further confirming this was indeed a case of AQP4 seropositive NMOSD.

She was commenced on azathioprine to reduce the risk of further relapse, especially to prevent a spinal cord relapse (myelitis). However, she developed gastrointestinal upset with azathioprine and has since refused the medication. Intriguingly, despite not on any immunosuppressants, there has been no relapse for 10 years since 2006. She was advised to seek immediate medical attention if there is new eye symptom or sudden limb weakness.

An optical coherence tomography (OCT) of the optic discs was recently performed for her, 22 years into the disease and after a total of 11 episodes of left ON. For the left eye, OCT showed severe retinal nerve fibre layer (RNFL) thinning in superior, inferior and nasal quadrants, and moderate thinning in temporal quadrant. It is interesting to note that for the right eye, the RNFL thickness is within normal range (Fig. 2). This is consistent with her clinical presentation that each time the ON has, for unknown reasons, only involved the left eye and not the opposite eye. Also, this OCT results affirmed that for NMOSD, without a clinical ON, that particular eye shall not be affected and shall not have significant subclinical thinning of RNFL. This is unlike MS where subclinical RNFL thinning does occur despite no clinical ON.

3. Discussion

NMOSD is an inflammatory disease of the central nervous system preferentially causing ON and transverse myelitis. In 2004, the discovery of NMO-IgG/AQP4 antibody has revolutionised our understanding of NMOSD (Lennon et al., 2004), and this has led to a renewed interest in this entity, especially in Asia where the ratio of NMOSD:MS was higher as compared to the West. With a positive serum AQP4 antibody and recurrent ON, this woman fulfills the 2015 criteria of the International Panel for NMO Diagnosis (Wingerchuk et al., 2015).

It is difficult to predict whether a particular attack of NMOSD will affect the optic nerve (ON: unilateral or bilateral), spinal cord (myelitis), brain or brainstem, or a combination of the above. There is a trend that older patients are more likely to have disease limited to spinal cord, and for younger patients the attacks are likely to involve multiple locations, including ON (Sato et al., 2015). Nevertheless, it is still not possible to predict exactly the location of a particular attack. Also, while a particular ON attack may be unilateral, frequently, with recurrent ON, the other eye will be affected eventually. In one study, up to 70% of NMOSD patients eventually had bilateral eye involvement (Merle et al., 2007). It is intriguing to note that in our case, all the 11 episodes of ON has occurred in the same eye only. As far as we know, this woman has the most reported number of ON episodes that affected the same eye, and never the opposite eye and also no myelitis.

ON in NMOSD is generally more severe than in MS. It has poorer recovery and can cause blindness even after 1st attack. In this woman, her ON seems to be milder and she has made a fairly good visual recovery each time. It was reported that the lesion length of ON affects the visual prognosis in AQP4 seropositive