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Case report

Monitoring of optic nerve function in Neurofibromatosis 2 children with optic nerve sheath meningiomas using multifocal visual evoked potentials

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ABSTRACT

Monitoring optic nerve sheath meningiomas (ONSM) in Neurofibromatosis type 2 (NF2) patients remains difficult. Other ocular manifestations of NF2 may obscure ophthalmic assessment of optic nerve function in these patients. Serial magnetic resonance imaging (MRI) used to assess the optic nerve is not without limitations, being expensive and often requiring general anaesthetic in children, with associated risks. This study was undertaken to describe the use of multifocal visual evoked potentials (multifocal VEP, mfVEP) in the regular monitoring of NF2 patients with ONSM. This study involved three NF2 patients with ONSM who undertook mfVEP testing at an academic ophthalmic centre. Same day mfVEP and routine ophthalmic testing were undertaken. Topographical function of the optic nerve was assessed, utilising tools such as asymmetry deviation and accumap severity index. Results were assessed alongside MRI and visual acuity (VA). From the three patients, five eyes had ONSMs, of which two caused unilateral blindness. The remaining three affected eyes had initial VAs 6/6, 6/24, and 6/18. Over follow up, ranging from 5 to 12 years, all tumours progressed, and VA declined for all patients. Multifocal VEP detected optic nerve functional loss corresponding with visual decline. This case series suggests mfVEP is effective in the objective topographic monitoring of optic nerve function in NF2 patients with ONSM. Due also to its safety in a paediatric population, the test may be considered in the routine monitoring of these patients, to be used to assist regular ophthalmic review and MRI scans.

1. Introduction

Neurofibromatosis Type 2 is a neurocutaneous disorder with a prevalence of 1 in 60,000 (1). Classic features of NF2 are vestibular schwannomas and other cranial nerve tumours, including ONSMs [1]. Typically ONSM progress, resulting in gradual loss of visual acuity, colour vision, and visual fields [2]. ONSMs may be treated with radiotherapy when progressing with visual compromise. However, potential side effects, including radiation induced retinopathy and optic neuropathy, prevent routine use in all patients [3]. Recommendations are for serial monitoring of ONSM progression with 3–6 monthly ophthalmic examination and routine magnetic resonance imaging (MRI) 6–12 monthly, offering radiotherapy or surgery if vision worsens [3–6].

In a study of 12 patients with NF2 under the age of 18, 83% had visual impairment [7]. As NF2 patients have other ocular manifestations which may impair visual outcome, including epiretinal membranes, cataracts, and retinal haemartomas, it is important to look further than clinical ophthalmic examination to properly assess ONSM progression [4,8,9]. Unfortunately, standard methods of VA are often unreliable in young children, and conventional forms of subjective perimetry require a high level of participant cognitive ability. A young age of ONSM symptom onset is a significant indicator of more aggressive disease, and faster progression [6,9]. Therefore, monitoring optic nerve function in these patients, to adequately time sight-saving intervention, is vital.

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While MRI is sensitive to detect OSNM growth at the level of 0.16 cm [3], it is costly and thus less feasible for frequent monitoring [10]. Additionally, in children, MRI scans often require general anaesthetic, imposing significant risks including post-operative nausea, vomiting, dental damage, respiratory depression, hypotension and cardiac arrest [11–13]. Thus our search for a new diagnostic tool, for the safe, objective, routine monitoring of ONSM in NF2 patients.

Conventional visual evoked potentials (VEP) methods have been shown as sensitive tools in the assessment of optic nerve function of optic gliomas in NF1 [14,15] while mfVEP has been used in the assessment of two cases of paediatric optic nerve gliomas [16]. We hope to find a sensitive test in children without the risks of MRI, hence our selection to study mfVEP. Multifocal VEP is a variation of traditional VEP testing, assessing amplitude and latency of the central 54 degrees of the visual field to provide topographical information on the function of the optic nerve regions. Furthermore, mfVEP has been demonstrated as efficacious in objective evaluation of other compressive optic nerve pathology such as that caused by pituitary adenomas [17–19]. Similarly, we expect mfVEP to be valuable in assessment of optic neuropathy caused by ONSM growth and compression.

We therefore report the use of objective mfVEP in the routine monitoring of 3 children with ONSM in NF2. Our hypothesis was that mfVEP is a safe and effective tool by which to routinely monitor their optic nerve function.

2. Materials and methods

2.1. Subjects

At our centre, eighteen patients had a NF2 diagnosis confirmed by a clinical geneticist. Three had ONSM detected by MRI scans.

Standard ophthalmic examination and MRIs were undertaken according to the treating consultant as per guidelines. Multifocal VEP testing was performed on the same day as routine ophthalmic examination.

2.2. Recording

Multifocal VEP testing was performed on the Accumap system (Accumap; ObjectiVision Pty. Ltd. Sydney, Australia), with standard stimulus conditions described in previous papers [20–29]. Monocular stimulation was utilised for all recordings.

Four gold cup electrodes were placed in a cross around the inion, allowing 4 recording channels to minimise the effect of cortical convolution [28].

Fifty-eight cortically scaled segments arranged in dartboard configuration were generated on a computer screen, serving as the visual stimulus. Two opposite checkerboard patterns undergo pseudo-random binary exchange with a maximum stimulation rate of 75 Hz. The sequences are cross-correlated with the electrical responses recorded to extract the VEP signal for each segment. Raw signals are analysed and scaled according to the individual's background EEG levels to standardise results [27].

In paediatric testing each recording lasts 13 s, with central fixation maintained by looking at a number in the central 1 degree of the stimulus. While central fixation is difficult for patients with low acuity, at our institute, trained technicians observe patient fixation. Forty runs are performed per eye, for a total stimulus time of 10 min per eye.

Accumap severity index (ASI) gives a guide to rate amplitude loss, with 0–11 being normal, 11–19 borderline, and greater than 20 abnormal. ASI was calculated by the OPERA software, allocating scores to abnormal points and clusters, assigning specific weighting on the location of defects and comparing these to an age appropriate normative database [16,29].

Asymmetry deviation was calculated by comparing intereye difference in amplitudes within each segment of the visual field tested. Only amplitude recordings were used in our results, as with our early recordings, the machines were inaccurate for latency in the presence of significant amplitude loss.

3. Results

3.1. Case 1

Patient 1 was diagnosed with NF2 aged 7 and a left sided ONSM. Initial ophthalmic examination revealed premacular fibrosis, and bilateral posterior subcapsular cataracts.

From baseline 6/6 in the left eye, VA dropped to 6/24 over a 10 month period. However, there were no MRI changes to tumour size or associated oedema. Serial mfVEPs showed steady worsening: ASI progressing from 201 to 241, asymmetry deviation (AD) progressing from 17 sectors to 29, and decreasing central and superonasal amplitudes when compared to the baseline mfVEP (Fig. 1A). This was confirmed with a repeat mfVEP.

Decompressive surgery was undertaken due to the rapid loss of VA. Central mfVEP signal amplitudes remained unchanged, but with peripheral signal loss, ASI decreased to 263, and VA did not recover. Unfortunately, our patient's condition deteriorated further, with decline of VA to 6/60 over a month, and 6/120 following a further 5 months. Again, mfVEPs displayed corresponding worsening, with ASI progressing to 294, AD involving 38 sectors and signal amplitude loss particularly in central areas. Over this period, MRIs displayed increase in ONSM associated oedema and resultant proptosis. Proton beam radiotherapy was trialled in the United States to salvage vision.

Following proton beam radiotherapy there have been no MRI changes noted. However, over the following 3 years, patient VA dropped further to 3/90. This decline in VA was preceded by mfVEP analysis 8 months prior, with widespread amplitude loss revealing significant worsening in ASI to 418, and AD to 45 sectors densest in the inferotemporal and central regions (Fig. 1B). Case 1 has been compiled as a table, serving as an illustrative case (see Table 1).

3.2. Case 2

Diagnosed with NF2 at 1 year of age following spinal lesion biopsy, this patient had bilateral ONSMs, and was already blind in the left eye. Other ophthalmic findings were a left sided combined retinal and pigment epithelial hamartoma, and bilateral pre-macular fibrosis.

Right VA dropped from initial 6/24 to 6/60 over 7 months. Repeat MRI showed no change in tumour size, nor oedema. However, repeat mfVEPs displayed new areas of signal amplitude loss in central, inferonasal, and superotemporal regions (Fig. 2A). Despite lack of MRI changes, the clinical deterioration warranted decompression surgery with adjuvant radiotherapy. This was unable to salvage VA. However, mfVEP displayed resolution of the pre-operative paracentral defects, albeit with loss of superior peripheral amplitudes.

6 months post-intervention, VA dropped further to 6/120, associated with worsening mfVEP results, with relapse of central amplitude loss. Four months after the VA and mfVEP changes, MRI displayed a mild increase in tumour size.

In the following 10 years, the tumour has remained stable on MRI. However, VA has fluctuated, from a worst of 4/36 to a most recent acuity of 6/120. Correspondingly, ASI has worsened from 0 to a worst of 126, before improving to the current 115 (Fig. 2B). Despite an overall picture of worsening amplitude loss, there has been more recent improvement, mirroring the trends in VA.

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