ABSTRACTS

Neuro-Ophthalmic Literature Review

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Sui Wong

INTRACTABLE VOMITING IN NMO

Yeo LL, Wieder N, Wang AS, Ting E, Rathakrishnan R, Soon D. Pearls & Oy-sters: a cause of intractable vomiting. *Neurology* 2014;83:e141–e144.

The authors reported a patient with optic neuritis who initially presented with intractable vomiting, dysphagia, and left hypoglossal nerve palsy. The symptoms subsided with intravenous methylprednisolone. Serum neuromyelitis optica immunoglobulin G (NMO-IgG) was positive, confirming a diagnosis of NMO. Brain magnetic resonance imaging (MRI) showed abnormal signal in the dorsal medulla and area postrema. The area postrema, a vomiting centre, is rich in aquaporin-4 and one of the antibody targets.

Panitha Jindahra

RETINOPATHY IN ACUTE AORTIC DISSECTION

Arao K, Kuribara A, Jinnouchi H, Matsumoto M, Fujiwara T, Kinoshita N, Kakehashi A, Ako J, Momomura S. Transient retinopathy in acute aortic dissection. *Ophthalmology* 2014;121:2261–2267.

This is a prospective observational study of 64 patients with Stanford type B acute aortic dissection. Retinopathy was demonstrated in 55% of cases in the acute phase and resolved subsequently within 2 to 3 months following conservative treatment. Retinopathy findings included cotton wool spots alone ($n=31$), dot haemorrhages alone ($n=1$), and both ($n=3$). Cases with retinopathy experienced more cardio-cerebrovascular events than those without. In addition, cases with retinopathy were associated with a history of hypertension and high peak C-reactive protein levels.

Panitha Jindahra

SEESAW DYSAUTONOMIA

Wu H, Ahmed K, Tan K, Blair NF. Seesaw dysautonomia: a manifestation of autonomic dysreflexia. *Neurology* 2014;83:2093–2095.

The authors reported a 58-year-old man who presented with several episodes of alternating anisocoria, unilateral hyperhidrosis ipsilateral to the larger pupil, and hypertension. These episodes occurred after an incomplete spinal cord injury at the level of C6–C7 many years past. Anisocoria seen in this case could be due to sympathetic overactivity of autonomic dysreflexia on one side with contralateral suppression on the other.

Panitha Jindahra

MALARIAL RETINOPATHY

MacCormick IJC, Beare NAV, Taylor TE, Barrera V, White VA, Hiscott P, Molyneux ME, Dhillon B, Harding SP. Cerebral malaria in children: using the retina to study the brain. *Brain* 2014;137:2119–2142.

To determine whether malarial retinopathy reflects cerebrovascular injury, the authors reviewed retinal and cerebral manifestations of malaria in children. In the brain, parasitised erythrocytes bind to vascular endothelium, causing sequestration. Microvascular obstruction and poor perfusion subsequently develop. Additionally, cerebral haemorrhage, brain swelling, and vessel leakage occur. Likewise, sequestration is also observed in retinal capillaries and the margins of larger retinal vessels. These vessels become white and orange. Fundus fluorescein angiogram demonstrates leakage from the vessels. Pale areas on the retina (retinal whitening) reflect impaired perfusion. White-centred retinal haemorrhages are frequent findings.

Panitha Jindahra

NATALIZUMAB IN MULTIPLE SCLEROSIS

Butzkueven H, Kappos L, Pellegrini F, Trojano M, Wiendl H, Patel RN, Zhang A, Hotermans C, Belachew S, on behalf of the TYSABRI Observational Program (TOP). Efficacy and safety of natalizumab in multiple sclerosis: interim observational programme results. *J Neurol Neurosurg Psychiatry* 2014;85:1190–1197.

The study supported the long-term safety of natalizumab and its efficacy in patients with relapsing remitting multiple sclerosis. It was an open-label observational study, conducted from 2007 to 2012 in 16 countries. Of 4821 patients enrolled, most were followed up for at least 2 years. About 8% of patients developed a serious adverse event. Infection was the most frequent (1.9%). Eighteen cases (0.4%) experienced progressive multifocal leucoencephalopathy after 11–44 doses. Mean annualised relapse rate declined significantly from 1.99 per year to 0.31 following the treatment. Expanded Disability Status Scale (EDSS) scores were also stable throughout the investigation.

Panitha Jindahra

GLYCINE RECEPTOR ANTIBODIES IN PERM AND RELATED SYNDROMES: CHARACTERISTICS, CLINICAL FEATURES AND OUTCOMES

Carvajal-González A, Leite MI, Waters P, Woodhall M, Coutinho E, Balint B, Lang B, Pettingill P, Carr A, Sheerin U, Press R, Lunn MP, Lim M, Maddison P, Meinck HM, Vandenberghe W, Vincent A. *Brain* 2014;137:2178–2192.

The authors described 45 cases with GlyR antibodies. Most cases developed progressive encephalomyelitis with rigidity and myoclonus (PERM), which is characterised by brainstem involvement and axial/limb rigidity. They presented with abnormal eye movement, speech/swallowing problems, walking difficulties, spasm, hyper-ekplexia, and autonomic disturbance. Other clinical features included stiff person syndrome (axial stiffness without brainstem involvement), optic neuritis, seizures, and cognitive impairment. Thymoma and lymphoma were not uncommon. They responded well to immunotherapies.

Panitha Jindahra

RETINAL OCT REVEALS IN VIVO EVIDENCE FOR GENETICALLY DETERMINED STRUCTURAL DYNAMICS ON A CELLULAR LEVEL THAT MIGHT BE OF DIAGNOSTIC RELEVANCE—A FIERCELY DISCUSSED OBSERVATION

(1) Abràmoff MD, Mullins RF, Lee K, Hoffmann JM, Sonka M, Critser DB, Stasheff SF, Stone EM. Human photoreceptor outer segments shorten during light adaptation. *Invest Ophthalmol Vis Sci* 2013;54:3721–3728.

This multimodal study by the Iowa group combined genetic, structural (optical coherence tomography [OCT]), and functional (electrooculography [EOG]) data to investigate anatomical changes in the outer retinal layers during dark and light adaptation. Data from 11 healthy control subjects were compared with findings from seven patients with Best vitelliform macular dystrophy (F. Best, *Ophthalmologica* 1905;13:199–212). The study was

inspired by the observation that in Best disease there is decreased responsiveness of the EOG to changes in light exposure. The study design was rigorous, correcting for possible diurnal variation contributing to a circadian component with all scans performed on early winter mornings (6:00–8:30 AM) over a 2-year period (2011–2012). Spectral-domain OCT was used with appropriate precautions against stray light and the use of an external fixation target. Longitudinal OCT images were taken at 6-minute intervals for a 30–45-minute observation period. The main findings were that of a reverse longitudinal pattern of the thickness of the outer retinal layers to light exposure between controls (getting smaller by about 3 μm within 15 minutes) compared with patients with Best disease (increasing by about 2 μm within 10 minutes). The structural data from the OCT matched the time profile of the functional data from the EOG in the two subjects investigated. Clearly, the changes observed with OCT were so small that macular volume scans were required to reach statistical significance. The argument might be even stronger if the authors would have provided evidence for different regional volume changes in the foveola, paramacular region, and close to the optic disc. Taken together, the authors showed for the first time a temporal relationship between the light phase of the EOG with volume thickness changes of the outer retinal layers using OCT that might not only be of diagnostic value, but also permit testing of hypotheses on the pathophysiology of Best disease *in vivo*.

(2) Kay DB, Land ME, Cooper RF, Dubis AM, Godara P, Dubra A, Carroll J, Stepien KE. Outer retinal structure in best vitelliform macular dystrophy. *JAMA Ophthalmol* 2013;131:1207–1215.

Combining adaptive optics scanning laser ophthalmoscopy with spectral-domain OCT allowed David Kay et al. to report in great detail four patients with one particular Best mutation: Arg218Cys. This carefully conducted study did not confirm the findings made by the Iowa group in the paper discussed above or a subsequent study on 15 patients with Best disease (Kay C, et al. Three-dimensional distribution of the vitelliform lesion, photoreceptors, and retinal pigment epithelium in the macula of patients with best vitelliform macular dystrophy. *Arch Ophthalmol* 2012;130:357–364). Borrowing from the 1979 movie *Kramer versus Kramer*, the discussion in the literature may become “Kay versus Kay”.

(3) Abràmoff MD, Mullins RF, Stone EM. Outer segment length in different Best disease genotypes. *JAMA Ophthalmol* 2014;132:1152–1153.

The Iowa group present a retrospective analysis of their data showing that in their only patient with Best and the Arg218Cys mutation (and one with the Asn133Lys mutation), the outer segment was shorter compared with the other mutations. There were methodological issues about light adaptation, too. But most importantly, it was suggested that the different functional and histopathological characteristics of BEST1 mutations might be the source of a potential inclusion bias.

(4) Stepien KE, Kay DB, Carroll J. Outer segment length in different Best disease genotypes—reply. *JAMA Ophthalmol* 2014;132:1153.

In their response, the Wisconsin group concede to methodological issues on light adaptation, but also raise other methodological issues about the OCT and image post-processing with automated retinal layer segmentation. It was suggested that the contrast of the outer retinal bands is lower during light adaptation. There are a number of other factors known to affect retinal layer reflectivity, such as variation of the OCT beam pathway during scan acquisition. Such potential sources for artefacts will need to be rigorously controlled for, ideally using validated OCT quality control criteria to test the important point made by the group, that there may be a future for imaging metrics as a secondary outcome measure for future treatment trials.

Axel Petzold

DECREASED ARTERIOLAR DIAMETER IN PROGRESSED NTG PATIENTS, NOT IN STABLE NTG PATIENTS

Lee TE, Kim YY, Yoo C. Retinal vessel diameter in normal-tension glaucoma patients with asymmetric progression. *Graefes Arch Clin Exp Ophthalmol* 2014;252:1795–1801.

In this retrospective study, the authors examined the central retinal vessel diameters of normal-tension glaucoma (NTG) patients, comparing those noted to have new retinal nerve fibre layer (RNFL) defects or progression of

existing defects against those deemed stable over a mean follow-up of 24.3 months. Progression was also confirmed by correlating RNFL defects with visual field changes. With a p value of less than 0.0001, the central retinal arteriolar equivalent (CRAE), as measured by IVAN software from retinal images, was noted to be thinner by about 21 microns in the progressed eyes, whereas stable eyes revealed a thinning of less than 1 micron over the course of follow-up. The central retinal venular equivalent (CRVE) was not noted to be significantly different between the groups. As the authors note, this corroborates recent data from the Blue Mountains Eye Study, which showed a higher correlation of incident primary open angle glaucoma (POAG) in eyes with a smaller CRAE, but not in those with a smaller CRVE. It is posited that the narrowing of the retinal arterioles could be either a cause of ischaemic or re-perfusion injury to the RNFL or a resultant effect of decreased perfusion demand in already-damaged tissue.

Evan Price

EARLY GCC THINNING IN NAION

Larrea BA, Iztueta MG, Indart LM, Alday NM. Early axonal damage detection by ganglion cell complex analysis with optical coherence tomography in nonarteritic anterior ischaemic optic neuropathy. *Graefes Arch Clin Exp Ophthalmol* 2014;252:1839–1846.

Ganglion cell complex (GCC) analysis via optical coherence tomography (OCT) is an emerging modality in the evaluation of optic neuropathies. In this retrospective case series, 22 patients with nonarteritic ischaemic optic neuropathy (NAION) underwent GCC and retinal nerve fibre layer (RNFL) thickness measurement in both the acute (2–6 weeks after the onset of symptoms) and chronic (at least 6 months later) phases. In the acute phase, whereas the mean RNFL was thickened by oedema or within normal values in 100% of cases, the average GCC was noted to be below normal values in 54.5% of patients. The minimum GCC was observed to be below normal values in 77.3% of patients. The authors also compared GCC thinning with visual field (VF) defects and suggest that the average GCC thickness in the acute phase of NAION may be predictive of the final VF defects.

Evan Price

BEYOND STEROIDS FOR THYROID EYE DISEASE

Salvi M. Immunotherapy for Graves' ophthalmopathy. *Curr Opin Endocrinol Diabetes Obes* 2014;21:409–414.

Active thyroid eye disease (TED) is mainly treated with steroids. Both oral and intravenous steroids are given, and both higher and lower intravenous dosing have been used. Of all these, some evidence suggests that higher-dose intravenous treatment has the greatest efficacy and lower side effects. Nevertheless, as this review explains, up to 20% of patients with TED have no response to any steroid dose. For this reason, other non-steroid immunosuppressants are being tried in the treatment of TED. Different targets for immunotherapy include the thyrotropin (TSH) receptor, the insulin-like growth factor (IGF)-1 receptor (teprotumumab), tumour necrosis factor-alpha (etanercept), interleukin-6 (tocilizumab), and interleukin-1. The compound that seems to have the greatest promise for TED, however, is rituximab, which targets B cells but also affects T cells. None of these medications have published placebo-controlled trials but some have shown open-label efficacy.

John H. Pula

REVERSAL OF PUPILLARY ATONIA AFTER REMOVAL OF AN ENCIRCLING BAND

Bremner FD, Zambarakji H, Griffiths C. Reversal of pupillary atonia after removal of an encircling band. *J Neuroophthalmol* 2014;34:268–270.

The authors describe a patient who developed an atonic pupil after placement of an encircling band during retinal detachment surgery. When the band was removed 18 months later, the pupil signs showed partial recovery, demonstrating a degree of reversibility of the parasympathetic paresis. We speculate that in this case mechanical deformation of the sclera by the encircling band had produced a conduction block of the short posterior ciliary nerve fibres as they pass forward in the underlying suprachoroidal space.

Michael Vaphiades

CEREBROSPINAL FLUID LEAK PRESENTING AS OCULORRHEA AFTER BLUNT ORBITOCRANIAL TRAUMA

Apkarian AO, Hervey-Jumper SL, Trobe JD. Cerebrospinal fluid leak presenting as oculorrhea after blunt orbitocranial trauma. *J Neuroophthalmol* 2014;34:271–273.

The authors report a patient who developed cerebrospinal fluid (CSF) oculorrhoea after blunt head trauma with associated facial fractures and a bout of vomiting. The oculorrhea ceased spontaneously within 6 days of the trauma. This manifestation of CSF leak must not be overlooked because of the threat of meningitis.

Michael Vaphiades

CHIASMAL GLIOMA IN SPASMUS NUTANS: A CAUTIONARY NOTE

Brodsky MC, Keating GF. Chiasmal glioma in spasmus nutans: a cautionary note. *J Neuroophthalmol* 2014;34:274–275.

The authors report an 8-month-old infant who had spasmus nutans with chiasmal glioma, a known association. The spasmus nutans spontaneously resolved. Magnetic resonance imaging showed no interval change in tumour size over the next 8 months. Clinical resolution of spasmus nutans does not preclude chiasmal glioma as the underlying cause.

Michael Vaphiades

VITREOUS SEEDING FROM A LARGE OPTIC DISC MELANOCYTOMA

Guo H, Li Y, Chen Z, Guo X. Vitreous seeding from a large optic disc melanocytoma. *J Neuroophthalmol* 2014;34:276–277.

The authors report a 17-year-old man with an optic disc melanocytoma that ruptured and seeded the vitreous with pigmented cells. Pathogenic mechanisms and visual prognosis are discussed.

Michael Vaphiades

CEREBROSPINAL FLUID PRESSURE IN ADULTS

Lee SC, Lueck CJ. Cerebrospinal fluid pressure in adults. *J Neuroophthalmol* 2014;34:278–283.

The authors performed a literature review of cerebrospinal fluid pressure in adults and concluded that the normal range of intracranial pressure measured by lumbar puncture in a typical clinical setting should be 6 to 25 cm H₂O with a mean of 18 cm H₂O, yet some normal individuals have pressures of 30 cm H₂O (or, occasionally, even higher). Also, patient's leg position in the lateral decubitus position is not that important in the pressure measurement. The authors conclude that pressure measurements should be interpreted in the clinical context.

Michael Vaphiades

INTERPRETATION OF LUMBAR PUNCTURE OPENING PRESSURE MEASUREMENTS IN CHILDREN

Avery RA. Interpretation of lumbar puncture opening pressure measurements in children *J Neuroophthalmol* 2014;34:284–287.

The authors performed a literature review of cerebrospinal fluid pressure in children and concluded that ≤ 28 cm H₂O can be considered “normal” for most children. The patient's depth of sedation, body mass index, and

sedation medication can sometimes result in small increases in pressure. Patient age and leg position (flexed vs. extended) in the lateral decubitus position do not seem to significantly impact these measures.

Michael Vaphiades

OPTIC NEUROPATHY AND GOLIMUMAB

Chang JR, Miller NR. Bilateral optic neuropathy associated with the tumor necrosis factor-alpha inhibitor golimumab. *J Neuroophthalmol* 2014;34:336–339.

The authors report a 62-year-old man who developed bilateral simultaneous anterior optic neuropathy while taking the tumour necrosis factor-alpha (TNF- α) inhibitor golimumab for prostate cancer. He had been on the medication for 1 year. Despite extensive work-up, no other aetiology for the optic neuropathies were detected. The authors concluded that this case represents a rare but well-documented serious adverse event associated with TNF- α inhibitors.

Michael Vaphiades

NONINVASIVE ASSESSMENT OF CEREBROSPINAL FLUID PRESSURE

Bruce BB. Noninvasive assessment of cerebrospinal fluid pressure. *J Neuroophthalmol* 2014;34:288–294.

The authors reviewed the currently available methods to noninvasively evaluate intracranial pressure. The authors concluded that numerous approaches have been applied to the problem, although none seems to represent a complete solution.

Michael Vaphiades

THE TAKEAWAY FRENZEL GOGGLES

Strupp M, Fischer C, Hanß L, Bayer O. The takeaway Frenzel goggles: a Fresnel-based device. *Neurology* 2014;83:1241–1245.

The authors developed and evaluated a new thin and light glasses for the examination of patients with nystagmus and to compare them with Frenzel goggles. They found that for suppression of nystagmus, the new Fresnel-based device or so-called M glasses is not inferior to Frenzel goggles. Doctors can carry it in their pocket, it is inexpensive and easy to handle and to fix to the patient's nose so that it can be used in daily practice for the bedside examination.

Michael Vaphiades

PRES WITH SPINAL CORD INVOLVEMENT

de Havenon A, Joos Z, Longenecker L, Shah L, Ansari S, Digre K. Posterior reversible encephalopathy syndrome with spinal cord involvement. *Neurology* 2014;83:2002–2006.

The authors reported two patients with the signs and symptoms of posterior reversible encephalopathy syndrome (PRES), but with clinical and radiologic involvement of the spinal cord. They also analysed an additional six cases in the MEDLINE database and analysed the clinical and imaging characteristics of the eight cases. They proposed a new syndrome named PRES with spinal cord involvement (PRES-SCI).

Michael Vaphiades

VEMURAFENIB IN ERDHEIM-CHESTER DISEASE

Cohen-Aubart F, Emile JF, Maksud P, Galanaud D, Idbaih A, Chauvet D, Amar Y, Benameur N, Amoura Z, Haroche J. Marked efficacy of vemurafenib in suprasellar Erdheim-Chester disease. *Neurology* 2014;83:1294–1296.

The authors report a 58-year-old man with Erdheim-Chester disease (ECD) with visual loss due to compression of the optic chiasm by a suprasellar lesion refractory to conventional treatment with interferon- α , who displayed reversal of this vision loss after 1 month of vemurafenib therapy. The authors discuss the drug.

Michael Vaphiades

PHOTOGRAPHIC ANALYSIS OF OBLIQUE MUSCLE DYSFUNCTION

Yoon CK, Yang HK, Kim JS, Hwang JM. An objective photographic analysis of ocular oblique muscle dysfunction. *Am J Ophthalmol* 2014;158:924–931.

In this prospective, observational study of 12 volunteers and 27 patients with oblique muscle overaction or underaction in at least one eye, the authors developed a new objective method for measuring ocular oblique muscle dysfunction using corneal contour in 9-gaze photographs transcribed into an ellipse. As the eyes moved the muscle dysfunction was analysed using the angular difference between the two eyes. The authors concluded this photographic analysis could provide an objective and accurate means of evaluating ocular oblique muscle dysfunction.

Michael Vaphiades

PAPILLOEDEMA GRADE AND DIFFUSION MRI IN IIH

Salvay DM, Padhye LV, Huecker JB, Gordon MO, Viets R, Sharma A, Van Stavern GP. Correlation between papilloedema grade and diffusion-weighted magnetic resonance imaging in idiopathic intracranial hypertension. *J Neuroophthalmol* 2014;34:331–335.

The authors studied 42 patients with papilloedema and idiopathic intracranial hypertension (IIH) who underwent orbital magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI). The hyperintensity of the optic nerve head (ONH) on DWI was graded and was compared with papilloedema grade. The authors found a significant correlation between the severity of papilloedema and ONH hyperintensity on DWI. They concluded that DWI may provide a surrogate marker for the presence and severity of papilloedema.

Michael Vaphiades

PERIPHERAL CONE DYSTROPHY

Vaphiades MS, Doyle JL. Peripheral cone dystrophy: a diagnostic improbability? *J Neuroophthalmol* 2014;34:366–368.

The authors reported a 19-year-old man with bilateral peripheral visual field loss, hemeralopia (day blindness), and photophobia. Examination and testing were in keeping with peripheral cone dystrophy. Cone dystrophy refers to a group of genetically heterogeneous disorders ranging from normal to mild pigmentary mottling to bull's eye maculopathy. It can be subdivided into central and peripheral forms. Peripheral cone dystrophy, the rarer of the two types, is discussed.

Michael Vaphiades

IGG4-RELATED OPHTHALMIC DISEASES

Sogabe Y, Ohshima K, Azumi A, Takahira M, Kase S, Tsuji H, Yoshikawa H, Nakamura T. Location and frequency of lesions in patients with IgG4-related ophthalmic diseases. *Graefes Arch Clin Exp Ophthalmol* 2014;252:531–538.

In this Japanese study of 64 patients, the authors report the location and frequency of immunoglobulin G4 (IgG4) lesions on radiological imaging (MRI or CT). The lacrimal gland was the most frequently involved location, found in 48% of patients. Interesting observations include the enlargement of trigeminal nerve branch found in 39% of patients, many bilateral, which were apparently asymptomatic. Eight patients had restriction of ocular movement, although the majority of these was due to lesions at the orbital fat tissue or a localised orbital mass. Extraocular muscle enlargement was found in 16 (25%), of which only three led to restriction of ocular movements. Six (9%) patients presented with visual disturbance due to optic nerve involvement. Elevated IgG4 levels were observed in all except two patients, and IgG4/IgG ratio was elevated in all but one.

Sui Wong

STENT FAILURE IN PSEUDOTUMOR CEREBRI

Goodwin CR, Elder BD, Ward A, Orkoulas-Razis D, Kosztowski TA, Hoffberger J, Moghekar A, Radvany M, Rigamoni D. Risk factors for failed transverse sinus stenting in pseudotumor cerebri patients. *Clin Neurol Neurosurg* 2014;127:75–78.

The authors from Johns Hopkins University examined the outcomes in 18 patients with IIH who were treated with venous stent for transverse sinus stenosis. Three patients required subsequent shunt placement. These three patients had a higher mean CSF opening pressure (50 cm H₂O, range: 40–55) compared with the other 15 patients (mean: 37, range: 25–50). Although the analysis showed statistical significance ($p=0.012$), the numbers are small and therefore results should be interpreted with caution. Nonetheless, this is an interesting observation that warrants investigation in future prospective studies.

Sui Wong