ABSTRACTS

Neuro-Ophthalmic Literature Review

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Sui Wong

THE IIHTT: PAPILLOEDMA OUTCOME OF THE OCT SUBSTUDY

Optical Coherence Tomography Substudy Committee and the NORDIC Idiopathic Intracranial Hypertension Study Group. Papilledema outcomes from the optical coherence tomography substudy of the Idiopathic Intracranial Hypertension Treatment Trial. *Ophthalmology* 2015;122:1939–1945.e2.

The Idiopathic Intracranial Hypertension Treatment Trial (IIHTT), published in *JAMA* last year, is a randomised double-masked controlled trial of weight management plus acetazolamide vs. placebo for the management of IIH patients with mild visual loss, with 6 months' follow-up. This paper reports the papilloedema outcomes from the OCT substudy. Eighty-nine patients (43 acetazolamide/46 placebo) of the 165 IIHTT patients were included in the OCT substudy. They had spectral-domain OCT imaging of the optic disc and macula at study entry, 3 months, and 6 months with Cirrus 4000 SD-OCT. The retinal nerve fibre layer thickness (RNFLT), total retinal thickness (TRT), and optic nerve head volume (ONHV) were derived from the optic disc scan; and the retinal ganglion cell layer + inner plexiform layer (RGC + IPL) was derived from the macular scan. The results were then compared with Frisén grading of papilloedema from digital optic disc photos. The two groups had similar OCT measurements at baseline. At 6 months, the acetazolamide group had significantly lower RNFLT, TRT, and ONHV than the placebo group. In both groups, the RNFLT, TRT, and ONHV also decreased significantly, but to a smaller extent, in those patients who lost 6% of body weight compared with those who did not. At 6 months, the RNFLT, TRT, and ONHV measurements showed moderate correlations with Frisén grading, but they did not correlate with visual acuity/visual field outcomes or cerebrospinal fluid (CSF) opening pressure. In both groups, there was mild thinning of RGC + IPL at 6 months, which meant both groups had minimal optic atrophy. The authors commented that OCT was a useful biomarker for monitoring the effects of treatment in IIH.

Carmen Chan

OCT FOR GRAVES' OPHTHALMOPATHY

Häner NU, Dysli M, Abegg M, Zinkernagel MS. Enhanced-depth optical coherence tomography for imaging horizontal rectus muscles in Graves' orbitopathy. *Graefes Arch Clin Exp Ophthalmol* 2015;253:1569–1573.

Optical coherence tomography (OCT) may be useful in Graves' ophthalmopathy (GO). Using enhanced-depth imaging anterior segment OCT (EDI AS-OCT), the authors measured the thickness of the horizontal rectus tendons in 15 patients with GO and 12 healthy controls. Mean medial rectus thickness was noted to be significantly thicker in the GO group as compared with controls (256.4 vs. 214.7 μm ; $p = 0.046$), whereas the lateral rectus was not noted to be significantly different in thickness. The authors note that this is consistent with the clinical observation that the inferior recti and medial recti are preferentially affected in GO. By analysing clinical activity score (CAS), they were also able to report that severity of GO was directly correlated with severity of medial rectus tendon thickening. It is interesting that thickening of the tendon itself was noted, as the tendon is usually spared in GO on imaging studies (a difference that the authors ascribe to decreased resolution on magnetic resonance imaging [MRI] as compared to OCT). The authors also note that one patient had EDI AS-OCT measurements done both before and after treatment with corticosteroids. In this patient, medial rectus thickness was noted to decrease from 336 to 182 μm over 2 months. Although the specificity of significant MR swelling on OCT is unclear, it appears that it may have an appropriate role in diagnosis and clinical monitoring.

Evan Price

VIRTUAL FISTICUFFS AND TRAUMATIC OPTIC NEUROPATHY

Huempferner-Hierl H, Böhne A, Wollny G, Sterker I, Hierl T. Blunt forehead trauma and optic canal involvement: finite element analysis of anterior skull base and orbit on causes of vision impairment. *Br J Ophthalmol* 2015;99:1430–1434.

The authors examine the structural mechanics of blunt forehead trauma using finite element analysis, with the goal of better understanding the mechanism of indirect traumatic optic neuropathy. A high-resolution virtual skull model composed of about 740,000 elements was generated from a computed tomography (CT) scan and was exposed to simulated impacts to the forehead from an impactor that was modelled to emulate a human fist. In the “low-impact” simulation, the stresses imparted to the model did not necessarily correlate with fracture, but they did propagate posteriorly to the optic foramen and near the chiasm. Furthermore, the analysis showed oscillation in the optic canal. It is noted that the exact mechanism of damage to the optic nerve itself remains hypothetical, but nerve oedema, haemorrhage, concussion/contusion, shearing, sheath haematoma, and chiasmal injury are all mentioned as possibilities. The authors also note that formal study of the transmission of force to intracanalicular soft tissues would require segmentation data that are not currently available and assert that further biomechanical studies would be helpful.

Evan Price

MANAGING THYROID EYE DISEASE

Rao R, MacIntosh PW, Yoon MK, Lefebvre DR. Current trends in the management of thyroid eye disease. *Curr Opin Ophthalmol* 2015;26:484–490.

This paper attempts to summarise current therapy of thyroid eye disease. It focuses on recent data regarding steroid management and newer biologicals such as rituximab, with a relatively lengthy discussion on some detailed aspects of orbital decompression. The review cannot be considered comprehensive, as limitations include no mention of various immunosuppressants such as methotrexate and limited discussion on the management of diplopia. There is also a lack of tables or diagrams, which would have been helpful for reference. However, the authors did an excellent job attempting to summarise the myriad approaches to the treatment of this confounding disease.

John H. Pula

LIVING WITH HEMIANOPIA

de Haan GA, Heutink J, Melis-Dankers BJ, Brouwer WH, Tucha O. Difficulties in daily life reported by patients with homonymous visual field defects. *J Neuroophthalmol* 2015;35:259–264.

The authors interviewed 44 patients with homonymous hemianopia or quadrantanopia using three standardised questionnaires: National Eye Institute Visual Functioning Questionnaire, Independent Mobility Questionnaire, and Cerebral Visual Disorders Questionnaire, to measure for the presence or absence of experienced difficulties. The study linked the content of these three questionnaires to the International Classification of Functioning, Disability, and Health (ICF), which is a classification of health and health-related domains. The investigators noted that besides well-known difficulties related to reading, orientation, and mobility, a high proportion of patients with homonymous visual field defects (HVFD) reported problems that previously have not been documented in the literature, such as impaired light sensitivity, colour vision, and perception of depth, and that these findings have implications for future study, assessment, and rehabilitation of patients with HVFD.

Michael Vaphiades

DIPLOPIA AND DENGUE FEVER

Mishra A, Shukla S, Aggarwal S, Chaudhary B. Lateral rectus palsy in a case of dengue fever. *Med J Armed Forces India* 2015;71(Suppl 1):S101–S103.

The authors present the second ever reported case of abducens nerve palsy complicating dengue fever in a previously healthy male. They discuss the disease and its neuro-ophthalmologic sequelae.

Michael Vaphiades

VISION AND CONCUSSION TESTING

Galetta KM, Morganroth J, Moehring N, Mueller B, Hasanaj L, Webb N, Civitano C, Cardone DA, Silverio A, Galetta SL, Balcer LJ. Adding vision to concussion testing: a prospective study of sideline testing in youth and collegiate athletes. *J Neuroophthalmol* 2015;35:235–241.

The authors conducted a prospective study to investigate how adding a vision-based test of rapid number naming could increase their ability to identify concussed athletes on the sideline at youth and collegiate levels. They concluded that by adding a vision-based performance measure to cognitive and balance testing enhanced the detection capabilities of current sideline concussion assessment.

Michael Vaphiades

A NEW APPROACH TO GCA

El-Dairi MA, Chang L, Proia AD, Cummings TJ, Stinnett SS, Bhatti MT. Diagnostic algorithm for patients with suspected giant cell arteritis. *J Neuroophthalmol* 2015;35:246–253.

The authors proposed a clinical algorithm that is highly predictive for a positive temporal artery biopsy (TAB) and is of value in the evaluation process of suspected cases of giant cell arteritis (GCA). They conducted a retrospective review of 213 consecutive cases of seen at a single academic centre over a 10-year period. Pathologic specimens were re-reviewed and agreement between the original and second readings was assessed. A composite clinical suspicion score was created by adding 1 point for each of the following criteria: anterior extracranial circulation ischaemia, new onset headache, abnormal laboratory results (erythrocyte sedimentation rate, C-reactive protein [CRP], or platelet count), jaw claudication, abnormal or tender superficial temporal artery, constitutional symptoms, and polymyalgia rheumatica; 1 point was subtracted if a co-morbid condition could explain a criterion. They found that TAB-positive patients were more likely to be older (age 75.2 ± 7.8), complain of jaw claudication, and have thrombocytosis and elevated CRP. None of the patients with a clinical score less than 2 had a positive TAB. Diabetes mellitus and kidney disease were often the explanation for the symptoms and abnormal clinical findings that led to a negative TAB because these diseases have vascular complications that may mimic GCA.

Michael Vaphiades

H1N1 INFLUENZA AND VISION LOSS

Breker DA, Stacey AW, Srinivasan A, Bursztyn LL, Trobe JD, Johnson MW. Vision loss caused by retinal and lateral geniculate nucleus infarction in H1N1 influenza. *J Neuroophthalmol* 2015;35:265–269.

The authors report a 13-year-old girl who developed encephalopathy and confluent ischaemic retinopathy from H1N1 influenza A. Brain magnetic resonance imaging (MRI) disclosed lateral geniculate body signal abnormalities indicative of haemorrhagic infarction. Despite aggressive treatment, vision did not improve from light perception in either eye. The authors concluded that H1N1 can cause simultaneous retinal and lateral geniculate body infarctions, a combination of findings not previously described in any condition.

Michael Vaphiades

APRACLONIDINE TESTING

Kauh CY, Bursztyn LL. Positive apraclonidine test in Horner syndrome caused by thalamic hemorrhage. *J Neuroophthalmol* 2015;35:287–288.

The authors report a case of a 69-year-old man with Horner syndrome due to thalamic haemorrhage with a positive apraclonidine test, suggesting that apraclonidine testing is useful in confirming the diagnosis within days of onset even in a lesion located at the most proximal portion of the oculosympathetic pathway.

Michael Vaphiades

ANOTHER USE FOR OCT

Vieira LM, Silva NF, Dias Dos Santos AM, Anjos RS, Pinto LA, Vicente AR, Borges BI, Ferreira JP, Amado DM, Cunha JP. Retinal ganglion cell layer analysis by optical coherence tomography in toxic and nutritional optic neuropathy. *J Neuroophthalmol* 2015;35:242–245.

The authors conducted an observational cross-sectional study in healthy subjects and in patients with toxic optic neuropathy. The study included 16 eyes of 12 healthy subjects and 16 eyes of 8 patients with toxic and nutritional optic neuropathy. They noted a decreased retinal ganglion cell layer (RGC) thickness and volume in the optic neuropathy group and concluded that RGL analysis may help in the diagnosis and management of these patients.

Michael Vaphiades

CHARLES BONNET SYNDROME AND RETINITIS PIGMENTOSA

O'Hare F, Bentley SA, Wu Z, Guymer RH, Luu CD, Ayton LN. Charles Bonnet syndrome in advanced retinitis pigmentosa. *Ophthalmology* 2015;122:1951–1953.

Chronic visual hallucinations associated with vision loss is known as the Charles Bonnet syndrome (CBS). The authors evaluated 72 participants with a history of retinitis pigmentosa (RP) and severe visual impairment via telephone interview. They noted that 27 of the 72 participants (at least 1/3) experienced visual hallucinations in keeping with CBS, which has important implications in routine ophthalmologic care and treatment trials.

Michael Vaphiades

POST-LUMBAR PUNCTURE TONSILLAR HERNIATION IN IIH

Borire AA, Hughes AR, Lueck CJ. Tonsillar herniation after lumbar puncture in idiopathic intracranial hypertension. *J Neuroophthalmol* 2015;35:293–295.

The authors report a 30-year-old woman who developed cerebellar tonsillar herniation requiring intubation after a lumbar puncture (LP). Brain magnetic resonance imaging at initial diagnosis showed minor tonsillar descent and computed tomographic venography revealed hypoplasia of the left transverse sinus. The patient previously had three uneventful LPs, all of which showed high opening pressures and normal cerebrospinal fluid composition. In retrospect, it was noted that her serum bicarbonate had fallen to 9 mmol/L (normal: 22–28 mm/L) 1 week before the LP (she was being treated with 1000 mg of acetazolamide daily). The authors hypothesised that the combination of cerebral oedema (due to worsening metabolic acidosis), poor venous drainage, and pre-existing minor tonsillar descent contributed to the cerebellar tonsillar herniation.

Michael Vaphiades

A SCORE FOR ANEURYSMS

Etminan N, Brown RD Jr, Beseoglu K. The unruptured intracranial aneurysm treatment score: a multidisciplinary consensus. *Neurology* 2015;85:881–889.

The authors developed an unruptured intracranial aneurysm (UIA) treatment score (UIATS) model that includes and quantifies key factors involved in clinical decision-making in the management of UIAs. An international multidisciplinary (neurosurgery, neuroradiology, neurology, clinical epidemiology) group of 69 specialists was convened to develop and validate the UIATS model using a Delphi consensus. This novel UIA decision guidance study captured an excellent consensus among highly informed individuals on UIA management, irrespective of their underlying specialty. Clinicians can use the UIATS as a comprehensive mechanism for indicating how a large group of specialists might manage an individual patient with a UIA.

Michael Vaphiades

VISUAL FIELD DEFECTS IN TBI

Jang SH, Seo JP. Damage to the optic radiation in patients with mild traumatic brain injury. *J Neuroophthalmol* 2015;35:270–273.

The authors report two patients with mild traumatic brain injury (TBI) and nine age-matched normal control subjects. Peripheral field defects were detected with automated perimetry in both patients. Injury of the optic radiation (OR) as demonstrated by diffusion tensor imaging (DTI) in the two study patients but were not detected on conventional brain magnetic resonance imaging (MRI) imaging nor on the DTI of the controls.

Michael Vaphiades

THIAMINE DEFICIENCY AND OCT CHANGES

Sia PI, Sia DI, Crompton JL, Casson RJ. Nerve fiber layer infarcts in thiamine deficiency. *J Neuroophthalmol* 2015;35:274–276.

Optic neuropathy is a rare manifestation of Wernicke encephalopathy and is usually associated with fundus appearances of optic disc swelling or optic disc pallor. The authors reported two cases of thiamine deficiency where the fundus demonstrated peripapillary retinal nerve fibre layer thickening (confirmed by OCT) but no florid disc swelling or pallor.

Michael Vaphiades

HAEMORRHAGE OF A HAEMANGIOMA

Grob SR, Campbell AA, Gross A, Cestari DM. Hemorrhage within the optic nerve from a cavernous hemangioma of the optic disc. *J Neuroophthalmol* 2015;35:277–279.

The authors present a 49-year-old woman with a known right optic disc cavernous haemangioma who haemorrhaged in the anterior portion of the right intraorbital optic nerve. She experienced pain with eye movements and worsening of a superior visual field defect while retaining 20/20 visual acuity. Magnetic resonance imaging was consistent with a haemorrhage in the anterior portion of the right intraorbital optic nerve. The authors are unaware of previous reports of haemorrhage into the optic nerve from a cavernous haemangioma of the optic disc.

Michael Vaphiades

DETECTING PRE-SYMPTOMATIC NA-AION WITH FA

Cestari DM, Lessell S, Mantopoulos D. Early diagnosis of subclinical interferon alpha-associated optic neuropathy using fluorescein angiography. *J Neuroophthalmol* 2015;35:280–283.

The authors report a case of a 57-year-old man who presented with decreased visual acuity in the left eye secondary to nonarteritic anterior ischaemic optic neuropathy (NAION) while on therapy with interferon- α for hepatitis C. Fundus fluorescein angiography revealed late leakage of both optic discs, consistent with bilateral disease. One week later, the patient developed clinical signs and symptoms consistent with NAION in the fellow eye. The authors concluded that fluorescein angiography may play an important role in identifying subclinical NAION in patients taking interferon- α .

Michael Vaphiades

DISK CUPPING IN METHANOL POISONING

Galvez-Ruiz A, Elkhamary SM, Asghar N, Bosley TM. Cupping of the optic disk after methanol poisoning. *Br J Ophthalmol* 2015;99:1220–1223.

The authors conducted a retrospective review of 50 consecutive patients with methanol poisoning. They found that optic disk cupping ≥ 0.8 c/d was present in at least one eye of 22 patients (43/100 eyes). Increasing severity of disk cupping was found to be significantly correlated with worse visual acuity and increasing visual field loss. In addition to arteritic ischaemic optic neuropathy (arteritic AION), methanol poisoning is an alternative diagnosis associated with significant disk cupping in non-glaucomatous optic neuropathies.

An-Guor Wang

NEUROPROTECTIVE EFFECT OF HUMAN SERUM ALBUMIN NANOPARTICLE WITH BRIMONIDINE

Kim KE, Jang I, Moon H, Kim YJ, Jeoung JW, Park KH, Kim H. Neuroprotective effects of human serum albumin nanoparticles loaded with brimonidine on retinal ganglion cells in optic nerve crush model. *Invest Ophthalmol Vis Sci* 2015;56:5641–5649.

Human serum albumin nanoparticle (HSA-NP) was used in this study as a drug carrier for its superior capability in penetrating deep tissue. HSA-NP is conjugated with low-molecular-weight neuroprotective drug, brimonidine, to provide stable intraocular release. By using an optic nerve crush model on adult rats, the authors found that HSA-NP-brimonidine had neuroprotective effects on retinal ganglion cells by inhibiting amyloid-beta deposition.

An-Guor Wang

SYPHILITIC OPTIC NEURITIS

Northey LC, Skalicky SE, Gurbaxani A, McCluskey PJ. Syphilitic uveitis and optic neuritis in Sydney, Australia. *Br J Ophthalmol* 2015;99:1215–1219.

The authors conducted a retrospective reviewed of ocular syphilis at Sydney Eye Hospital from 2007 to 2012. Twenty-five patients with 37 eyes were diagnosed as having ocular syphilis, with a mean age of 43.7 years and a male predominance (92%). Twenty-five (67.6%) eyes demonstrated posterior segment involvement, and 10 (27%) eyes had optic neuropathy. Visual prognosis in cases of optic neuropathy was generally good, demonstrating either improvement or at least stabilisation.

An-Guor Wang

MORE ON MUSK-POSITIVE MYASTHENIA

Tsonis AI, Zisimopoulou P, Lazaridis K, Tzartos J, Matsigkou E, Zouvelou V, Mantegazza R, Antozzi C, Andreetta F, Evoli A, Deymeer F, Saruhan-Direskeneli G, Durmus H, Brenner T, Vaknin A, Berrih-Aknin S, Behin A, Sharshar T, De Baets M, Losen M, Martinez-Martinez P, Kleopa KA, Zamba-Papanicolaou E, Kyriakides T, Kostera-Pruszczyk A, Szczudlik P, Szyluk B, Lavrnic D, Basta I, Peric S, Tallaksen C, Maniaol A, Casasnovas Pons C, Pitha J, Jakubikova M, Hanisch F, Tzartos SJ. MuSK autoantibodies in myasthenia gravis detected by cell based assay—a multinational study. *J Neuroimmunol* 2015;284:10–17.

This multicentre study involving 13 countries looked at the yield of cell-based assay for anti-muscle specific kinase (MuSK) antibodies on previously seronegative patients. Sera from 633 patients who were seronegative to anti-acetylcholine receptor (anti-AChR) and anti-muscle specific kinase (anti-MuSK) radioimmunoassays and anti-low-density lipoprotein receptor-related protein 4 (anti-LRP4) were tested. Controls included healthy controls (162) and other neuroimmune diseases (78 multiple sclerosis and 50 neuromyelitis optica). Results noted with particular interest include the following:

- (1) 13% of previously triple-seronegative patients were positive on the cell-based anti-MuSK assay. This suggests that the radioimmunoassay is not as sensitive as the cell-based assay.
- (2) A proportion of patients had double-positivity: 12.5% were seropositive for both anti-AChR and anti-MuSK; 19% for both anti-MuSK and anti-LRP4. The significance of this is unclear.
- (3) False positives can occur: 5% of neuroimmune disease control patients and 2% of healthy controls were seropositive on the anti-MuSK cell-based assay.
- (4) Thymic hyperplasia is noted in just over 20% of anti-MuSK and 30% of LRP4 MG, which is more than previously described in the literature. None of the anti-MuSK patients had thymoma.
- (5) There was no geographical distribution effect on anti-MuSK. In other words, this study did not confirm the previously reported geographical distribution of increased anti-MuSK closer to the equator.
- (6) Ocular myasthenia was the presenting feature in almost 30% of the cell-based assay anti-MuSK positive patients.

Sui Wong

CELL-BASED ASSAYS IN MYASTHENIA GRAVIS

Rodriguez Cruz PM, Huda S, López-Ruiz P, Vincent A. Use of cell-based assays in myasthenia gravis and other antibody-mediated diseases. *Exp Neurol* 2015;270:66–71.

This review details the use of cell-based assays in improving the diagnosis in myasthenia gravis (MG) and other antibody mediated diseases (e.g., neuromyelitis optica). The sensitivity of anti-MuSK cell-based assays is reported as 97% (false positives can occur, in keeping with the referenced paper by Tsonis et al.); the observation of double-positives (anti-AChR with anti-LRP4) is of uncertain significance. The review suggests that serial measurements of antibody titres in MG or aquaporin 4 for neuromyelitis optica can help guide therapy.

Sui Wong

OCT FOR MEASURING AND MONITORING PAPHILLOEDEMA

Chang YC, Alperin N, Bagci AM, Lee SH, Rosa PR, Giovanni G, Lam BL. Relationship between optic nerve protrusion measured by OCT and MRI and papilledema Severity. *Invest Ophthalmol Vis Sci* 2015;56:2297–2302.

Chang and colleagues show that optical coherence tomography (OCT) measurements of optic nerve head protrusion (from the retinal pigment epithelium) correlates with Frisen grading. Previous work by others had shown magnetic resonance imaging (MRI) to be a reliable method to measuring optic nerve head protrusion, and in accordance the mechanical nature of papilloedema from raised intracranial pressure. In this study, 11 patients with idiopathic intracranial hypertension were examined, showing that both MRI and OCT are reliable and consistent measures of papilloedema. OCT in this manner can therefore compliment clinical observations and patient monitoring.

Sui Wong

DRAINING FLUID FROM HEAD TO CHEST

Elder BD, Sankey EW, Goodwin CR, Jusué-Torres I, Khattab MH, Rigamonti D. Outcomes and experience with lumbopleural shunts in the management of idiopathic intracranial hypertension. *World Neurosurg* 2015;84: 314–319.

This is a small series of five patients over a 23-year period who had lumbopleural shunts for treatment of idiopathic intracranial hypertension. The numbers are small and therefore caution has to be taken in drawing conclusions. Nevertheless, the paper is a reminder that there are alternative methods to lumboperitoneal or ventricular-peritoneal shunts, particularly in patients who may not tolerate peritoneal draining (e.g., from previous abdominal disease or peritonitis). The authors report the usefulness of this technique in the control of intracranial pressure, although revisions may be necessary and overdrainage can be problematic, requiring the use of an antisiphon device or valve change.

Sui Wong