ABSTRACTS

Neuro-Ophthalmic Literature Review

David A. Bellows, Noel C. Y. Chan, John J. Chen, Hui-Chen Cheng, Peter W. MacIntosh, Jenny A. Nij Bijvank, and Michael S. Vaphiades

Can we measure intracranial pressure without the needle?

Price DA, Grzybowski A, Eikenberry J, Januleviciene I, Verticchio Vercellin AC, Mathew S, Siesky B, Harris A. Review of non-invasive intracranial pressure measurement techniques for ophthalmology applications. *Br J Ophthalmol* 2020;104:887–892

I am certain that we would all welcome a method of measuring intracranial pressure that eliminates the risk, discomfort, expense, unreliability, and inconvenience of invasive techniques such as lumbar puncture, external ventricular drainage and intraparenchymal probes. The authors conducted a literature review of the current non-invasive methods of measuring intracranial pressure and compared these with the “gold standard” methods in their ability to screen for elevated intracranial pressure and to estimate intracranial pressure in patients with glaucoma.

The currently available non-invasive techniques of measuring intracranial pressure included in this review are ultrasonography to measure the diameter of the optic nerve sheath, magnetic resonance imaging (MR-ICP), computerised tomography (CT), transcranial doppler (TCD), ophthalmodynamometry, electroencephalography (EEG), intraocular pressure (IOP), optical coherence tomography (OCT), visual evoked potential (VEP) and pupillometry.

In cases of suspected pseudotumour cerebri the authors found that measurements of optic nerve sheath diameter (ONSD) using ultrasound, MR and CT were the most studied options and had high sensitivity. However, they note that “normal” ONSD seems to be population specific and would likely need to be determined individually for each institution.

MR-ICP was found to be closest to providing a reliable non-invasive technique for measuring intracranial pressure in patients with glaucoma.

However, this technique is generally poor at predicting small changes in the range of normal intracranial pressure and there is no set threshold for low intracranial pressure increasing glaucoma risk.

The value of these non-invasive techniques, particularly in patients with pseudotumour cerebri, may be enhanced if they are used to track changes in intracranial pressure after first being “calibrated” with an invasive procedure.

David A. Bellows

Novel visual field nomenclature for detecting progression in optic neuropathies associated with thyroid eye disease

Freitag SK, Tanking T. A nomenclature to describe the sequence of visual field defects in progressive thyroid eye disease-compressive optic neuropathy (An American Ophthalmological Society Thesis). *Am J Ophthalmol* 2020;213:293–305.

Optic neuropathy is one of the potential blinding conditions in patients with thyroid eye disease (TED) which warrants urgent medical treatment. Early detection by careful monitoring of visual function is therefore crucial in susceptible patients.

However, the absence of relative afferent pupillary defect (RAPD) or disc swelling do not exclude TED associated optic neuropathy. Previous literature has detected 76% of bilateral cases with no RAPD while only 20–50% had disc swelling. Visual acuity may decline gradually without being noticed by the patient and 50–70% of eyes with confirmed TED-compressive optic neuropathy (TED-CON) have visual acuity of at least 20/40. Visual field (VF) examination is therefore prudent in the clinical examination and continuous surveillance of this group of patients. Yet, recent studies had shown that the VF defects in TED-CON did

not fit into pre-existing nomenclatures, which were systems predominantly used for describing glaucomatous VF defects from glaucoma. This is a retrospective study trying to create a novel nomenclature characterising the longitudinal sequence of VF defects in patients with TED-CON.

VF defects were analysed by two independent reviewers and classified into one of the 10 categories which were further divided into three stages reflecting the observed progression patterns. Stage 1 refers to different severities (a, b & c) of inferior field defects. Stage 2 refers to the addition of superior VF loss while stage 3 refers to the severe widespread loss in all four quadrants. Miscellaneous VF defects including predominant superior VF defect, central scotoma, enlarged blind spot and scattered loss were grouped as Stage X. Reviewing 234 VFs from 37 eyes of 23 patients with TED-CON, the most common VF defect was stage 1 (62%). There were only 6 of 37 eyes (16.2%) with VF defects outside the typical pattern (Stage X). Longitudinal analysis of the VF defects showed that 31 of 37 eyes (83.8%) shared similar progression patterns in the order of the nomenclature although not all progressed to the most severe spectrum. The reverse order of VF defect progression was noted with improving TED-CON.

The authors proposed the use of this nomenclature for better monitoring of the visual function in patients with suspected TED-CON. The longitudinal VF changes described also provide clinicians with information as of where the spectrum of progression a patient's visual field falls. Further studies with larger cohorts will be valuable in evaluating the clinical application of this nomenclature.

Noel C. Y. Chan

The pattern of peripapillary choroidal microvasculature dropout may differentiate compressive optic neuropathy from open angle glaucoma

Lee EJ, Kim J-A, Kim T-W, Kim H, Yang HK, Hwang J-M. Glaucoma-like parapapillary choroidal microvasculature dropout in patients with compressive optic neuropathy. *Ophthalmol* 2020. Article in press. doi: 10.1016/j.ophtha.2020.06.001

The authors conducted a cross-sectional observational study to characterise peripapillary choroidal

microvasculature dropout (MvD) in patients with compressive optic neuropathy (CON) by parasellar tumour as compared to those with open-angle glaucoma (OAG) using optical coherence tomography angiography (OCTA). A total of 88 eyes of 44 patients with CON, 88 eyes of 88 patients with OAG, and 88 eyes of 44 control subjects were enrolled. Patients with CON and OAG were matched by age, spherical error (SE) and retinal nerve fibre layer thickness (RNFLT) on OCT. Control subjects were matched by age and SE. They found that MvD was observed in 30 eyes (34.1%) in the CON group and 48 eyes (54.5%) in the OAG group ($p = .011$). In the CON group, all MvDs were located in the temporal parapapillary sector. Instead, MvDs in the OAG group were located in the temporal-inferior and temporal-superior sectors. The locations of MvDs were accompanied by significant reductions in retinal vessel density and RNFLT in the CON group but not in the OAG group. The authors highlight the different features of MvD between CON and OAG, which may help for differential diagnosis.

Hui-Chen Cheng

Awareness of immune checkpoint inhibitor associated optic neuritis

Francis JH, Jaben K, Santomasso BD, Canestraro J, Abramson DH, Chapman PB, Berkenstock M, Aronow ME. Immune checkpoint inhibitor associated optic neuritis. *Ophthalmol*. 2020. Article in press. doi: 10.1016/j.ophtha.2020.05.003

Immune checkpoint inhibitors (ICIs) are a group of systemically administered immunotherapy agents, which can enhance the adaptive immune response and are now widely used to treat many forms of cancer. The authors conducted a retrospective case series to describe the clinical characteristics of ICI-associated optic neuritis (ON). They enrolled 18 eyes with ICI-associated optic neuritis in 11 patients diagnosed between 2017 and 2020. They found that all three classes of ICIs (anti-CTLA4, anti-PD-1, and anti-PD-L1) have the potential to induce ON. Timing of onset ranged from 2 to 95 cycles (median, 4 cycles). Ninety percent of patients complained painless visual loss and/or floaters, 64% of patients had bilateral optic nerve involvement and 67% of eyes had dyschromatopsia. Visual fields showed variable

patterns including diffuse (28%), arcuate/altitudinal (39%), central/cecocentral (22%), and no defect (11%). Magnetic resonance imaging showed a propensity to spare the retrobulbar and proximal nerve. In this series, the ICI was discontinued in all patients. All but one patient received steroids. Two patients received rituximab, intravenous immunoglobulin (IVIG), and/or plasmapheresis. Of 16 eyes with worse than 20/20 baseline vision, the visual acuity (VA) improved in 12, was stable in two, and worsened in two. The authors suggested that ON in the context of ICI should raise the suspicion for drug-associated disease.

Hui-Chen Cheng

Risk factors of transient cortical blindness after cerebral angiography

Li M, Liang H, Liu C, Liu H, Zheng Y, Shi W, Wang J. Risk factors of transient cortical blindness after cerebral angiography: A multicenter study. *Front Neurol.* 2019;10:1005. doi: 10.3389/fneur.2019.01005

Transient cortical blindness has a reported incidence of 0.3–1% after cerebral angiography. The authors undertook a retrospective, multi-centre study of 5126 patients at five high-volume medical centres to identify risk factors related to transient cortical blindness after cerebral angiography. The exact mechanism is unknown but postulated to be related to contrast neurotoxicity.

The following criteria were used for inclusion: (1) cervical and intracranial vascular disease; (2) aged 18–75 years; and (3) patients who underwent cerebral angiography. The exclusion criteria were: (1) severely abnormal lung, kidney, or liver function; (2) hyperthyroidism; (3) coagulation disorder; and (4) mental illness. The authors then analysed age, sex, weight, cigarette smoking, hypertension, diabetes, dose of contrast agent and delivery of contrast agent to the posterior circulation.

Of 5126 patients who underwent cerebral angiography, 18 (0.35%) suffered transient cortical blindness. Though self-limiting and reversible, patients diagnosed with cortical blindness were treated with intravenous nimodipine, mannitol, low molecular weight dextran and dexamethasone and all patients completely recovered vision within 2 h to 4 days.

No significant differences were found between the transient cortical blindness group and the control group regarding gender, age, and smoking. Patients in the transient cortical blindness group weighed less, had higher levels of hypertension, larger boluses of contrast agent, and were more likely to be injected into the posterior circulation than the control group. Multivariate logistic regression analysis showed that dose of contrast agent and contrast agent injected into the posterior circulation were independent risk factors for transient cortical blindness.

The limitations of the study include its retrospective design and limited number of patients who had transient cortical blindness.

Peter W. MacIntosh

Predicting the diagnosis of MS with OCT

Pihl-Jensen G, Wanscher B, Frederiksen JL. Predictive value of optical coherence tomography, multifocal visual evoked potentials, and full-field visual evoked potentials of the fellow, non-symptomatic eye for subsequent multiple sclerosis development in patients with acute optic neuritis. *Mult Scler.* 2020;1–10. Advanced online publication. doi:10.1177/1352458520917924

This prospective cohort study investigated the predictive value of optical coherence tomography (OCT) and visual-evoked potentials (VEP) measurements of the non-symptomatic, fellow eye of optic neuritis (ON) patients, for conversion to MS.

A total of 79 patients were analysed, of which 28 (35%) developed MS during the follow-up period of 1.3 to 4 years. In the univariate cox regression models investigating the time to the diagnosis of MS, OCT mean GCIPL thickness, OCT GCIPL thickness inferonasal sector, OCT mean pRNFL thickness, and mfVEP mean latency significantly predicted MS development. Additionally, multivariate models were built, investigating one OCT parameters at a time (because of collinearity) and also included mfVEP, magnetic resonance imaging (MRI) at baseline displaying ≥ 1 demyelinating lesion, cerebrospinal fluid oligoclonal band and immunomodulatory treatment during follow-up. These analyses showed that all three OCT parameters independently predicted MS

development, which was not the case for mfVEP. An increase of 1 μm in the mean GCL IPL led to an increase in hazard rate of MS development of 10.7% ($p = .021$). Next, receiver operating characteristic analyses were provided for determining optimal thresholds and corresponding sensitivity and specificity of the OCT parameters on MS development.

This study shows that OCT of the fellow-eye in ON patients might be predictive for conversion to MS. This is useful in cases with acute ON in which a diagnosis of MS is not ascertained at the time of ON, and might aid in treatment decisions. The number of events in relation to the number of variables investigated in the multivariate models was relatively small, and therefore larger cohorts investigating more clinical and MRI variables could confirm the independent predictive value of OCT parameters in the development of MS.

Jenny A. Nij Bijvank

Demographics of a large international population of patients affected by Leber's hereditary optic neuropathy

Poincenot L, Pearson AL, Karanjia R. Demographics of a large international population of patients affected by Leber's hereditary optic neuropathy. *Ophthalmol.* 2020;127:679–688.

The authors performed a cross-sectional study to study the demographics of Leber's hereditary optic neuropathy (LHON) using a large international database of 1517 people affected by LHON with a known pathogenic genetic mutation. They found that both females and males can experience symptom onset at any age with a 3:1 male-to-female ratio. In patients younger than 5 years and older than 45 years, the male-to-female ratio was approximately 1:1, and after 50 years 10% of individuals become affected. The authors found that the m.11778, m.14484, and m.3460 mutations were the most common LHON point mutations. The authors concluded that LHON is a disease that affects both females and males of all ages. This should prompt physicians to obtain genetic testing for LHON in all patients who meet the clinical criteria, regardless of whether they fit the demographics traditionally associated with the disease.

Michael S. Vaphiades

Upper cranial nerve involvement and immunoglobulin G4-related optic neuropathy

Lai KKH, Chan RYC, Chin JKY, Li KKW, Young AL, Yuen HKL, Ko STC, Chong KKL. Upper cranial nerve involvement and immunoglobulin G4-related optic neuropathy. *Ophthalmol.* 2020;127:699–703.

Immunoglobulin G4-related ophthalmic disease (IgG4-ROD) is an immune-mediated fibroinflammatory disease characterised by tumefactive lesion(s) with prominent immunoglobulin G4+ plasma cells infiltrating into multiple organs. This disease affects the lacrimal glands, extraocular muscles, periorbital and optic nerves, and eyelid, orbital, and palpebral soft tissues. The authors conducted a retrospective review of medical records, orbital images, and histology slides of all patients with biopsy-proven IgG4-ROD from all seven oculoplastic units covering the territory-wide and government-supported (Hospital Authority) ophthalmology service in Hong Kong from 2005 to 2018. They found that six (5.3%) of the 112 patients with IgG4-ROD (four females) had IgG4-related optic neuropathy (IgG4-RON). Upper cranial nerve involvement leading to sensory or motor disturbance clinically with the corresponding nerve enlarged radiologically was observed only in patients with IgG4-RON in the study. Four eyes had compressive optic neuropathy, and two eyes had infiltrative optic neuropathy. Three of the six patients (50%) with IgG4-RON presented with poor vision had irreversible, permanent visual loss (BCVA worse than 20/200).

Michael S. Vaphiades

PSP-like syndrome after aortic surgery in adults (Mokri syndrome)

Sarah M. Tisel, J. Eric Ahlskog, Joseph R. Duffy, Joseph Y. Matsumoto, Keith A. Josephs. PSP-like syndrome after aortic surgery in adults (Mokri syndrome). *Neurol Clin Pract* 2020;10(3):245–254.

The authors retrospectively studied 25 patients detected in the Mayo Clinic electronic medical records who were evaluated for neurologic symptoms after cardiac-aortic surgery in the past 30 years. A typical triad of supranuclear gaze palsy (100%), gait imbalance (80%), and dysarthria (96%) was noted. Part or all of the triad was observed before hospital discharge and stabilised over the course of days-weeks. A second phase of symptom worsening plus new symptoms developed up to

a year later and this decline continued for up to several years before stabilisation. Delayed epileptic seizures occurred in 32% of patients. Brain magnetic resonance imaging revealed only non-specific findings. The authors concluded that this syndrome remains unexplained, however profound hypothermia which is a commonly used to perform these surgeries may be implicated.

Michael S. Vaphiades

Nonarteritic anterior ischaemic optic neuropathy: Exceptions to the rules

Vaphiades MS, Al-Sadah ZM, Kline LB.
Nonarteritic anterior ischaemic optic neuropathy:

Exceptions to the rules. *J Neuro-Ophthalmol* 2020; 1–3. Advance online publication. doi: 10.1097/WNO.0000000000000949

The authors present a 61-year-old woman with nonarteritic anterior ischaemic optic neuropathy (NAION) who had persistent optic disc oedema (ODE) in the right eye for 19 months before resolution. The temporal profile of the patient's clinical course highlights two aspects of NAION: (1) incipient NAION and (2) prolonged resolution of ODE. The authors review the literature and explore the pathogenesis of this rare variant of NAION.

Michael S. Vaphiades