ABSTRACTS

Neuro-Ophthalmic Literature Review

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and Sui Wong

MACULAR OCT DEMONSTRATES TRANSSYNAPTIC RETROGRADE RETINAL DEGENERATION

Meier PG, Maeder P, Kardon RH, Borruat FX. Homonymous ganglion cell layer thinning after isolated occipital lesion: Macular OCT demonstrates transsynaptic retrograde retinal degeneration. *J Neuroophthalmol* 2015;35:112–116.

Traditionally, occipital lobe lesions are not thought to be a cause of optic atrophy. However in recent years, transsynaptic retrograde degeneration has been convincingly demonstrated in vivo, by OCT and MRI. Previous studies have shown that patients with both congenital and acquired homonymous hemianopia from retrogeniculate lesions had thinning of the peripapillary retinal nerve fibre layer (RNFL). There was also MRI evidence of optic tract atrophy after an ipsilateral occipital lobe lesion. In this case report, the authors describe a 46 year-old man with a right occipital lobe abscess. Two years after the lesion was treated, he still had a residual homonymous left inferior scotoma. OCT of the peripapillary RNFL showed mild sectoral thinning only. The macular OCT retinal ganglion cell-inner plexiform layer (RGC-IPL) thickness map demonstrated temporal macular thinning of the right eye and nasal macular thinning of the left eye, which respected the vertical meridian and corresponded with the visual field defect. This demonstrated that transsynaptic retrograde degeneration after an occipital lesion extended to the retinal RGC-IPL layers.

Carmen Chan

WHICH LABORATORY MARKERS INFLUENCE OUR DECISION TO PERFORM TEMPORAL ARTERY BIOPSIES?

De Lott LB, Burke JF; Michigan Neuro-Ophthalmology Research Consortium. Use of laboratory markers in deciding whether to perform temporal artery biopsy. *JAMA Ophthalmol* 2015;133:605–606.

In suspected cases of giant cell arteritis (GCA), our decision to perform a temporal artery biopsy (TAB) is usually based on patient demographics (e.g. age, sex), history, clinical examination, and laboratory markers. Which laboratory markers do we base our decision on? In this research letter, the authors sought to answer this question by performing a retrospective case-notes review study on all the patients who underwent TAB at 8 US institutions from 2007–2012. 404 patients met the inclusion criteria and 90 (22.3%) had biopsy proven GCA. As expected, older age, elevated ESR, elevated platelet count, and elevated CRP were significantly associated with a positive TAB result. Using multiple logistic regression analysis, after controlling for sex, CRP and ESR, age, and platelet count continued to predict the biopsy result. The authors deduced from the data that physicians integrate ESR, CRP, and patient sex into TAB decisions but may not completely take into account the age and platelet count. This paper does contain quite a lot of statistics and it is best understood when read with the supplemental online content.

Carmen Chan

VERTICAL GAZE PALSY FROM BILATERAL THALAMIC INFARCTION

Gooneratne IK, Caldera MC, Liyanage DS, Pathberiya L, Vithanage K, Gamage R. Pearls & Oy-sters: Ocular motor abnormalities in bilateral paramedian thalamic stroke. *Neurology* 2015;84:e155–158.

Three cases of bilateral thalamic infarction from artery of Pocheron occlusions were described. The artery of Pocheron is a rare variant in the posterior cerebral circulation arising from the posterior cerebral artery. It supplies blood to bilateral medial thalami. The patients developed vertical gaze palsy which was corrected by oculoccephalic maneuvers, suggesting they were supranuclear in origin. This might be due to disturbances of supranuclear input from the thalamus or thalamo-midbrain junction. Bilateral internuclear ophthalmoplegia was also observed. Other neurological deficits included impaired consciousness and imbalance.

Panitha Jindahra

LHON AND MS

Matthews L, Enzinger C, Fazekas F, Rovira A, Ciccarella O, Dotti MT, Filippi M, Frederiksen JL, Giorgio A, Küker W, Lukas C, Rocca MA, De Stefano N, Toosy A, Yousry T, Palace J; MAGNIMS Network. MRI in Leber's hereditary optic neuropathy: The relationship to multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2015;86:537–542.

The authors retrospectively reviewed brain MRIs in patients with multiple sclerosis (MS), Leber's hereditary optic neuropathy (LHON), & LHON and MS association (LMS). They found that all LMS cases and 26% of LHON cases had white matter lesions. All LMS and 25% of LHON cases with white matter lesions had typical MS lesions on brain MRI. There was a preponderance of LHON women to have typical MS brain lesions (relative risk 8.3). The findings supported the theory that mitochondrial disturbance might play a part in MS pathology.

Panitha Jindahra

VZV IN TEMPORAL ARTERITIS

Gilden D, White T, Khmeleva N, Heintzman A, Choe A, Boyer PJ, Grose C, Carpenter JE, Rempel A, Bos N, Kandasamy B, Lear-Kaul K, Holmes DB, Bennett JL, Cohrs RJ, Mahalingam R, Mandava N, Eberhart CG, Bockelman B, Poppiti RJ, Tamhankar MA, Fogt F, Amato M, Wood E, Durairaj V, Rasmussen S, Petursdottir V, Pollak L, Mendlovic S, Chatelain D, Keyvani K, Brueck W, Nagel MA. Prevalence and distribution of VZV in temporal arteries of patients with giant cell arteritis. *Neurology* 2015;84:1948–1955.

This study demonstrated evidence of varicella-zoster virus (VZV) infection in giant cell arteritis (GCA)-positive temporal artery (TA) biopsies. Immunohistochemistry for VZV antigen, ultrastructural examination for virions, and PCR for VZV were analyzed in both GCA-positive TA and normal TA biopsies. VZV antigen was significantly greater in the GCA-positive TA group (74%) than in the normal TA group (8%). It was identified in all arterial layers particularly the adventitia. The antigen distribution, located in skip areas, was similar to that found in GCA. VZV DNA and virions were also demonstrated in the GCA group. VZV might have a role in GCA pathology and that antiviral medication would be useful in GCA treatment.

Panitha Jindahra

THE PULFRICH EFFECT

Lanska DJ, Lanska JM, Remler BF. Description and clinical application of the Pulfrich effect. *Neurology* 2015;84:2274–2278.

Problems with depth perception during movement can be acquired with unilateral neurological and ophthalmological pathology, notably optic neuritis. Patients might find it difficult to describe this specific problem and doctors may not necessarily be aware about the phenomenon also known as the Pulfrich effect. This paper published in the Historical section of Neurology can be divided into three parts, (i) history, (ii) physiology

and (iii) application. The paper grows in strength along these parts, starting with a review of the historical literature and some fanciful but rather free translations from the German original.

Part I—History

The key historical point is that Carl Pulfrich (*24.9.1858 Düsseldorf, †12.8.1927 Baltic Sea) was employed by the Carl Zeiss Company to develop stereoscopy into a powerful quantitative technique. All seemed going well until the eminent astronomer Max Wolf (*21.6.1863 Heidelberg, †3.10.1932 Heidelberg) published in 1920 the observation that measurements were not precise with variation of object brightness (in this case a star, *Veränderlicher Nr. 19* in the region of Cygni). Whilst historically Max Wolf made the discovery using a stereo-comparator very different to what the authors show in their supplementary material, their manuscript gains however in strength as they move on to explain what eventually became known as the Pulfrich effect because of experiments subsequently conducted by Pulfrich.

Part II—Physiology

Inequalities in binocular illumination lead to unequal visual-perceptual latencies. In practical terms, a neutral density filter placed in front of one eye gives the impression of an ellipsoid trajectory of an object which in reality moves horizontally back and forth across the field of vision. The authors make the point that “overlooked by many modern authors . . .” “the true line of object motion . . .” “is displaced away from the observer”. The manuscript also catches up on the fine details of the observations reported by Pulfrich and his team, namely that there is no ideal ellipsoid trajectory in reality, but a perceived shift in depth due to irregular movements. A fine point, but relevant to a patient’s “real life”. For those readers who are now tempted to test this phenomenon by hanging a swinging pendulum in front of a dark or light wall, it may be added that a high-contrast patterned background will be help to enhance binocular disparity and therefore the perceived Pulfrich effect.

Part III—Application

The Pulfrich effect can be observed in patient with ophthalmological conditions as first recognised by Pulfrich himself. Being more specific about the actual clinical diagnosis, the Pulfrich effect was first described in unilateral retrobulbar optic neuritis by Harold Barr Grimsdale (*12.11.1866 Liverpool, 5.5.1942, London, briefly after his house was demolished during the London air raids). Grimsdale was first to describe that a patient could be helped by placing a neutral density filter in front of the better eye. This can readily be done using tinted spectacles. Reminding us about the relative simplicity of treating patients is the strongest point of this manuscript. Taking all of above observations together, in “real life” patients have difficulties with perception of movement in depth, particularly in a visually busy environment such as traffic, shopping malls (note my point on binocular disparity), for a whole range of ophthalmological and neurological reasons, all of which can be alleviated easily and non-invasively.

Axel Petzold

RETINAL INJURY AFTER OPTIC NEURITIS

Gabilondo I, Martínez-Lapiscina EH, Fraga-Pumar E, Ortiz-Perez S, Torres-Torres R, Andorra M, Llufríu S, Zubizarreta I, Saiz A, Sanchez-Dalmau B, Villoslada P. Dynamics of retinal injury after acute optic neuritis. *Ann Neurol* 2015;77:517–528.

The group from Barcelona investigated the change of individual retinal layer thicknesses in 27 patients (26 unilateral and 1 bilateral optic neuritis) following an episode of acute optic neuritis. In addition to spectral domain optical coherence (OCT) data the authors also assessed visual function for high and low contrast acuity, colour vision and visual fields. A comprehensive study in the field. Most patients ($n = 20$) were seen within 15 days after onset. Follow-up intervals were systematic on a monthly basis for six months. Therefore this study captures the very early phase of optic neuritis, but falls short of the about 12 months interval after which retinal layer atrophy following optic neuritis subsides. The main message of the paper is summarised in Figures 1 and 2 illustrating atrophy of two inner retinal layers, the retinal nerve fibre layer (RNFL) and ganglion cell complex (GCL + IPL).

Atrophy rates are related to clinical severity of acute optic neuritis. The macular area does show more substantial atrophy at an earlier stage compared to the optic disc. Interestingly atrophy stops at level of the inner nuclear layer (INL) which may represent a barrier to the underlying mechanism of trans-synaptic retrograde axonal degeneration. Interestingly, there is some early thickening of mainly two outer retinal layers, the outer plexiform layer and outer nuclear layer. This represents a consistent finding in the literature which is not yet understood. Another finding of this study was that the location of peripapillary RNFL loss was related to the approximate corresponding anatomical area in the perimacular rim. Finally, the quantitative structural data were related to functional data of visual function. Interestingly these data were presented as an area under the curve (AUC) for the relationship of GCL + IPL change to colour vision (best AUC), low contrast visual acuity (second best) and visual field (poorest AUC). Taken together future treatment trials on acute optic neuritis may consider inclusion of OCT as a structural outcome measure and colour vision testing (or low contrast visual acuity) as a clinical measure. The sample size calculations provided suggest that 25 patients per group may suffice. This is encouraging.

Axel Petzold

ASYMMETRIC PAPILLEDEMA IN IIH

Bidot S, Bruce BB, Saindane AM, Newman NJ, Biousse V. Asymmetric papilledema in idiopathic intracranial hypertension. *J Neuroophthalmol* 2015;35:31–36.

The authors identified 559 adult idiopathic intracranial hypertension (IIH) patients with asymmetric papilledema. They noted these patients were older had lower cerebrospinal opening pressure and were more likely to be asymptomatic compared with patients with symmetric papilledema. They also noted that the bony optic canal was smaller on the side of the lowest-grade edema all 8 patients (100%) in whom the imaging was sufficient for reliable measurements. They concluded that IIH with very asymmetric papilledema is uncommon and may result from differences in size of the bony optic canals, supporting the concept of compartmentation of the perioptic subarachnoid spaces.

Michael Vaphiades

ISOLATED OCULAR MOTOR NERVE PALSIES

Jung JS, Kim DH. Risk factors and prognosis of isolated ischemic third, fourth, or sixth cranial nerve palsies in the Korean population. *J Neuroophthalmol* 2015;35:37–40.

The authors performed a pair-matched case-control study of 54 Korean patients who were diagnosed with ischemic third, fourth, or sixth cranial nerve palsy and evaluated demographics. They noted that ischemic ocular motor cranial nerve palsy is closely related to diabetes mellitus, hypertension, and hyperlipidemia in Korean patients. Compared with the fourth or sixth nerve palsy groups, the third nerve palsy group showed a tendency to have multiple risk factors. Recovery takes longer when 2 or more risk factors were present or when abnormal findings were observed on neuroimaging.

Michael Vaphiades

FACE RECOGNITION IN PATIENTS WITH MIGRAINE

Yetkin-Ozden S, Ekizoglu E, Baykan B. Face recognition in patients with migraine. *Pain Pract* 2015;15:319–322.

The authors evaluated 74 migraineurs, with or without aura and 37 healthy control subjects with a variety of different tests for face recognition. The migraineurs showed significantly lower performance (prosopagnosia) indicating impaired visuospatial perception. In the subgroup analysis, these impairments were more pronounced in the group with migraine without aura. The authors theorized that the findings could be based on functional differences in the migraineurs' brain or genetic.

Michael Vaphiades

Neuro-Ophthalmology

OPTIC NERVE INVOLVEMENT IN RETINAL MIGRAINE

Codeluppi L, Bonifacio G, Chiari A, Ariatti A, Nichelli PF. Optic nerve involvement in retinal migraine. *Headache* 2015;55:562–564.

Retinal migraine is a rare entity characterized by headache associated with transient monocular visual loss. While fully reversible and a normal ophthalmological examination between the attacks is the hallmark, persistent visual loss has been reported. The authors present a patient with persistent monocular visual loss in the right eye after retinal migraine in whom a signal hyperintensity along with a slight distention of the perioptic subarachnoid space in the right optic nerve was detected on magnetic resonance imaging scan, suggesting optic nerve involvement.

Michael Vaphiades

EFFECT OF DIABETES MELLITUS ON GIANT CELL ARTERITIS

Abel AS, Yashkin AP, Sloan FA, Lee MS. Effect of Diabetes Mellitus on Giant Cell Arteritis. *J Neuroophthalmol* 2015;35:134–138

The authors reviewed the records of 151,041 patients diagnosed with diabetes mellitus (DM) with matched controls and then used statistical analysis to assess the impact of the DM diagnosis on a giant cell arteritis (GCA) diagnosis. They concluded that DM diagnosis is not protective against a GCA diagnosis in the Medicare population. They also found that a DM diagnosis increases the risk of GCA diagnosis within 5.7 years for Medicare beneficiaries older than 68 years.

Michael Vaphiades

CLINICAL FEATURES IN PEDIATRIC NEUROMYELITIS OPTICA

Absoud M, Lim MJ, Appleton R, Jacob A, Kitley J, Leite MI, Pike MG, Vincent A, Wassmer E, Waters P, Woodhall M, Hemingway C, Palace J. Paediatric neuromyelitis optica: Clinical, MRI of the brain and prognostic features. *J Neurol Neurosurg Psychiatry* 2015;86:470–472.

The authors conducted a retrospective case review of paediatric neuromyelitis optica (NMO) from the UK national NMO service database (2009–2012). They have included twenty NMO cases (12 AQP4-Ab positive, 8 AQP4-Ab negative; median age = 10.5yrs) with median follow-up of 6.1yrs. In AQP4-Ab positive cases, 10/12 had visual acuity worse than 6/60 in at least one eye, while none of 8 AQP4-Ab negative cases had visual acuity less than 6/60. Three AQP4-Ab negative cases but no AQP4-Ab positive cases were wheelchair dependent on follow-up. The authors conclude that pediatric NMO is associated with visual impairment in AQP4-Ab positivity and physical disability in AQP4-Ab negative relapsing cases.

An-Guor Wang

HEADACHES AND RAISED INTRACRANIAL PRESSURE

Ducros A, Biousse V. Headache arising from idiopathic changes in CSF pressure. *Lancet Neurol* 2015;14:655–668.

De Simone R, Ranieri A. The role of intracranial hypertension in the chronification of migraine. *Neurol Sci* 2015;36:S23–S28.

Mulla Y, Markey KA, Wooley RL, Patel S, Mollan SP, Sinclair AJ. Headache determines quality of life in idiopathic intracranial hypertension (IIH). *J Headache Pain* 2015;16:45.

The above three articles provides a complementary trio, reminding us of the importance of headache in association with CSF pressure disorders.

Ducros & Biousse have written a comprehensive summary on headaches associated with CSF pressure, both idiopathic intracranial hyper- and hypotension; nicely bringing together their respective expertise on headache disorders and neuro-ophthalmology. The section on raised intracranial pressure will be of particular interest to the readers of this journal, in view of the associated visual dysfunction.

This thorough review includes the pathophysiology, clinical presentation, diagnosis, and management of IIH. Of particular interest also, is the section of headache management in IIH. Chronic headaches that persist despite normalization of intracranial pressure is common. The authors remind the readers of the treatment of coexisting conditions that may exacerbate headaches, including migraine, tension type headaches, and medication overuse. Depression and anxiety are associated features. The authors do not recommend surgical treatment or venous stenting for patients with isolated chronic headaches or mild or moderate papilloedema without visual loss.

The latter point by Ducros & Biousse leads us on to the slightly controversial opinion from De Simone & Ranieri. De Simone and Ranieri propose that patients with a diagnosis of chronic migraine may be misdiagnosed. Instead these patients may have IIH without papilloedema (IIHWOP), and their condition may be cured by a single lumbar puncture. This controversial conclusion was based on a small, prospective, unblinded study where 38/44 patients who had lumbar puncture (LP) showed an opening pressure (OP) of >20 cm H₂O, of which 19 had an OP >25 cm H₂O. Removal of 20–30 ml cerebrospinal fluid (CSF) improved the headache in 77%, although 55% of patient's headaches recurred episodically. De Simone and Ranieri also highlighted another study where venous sinus stenosis was observed in patients with IIHWOP. Nevertheless this theory is worth further examination – perhaps a multi-centre randomised controlled trial of chronic migraine patients (with or without venous stenosis) treated with a double-blinded LP?

Returning to the early point raised in the review by Ducros and Biousse about headaches in IIH, a study by Mulla and colleagues emphasizes the importance of managing this. In this small prospective cohort study ($n=20$ completed visits), the effect on quality of life (QOL) was assessed following a dietary intervention (resulting in significant weight loss from baseline mean BMI 38.2 to mean BMI 32.6 at 6 months). QOL was measured using the SF-36 scale. Surprisingly, significant weight loss was not associated with improved QOL. Headache was the only clinical outcome that correlated with improved QOL. This emphasizes the importance of managing headache in this group of patients.

Sui Wong

ELECTRODIAGNOSTICS IN MONITORING RAISED ICP

Afonso C, Raza AS, Kruez AC, Hokazono K, Cunha LP, Oyamada MK, Monteiro MLR. Relationship between pattern electroretinogram, frequency-domain OCT, and automated perimetry in chronic papilloedema from pseudotumour cerebri syndrome. *IOVS* 2015;56:3656–3665

Moss HE, Park JC, McAnany JJ. The photopic negative response in idiopathic intracranial hypertension. *IOVS* 2015;56:3709–3714

The above two small studies by Afonso et al and Moss et al highlight the potential usefulness of electrodiagnostics in the monitoring of patients with papilloedema from raised intracranial pressure.

Afonso and colleagues studied patients (24 pseudotumour cerebri; 26 normal controls) who had resolved chronic papilloedema and showed that pattern electroretinogram (PERG) amplitude reduction is correlated with OCT and automated field changes.

Of further interest, and perhaps more useful, is the study by Moss and colleagues. They evaluated the photopic negative response (PhNR) as an index of retinal ganglion cell (RGC) function in IIH ($n=10$ IIH; 15 normal controls). They showed that patients with IIH can have reduced PhNR amplitudes, which correlate significantly with visual function as assessed by perimetry and severity of papilloedema.

PhNR has advantages over PERG by being a relatively brief test not requiring refractive correction, and also minimal patient demands. Therefore PhNR can be a particularly useful adjunct for monitoring treatment in tricky patients e.g. those with unreliable perimetry or functional visual loss. Additionally, PhNR captures RGC function throughout the entire visual field, not just the central portions stimulated by PERG, and is of particular relevance in papilloedema where early visual loss occurs in the periphery.

Sui Wong