

Results: 20 B-MB were identified; by WHO definition, most of these resided within the classic category (N = 19), while one was LCA. 13 of 20 B-MB displayed “scattered” nodules; by molecular subtype, these included eight group 4, four group 3 and one WNT tumors. Seven of the 20 B-MB exhibited “frequent” nodules; by molecular subtype, these included six group 4 and one group 3 tumors. Statistical analysis confirmed this non random distribution of B-MB across molecular subtypes.

Conclusion: Our data confirm the work of Ellison et al. that suggested B-MB is genetically different than DN-MB. In particular, B-MB resides in the non-WNT/SHH molecular category, but especially amongst group 4 when nodularity is “frequent”.

5. Automated analysis of 1p/19q status by FISH in oligodendroglial tumours.

P.V. Gould¹, C. Duval¹, M. de Tayrac², F. Sanschagrin¹, K. Michaud³, S. Saikali¹

¹Department of medical biology, CHU de Québec, Québec, Canada; ²Department of genomic and molecular genetics, CHU de Rennes, Rennes, France; ³Department of Neurosurgery, CHU de Québec, Québec, Canada

doi:10.1017/cjn.2015.253

Automated analysis of 1p and 19q status in oligodendroglial tumors by fluorescence in-situ hybridization (FISH) can be achieved by image-analysis software present in the majority of institutions using the FISH technique. Despite the widespread availability of this software, there are no specific guidelines in the literature on how to use it.

We studied which green/red (G/R) probe signal combinations are predictive of 1p/19q co-deletion in a retrospective series of 53 oligodendroglial tumours and defined a new algorithm with a reduced sequence of combinations compared to previous studies. This algorithm was then tested and refined on a prospective series of 45 oligodendroglial tumours. The new algorithm scores 24 G/R combinations, which represent less than 50 % of the total observed combinations in our series. This algorithm excludes some previously described combinations and redefines the place of others. G/R combinations of 5/2, 6/2 and 6/3 associate with deletion status combinations, combinations of 1/2 associate with normal chromosome status, and combinations of 3/3 and 4/4 associate with imbalanced chromosome status.

The new algorithm when applied to the combination and ratio methods of signal probe analysis gives a high concordance between manual and automated analysis on examination of 100 tumour cells (91% concordance for 1p and 89% concordance for 19q) and total concordance on examination of 200 tumour cells. This highlights the value of automated analysis to identify cases with imbalanced chromosome status, in which a larger number of tumour cells should be studied by manual analysis. Our algorithm can be easily programmed on all existing FISH analysis software platforms and should facilitate multicentric evaluation and standardization of 1p/19q assessment in gliomas.

6. Surfen, a proteoglycan antagonist, reduces lysolecithin-induced demyelination with related effects on macrophage function

J. Warford¹, L. Madara², D.W. Hoskin^{1,2}, A.S. Easton^{1,2}

¹Department of Pathology, Dalhousie University, Halifax;

²Department of Microbiology and Immunology, Dalhousie University

doi:10.1017/cjn.2015.254

Proteoglycans are components of the extracellular matrix and have roles in brain development and responses to injury. Connective tissue components are known to be major inhibitors of remyelination in mouse models of demyelination and are found at the border of active demyelinating lesions in Multiple Sclerosis. Surfen (bis 2-methyl, 4- amino, 6-quinolyl amide) is a small molecule antagonist previously shown to bind preferentially to heparan sulfate and related proteoglycans.

We have previously reported that surfen reduces T cell proliferation *in vivo* and *in vitro*. Here we report the effects of surfen on an *in vivo* model of demyelination and its effects on macrophage function *in vitro*. Demyelination was induced by injecting the detergent lysolecithin into the spinal cord dorsal columns of adult C57Bl/6 mice. Relative to vehicle treated mice, co-injection of surfen (100 µM) with lysolecithin reduced total lesion area seven days post-injection. Because macrophages dominate these lesions and influence remyelination, murine bone marrow derived macrophages were assessed using assays of chemotaxis and phagocytosis. Macrophages chemotaxis was increased in response to surfen (10 µM) relative to vehicle by approximately 15% (p < 0.05). Phagocytosis of *E. coli* was not affected by surfen.

These effects of surfen on experimental demyelination and macrophage function suggest that proteoglycan binding may promote aspects of myelin repair relevant to Multiple Sclerosis.

7. The pathogenesis of Friedreich cardiomyopathy: myocarditis

A.H. Koeppe, R.L. Ramirez, A.B. Becker, S.T. Bjork, P.J. Feustel, J.E. Mazurkiewicz

VA Medical Center, Albany, N.Y., USA, and Albany Medical College

doi:10.1017/cjn.2015.255

Fra-taxin deficiency causes the complex neurological and cardiac phenotype of Friedreich ataxia (FRDA). The most common cause of death is cardiomyopathy. The results presented here are based on a systematic study of fixed and frozen archival heart specimens and include measurement of cardiomyocyte hypertrophy, fra-taxin assay, X-ray fluorescence (XRF) of iron (Fe) and zinc (Zn), inductively-coupled plasma optical emission spectrometry of these metals in digests of left ventricular wall (LVW), right ventricular wall (RVW), and ventricular septum (VS), Fe histochemistry, and immunohistochemistry and double-label immunofluorescence microscopy of cytosolic and mitochondrial ferritins, and of the inflammatory markers CD68

and hepcidin. Frataxin levels in LVW were extremely low at less than 15 ng/g wet weight (normal: 214.1 ± 81.2). On cross-sections, cardiomyocytes were significantly larger than normal with case means ranging from 635-1856 μm^2 for LVW and 483-1150 μm^2 for VS (normal LVW, 140-460; normal VS, 237-613). Fe accumulations varied from minute granules to coarse aggregates in fibers undergoing phagocytosis. Measured by XRF, regional Fe concentration in LVW and VS were significantly increased while Zn remained normal. Total heart Fe and Zn did not differ from normal levels. Cytosolic and mitochondrial ferritins exhibited extensive co-localization, representing translational and transcriptional responses to Fe, respectively. All cases met the criteria of myocarditis. Inflammatory cells contained CD68 and ferritin, and most expressed the Fe-regulatory hormone hepcidin. In conclusion, inflammation plays a major role in the pathogenesis of FA cardiomyopathy, and hepcidin-induced retention of Fe in macrophages contributes to cardiac damage in FRDA.

8. Maturation of the Fetal Olfactory Bulb

Harvey B. Sarnat

University of Calgary, Calgary, Alberta, Canada

doi:10.1017/cjn.2015.256

The olfactory bulb exhibits architecture unique amongst laminar cortices, lacking molecular and subplate zones and having superficial synaptic glomeruli. Its ontogenesis also is unique because neuroblasts do not migrate radially but stream in from the rostral telencephalon; an ependymal-lined olfactory ventricle is transitory. The olfactory is the only sensory system to not project to the thalamus but incorporates a thalamic equivalent. It is a repository of progenitor cells in the mature brain. The aim was to define olfactory bulb development in the human foetus: synaptogenesis and cellular maturation.

Immunoreactivity in paraffin sections of synaptophysin, NeuN, calretinin, vimentin and nestin was examined at autopsy in olfactory bulb in 20 fetuses, 9-40wks gestation. Synaptophysin reactivity was seen around the somata of mitral and tufted neurons at 9wks, synaptic glomeruli at 13wks. The granule cell layer in the core exhibited NeuN-reactive nuclei in cells of the outer half at 20wks; 60% of granular neurons reacted by term. Synaptophysin reactivity in the granular layer initiates at 15wk. GABAergic calretinin-reactive neurons and neurites and synaptic glomeruli appeared at 13wks. Nestin- and vimentin-reactive bipolar progenitor cells were shown at all gestational ages, mainly in the granular layer, the ratio to other cells remaining constant. Synapses form in the small accessory olfactory bulb of the nervus terminalis earlier than in the main bulb. Development of synaptic vesicles in the human fetal olfactory bulb is precise both spatially and temporally, but not yet fully mature at term.

In brain malformations and congenital metabolic and genetic diseases, the olfactory bulb may be affected and provide additional neuropathological data. Therapeutic autologous transplantation of olfactory progenitor cells focus renewed interest in the olfactory bulb.

9. Congenital Lymphocytic Choriomeningitis Virus: A Neuropathological Study

C. Fallet-Bianco

CHU Sainte-Justine, Montréal, Québec, Canada

doi:10.1017/cjn.2015.257

Lymphocytic choriomeningitis virus (LCMV) carried and secreted by mice, infects great numbers of people. LCMV infection acquired during childhood or adulthood is usually moderately symptomatic with a full recovery. When the infection occurs prenatally, it results in a wide spectrum of severe brain lesions described mainly on imaging. Neuropathological data have never been reported.

We present 2 fetuses with a prenatal diagnosis of microcephaly with ventriculomegaly, abnormal gyration, and ponto-cerebellar hypoplasia in one case. Parents elected to terminate the pregnancy. A complete autopsy demonstrated no dysmorphic features, no visceral or skeletal malformation. Histological examination of viscera did not show any significant lesion.

Neuropathological examination confirmed microcephaly and ventriculomegaly with a thick yellowish band surrounding the ventricles. Identical histological lesions were observed in both cases associating a polymicrogyria and a diffuse necrosis of parenchyma with massive calcifications all around the ventricles. The most characteristic feature was the unusual aspect of necrosis, distinct from that observed in other infections, characterized by a finely granular appearance looking like sand. Small lymphocytic infiltrates were observed in the leptomeninges and in the choroid but not in the retina. The congenital LCMV infection was confirmed by serologic testing.

This study confirms the strong neurotropism of LCMV and demonstrates that prenatal infection has some particular features such as absent systemic signs, and distinct appearance of the necrosis that allow to distinguish it from other congenital infections and other non infectious conditions.

10. Cerebral hyaline astrocytic inclusions in treatment-resistant epilepsy and global developmental delay

M. Signaevski¹, C. Sanguansermisri¹, M. Connolly¹, LN. Hazrati², C. Dunham¹

¹University of British Columbia, Vancouver, Canada; ²University of Toronto, Toronto, Canada

doi:10.1017/cjn.2015.258

Cerebral hyaline astrocytic inclusions (HAI) have been observed in a subset of patients with epilepsy, structural brain anomalies, and developmental delay. We present a case of a 2.5-year-old male with epilepsy and global developmental delay. Chromosomal microarray detected a copy loss at 22q13 that resulted in a partial deletion of SHANK3 gene. The EEGs revealed seizure activity arising from left frontal central region. Invasive video electrocorticography captured clusters of epileptic spasms, all originating from left antero-lateral frontal lobe rostral to the motor cortex. We utilized routine histology to identify the inclusions and mapped their distribution in the resected portion of