infusion in our rat model, using powerful anti-inflammatory but non-toxic drugs is to begin soon.

Abstract A15

Proteoglycans as a double-edged sword in multiple sclerosis: Implications for future approaches to immunomodulatory therapy

J Warford, AC Lamport, DW Hoskin, AS Easton

Department of Pathology, Dalhousie University, Halifax, NS

doi:10.1017/cjn.2017.16

Proteoglycans are components of the extracellular matrix that have been identified as barriers to endogenous remyelination. Surfen (bis 2-methyl, 4-amino, 6-quinolyl amide) is a small molecule proteoglycan antagonist. We have previously reported that surfen reduces T cell proliferation in vivo and in vitro while also decreasing the production of chemotactic and pro-inflammatory factors produced by macrophages. Here we extend these studies to clinically relevant mouse models of chronic neuroinflammation (experimental autoimmune encephalomyelitis; EAE) and focal demyelination (lysolecithin). In the EAE model, surfen treated mice displayed a reduced disease severity that was associated with decreased percentages of CD4+CD45+ T cells and CD11b/F480 myeloid populations in the spinal cord. The chemokines RANTES, CCL2, and CCL3 were reduced in the spinal cords of surfen treated mice, resembling previous in vitro macrophage results and implicating a chemotactic mechanism that reduces cell infiltration. By contrast, when surfen was administered into a developing brain lesion using the lysolecithin model of demyelination it produced significantly larger lesions. The opposing effects of surfen observed in EAE and the lysolecithin model suggests that distinct proteoglycan families influence inflammation and remyelination differently depending on the stage of repair.

Abstract A16

Biopsy pathology in a large cohort of juvenile dermatomyositis is heterogeneous and, for the most part, independent of autoantibody phenotype

Shireena A Yasin[1,], Peter W Schutz[1,2,*,#], Claire T Deakin[1], Erdal Sag[1], Hemlata Varsani[1], Stephanie Simou[1], Sarah Tansley[3], Neil McHugh[3], Janice L Holton[2,4], Lucy R Wedderburn[1,5], Thomas S Jacques[6], on behalf of the UK Juvenile Dermatomyositis Research Group*

[1]Infection, Immunity, Inflammation Programme, UCL GOS Institute of Child Health, London, UK; [2]Division of Neuropathology, UCL Institute of Neurology, London, UK; [3]Royal National Hospital for Rheumatic Diseases, Royal United Hospitals Foundation Trust, Bath; and University of Bath, UK; [4]MRC Centre for Neuromuscular Diseases, UCL Institute of Neurology, London, UK; [5]Rheumatology Unit, Great Ormond Street Hospital for Children, London, UK; [6]Developmental Biology and Cancer Programme, UCL Institute of Child Health and Department of Histopathology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

doi:10.1017/cjn.2017.17

Background: Juvenile dermatomyositis has come to encompass several subtypes based on an emerging correlation between autoantibodies and clinical presentation. We hypothesised that myopathological findings may align with clinico-serological subtypes, potentially indicating differences in pathogenesis.

Methods: We studied a large cohort of 101 muscle biopsies from JDM patients in the UK JDM Cohort and Biomarker Study using the international JDM score tool and performing histological analysis of dominant fiber pathology. Autoantibody data were available for the majority of patients and were correlated with histological findings.

Results: Major autoantibody groups in our cohort were anti-TIF1γ (18/101), -NXP2 (15/101), -MDA5 (11/101), -Mi2 (5/101), and -PmScl (6/101). JDM biopsy severity scores varied within antibody groups except for MDA5 with consistently low, and Mi2 with consistently high scores. Dominant fiber pathology was grouped under 8 descriptive labels (minimal change (24/101), diffuse endomysial macrophage infiltrates (40/101), perifascicular atrophy (22/101), macrophage rich necrosis (6/101), scattered necrosis (2/101), clustered necrosis (2/101), inflammatory fiber invasion (2/101), chronic myopathic change (1/101)). All major autoantibody groups showed a mix of fiber pathologies with the exception of MDA5, which consisted predominantly of minimal change biopsies.

Conclusion: JDM patients demonstrate a range of muscle biopsy findings in our cohort with perfascicular atrophy represented in only about one third of biopsies. Dominant fiber pathology or severity scores do not clearly predict autoantibody groups. Heterogeneity of muscle histology in JDM is not fully understood but may indicate differences in activation of inflammatory signaling pathways in muscle between patients.

Abstract A17

Myopathology of Isolated Congenital Ptosis

H.B. Sarnat, L. Flores-Sarnat, Femida Kherani

University of Calgary and Alberta Children's Hospital, Calgary, Alberta, Canada

doi:10.1017/cjn.2017.18

Isolated congenital ptosis is incomplete retraction of the upper palpebrae since birth, usually bilateral, and not associated with external ophthalmoplegia, facial weakness or other neurological deficits, neuromuscular disease (myasthenia; congenital myopathies), systemic metabolic disease (mitochondrial cytopathy; organic acidurias) or structural lesions of the eyelid (plexiform neurofibroma; haemangioma; Meibomian or epithelial cysts; abscess). It may occur as a Mendelian trait, especially if the parents are consanguinous, or a genetic defect may not be evident from family history. Treatment is surgical resection of palpebral tissue from the conjunctival side of the eyelid.

We performed pathological examination of such resections in 28 infants and children, including immunocytochemical markers for smooth and striated slow and fast muscle myosin. Results showed structural lesions in 3; agenesis or hypoplasia of the striated levator palpebrae muscle with preservation of the smooth Müller muscle in 23, selective agenesis of Müller muscle in 1 case, and no evident lesions in 1 patient. Mild subconjunctival

*Contributed equally.

#Present affiliation: Division of Neuropathology, Vancouver General Hospital, Vancouver BC, Canada.

and perivascular lymphocytic infiltrates were almost universal, but probably secondary inflammation from chronic rubbing of the eyes and not pathogenetic. Many examples of congenital absence of specific striated muscles throughout the body are known and congenital ptosis is another. Isolated absence of smooth muscles is rarer. The upper eyelid is one of only a few sites in the body where smooth and striated muscle must work together for function, the absence of one not fully compensated by the other.

Abstract A18

Lissencephaly and circumferential skin creases associated with TUBB mutation broaden the spectrum of tubulinopathies

C. Fallet-Bianco[1], S. Boissel[2], F. Rypens[1], D. Bouron-Dal Soglio[1], J. Michaud[2]

[1]CHU Sainte-Justine-Université de Montréal, Montréal (QC), Canada; [2]CHU Sainte-Justine Research Center, Université de Montréal, Montréal (QC), Canada

doi:10.1017/cjn.2017.19

Mutations in tubulin genes cause cortical malformations, rarely with minor dysmorphic features. Congenital circumferential skin creases are rare disorders characterized by ring creases associated with facial dysmorphism, intellectual disability and imaging brain data from normal to malformations involving corpus callosum and vermis. The cause was unknown until recent data demonstrated that mutations in TUBB are responsible for this syndrome for which neuropathological data have never been described.

A termination of pregnancy was performed at 28 WG for brain malformations. Karyotype was normal and whole-exome sequencing was performed for subject and parents. Examination disclosed severe dysmorphic features, circumferential creases and microcephaly. Neuropathological study demonstrated microlissencephaly, callosal agenesis, dysmorphic basal ganglia, cerebellar hypoplasia. Histological examination showed cortical glomerular structures, abnormal cortico-spinal tracts, heterotopic axonal fascicles, unusually large germinal zones, abnormal hippocampi, roughly-shaped dentate and olivary nuclei. Whole-exome sequencing demonstrated a heterozygous missense mutation in TUBB gene occurring de novo.

Neuropathological features are identical to those observed in other tubulinopathies. However, mutations in TUBB gene have not yet been reported in tubulinopathies with isolated cortical malformations. The association of circumferential skin creases, facial dysmorphism and a characteristic brain malformation resulting from a mutation in TUBB gene constitutes a new entity expanding the spectrum of tubulinopathies.

Abstract A19

The neuropathology of the brain malformation in fetal PI3KR2 related disease

P. Diamandis[1], S. Keating[2], D. Chitayat[2], G. Mirzaa[3], P. Shannon[4]

[1]University Health Network, Toronto, Ontario; [2]Mount Sinai Hospital, Toronto, Ontario; [3]Seattle Children's Research Institute, Seattle, Washington; [4]Mount Sinai Hospital, Toronto, Ontario, Canada

doi:10.1017/cjn.2017.20

Activating germline mutations in PI3KR2 (Phosphatidylinositol 3-kinase regulatory subunit 2) have been associated with a syndrome of macrencephaly, polydactyly and Polygyria (MIM#603387), which is well described in the clinical and radiological literature not histologically. We present the first pathological description of the condition of which we are aware in a 20 week gestation fetus. Midgestation ultrasound demonstrated complex congenital heart disease, and the pregnancy was interrupted at 20 weeks gestation. Neuropathological examination demonstrated cerebral macroencephaly, with a weight greater than twice that expected for gestational age. The hemispheres were symmetrically swollen with blunted Sylvian fissures, mildly enlarged lateral ventricles and thickened cerebral mantles. Histology demonstrated leptomeningeal and subcortical heterotopia, as well as premature and abnormal neocortical lamination, principally in the frontal lobes. Cajal Retzius cells displayed enlarged Reelin (+) varicosities extending into the superficial cellular layers of the cortex, and layer II demonstrated a population of large pyramidal cells. An intracortical calretinin (+) hypocellular band was sometimes present.

Titles of Diagnostic Case Presentations

1. Atypical teratoid/rhabdoid tumour of the sella turcica

R. J. B. Macaulay

Department of Anatomic Pathology, Moffitt Cancer Center, Tampa, FL

2. Cortical ependymoma presenting with long - term refractory epilepsy

H. Alghefari, B AlYamany, LC Ang

London Health Science Center Ontario, Canada

3. Osmotic Demyelination Syndrome secondary to recurrent hypoglycemia

J. Karamchandani and R. Auer

Department of Pathology, McGill University, Montreal, QC;

Department of Pathology, University of Saskatchewan, Saskatoon, Saskatoon, SK

4. Amyloid beta-related angiitis

S. Magaki, S. Karnezis, L. Macyszyn, and H. V. Vinters

UCLA Medical Center, Los Angeles, CA

5. Intravascular large B cell lymphoma

L.M. Schmitt and L. Resch

Division of Neuropathology, University of Calgary, Calgary, Alberta