Autopsy, however, disclosed a diffuse large B-cell lymphoma in the cerebellum with widespread dissemination throughout the brain. In the background were multifocal gliotic regions of myelin/axonal loss with intermixed infiltrates of T-cells and microglia/macrophages. The biopsy sites and resection cavity showed similar findings. Overlapping features between these chronic lesions and that in the surgical specimens suggest a shared pathogenesis, supporting a concept that the sentinel lesion represents a reaction to an emerging PCNSL, either immune mediated or resorptive due to spontaneous or induced regression. Moreover, as demonstrated, PCNSL should remain a persistent consideration in the differential diagnosis, even though clinical, imaging, and pathology indices may fail in resolution between tumefactive MS, sentinel lesion, or overt PCNSL.

Abstract A5

Intraventricular ganglioglioma with hemorrhage

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Gangliogliomas represent a rare form of neuroepithelial tumours, which even more rarely present with hemorrhage or localize intraventricularly. To date, only two cases of ganglioglioma with both of these features have been reported. Our patient is a 23-year-old woman who presented with signs and symptoms of increased ICP, with a post-subtotal resection diagnosis of WHO Grade I ganglioglioma localizing bilaterally to the lateral ventricles. One year following the operation, the tumour showed radiologic evidence of interval hemorrhage, which was verified histopathologically following a second subtotal resection. Greater than 95% of the lesion represented a large hematoma with organization and well-defined fibrous pseudo-capsule, with very scanty fragments of adjacent/peripheral low-grade glial tumour. This case represents a very rare presentation of intraventricular ganglioglioma with hemorrhage.

Abstract A6

Histone H3 mutations in astrocytomas in young adult patients

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Histones are nuclear proteins involved in control of both DNA replication/repair and transcription, which are regulated by methylation and acetylation at specific residues. Recurrent point mutations have been described in histone H3 in pediatric gliomas. Using Droplet Digital (ddPCR) Assay we investigated the presence of the K27M mutation (in the genes for either H3.3 or H3.1) and G34V/R in all 39 patients under the age of 40 (over 18) operated at St. Michael's hospital for astrocytoma from 2004 to 2015 in whom enough material was available. 6 patients (average age 21 ± 5.2) harboured H3K27M mutations; tumor histology ranged from pilocytic to glioblastoma, all were located in the midline, and none was associated with mutations in IDH1 or BRAF. 10 patients (average age 30 ± 6.8) harboured H3G34R mutations; tumor histology ranged from diffuse astrocytoma to glioblastoma, all were located in the hemispheres, and were frequently associated with mutations in IDH1 (R132H, 60%) and sometimes BRAF (V600E, 10%). We also found 17 patients harboured the IDH1 R123H mutation, which co-occurred with H3G34R in 6, and 4 patients harboured the BRAF V600E, in one case along with H3G34R. Only 26% of patients did not carry at least one of the mutations investigated; Histone mutations are present in 35% of midline tumours and 40% of hemispheric astrocytomas in this age group.

Abstract A7

Impaired TDP-43 Repression of Nonconserved Cryptic Exons in Alzheimer's Disease

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Initially implicated in the pathogenesis of amyotrophic lateral sclerosis/frontotemporal dementia (ALS-FTD), TDP-43 proteinopathy has been documented in 30-70% of subjects with Alzheimer's disease (AD) neuropathology. Moreover, TDP-43 pathology has been shown to be significantly associated with cognitive impairment and brain atrophy in AD. Previously, we showed that TDP-43 serves as a splicing repressor of nonconserved cryptic exons and that such function is compromised in brains of ALS and FTD patients. It is not known whether TDP-43 cytoplasmic aggregates are a prerequisite for the incorporation of cryptic exons or how extensively such splicing defects occur in AD. Here, we report that cryptic exon incorporation occurs in all AD cases exhibiting TDP-43 pathology. Furthermore, in AD cases exhibiting both TDP-43 cytoplasmic inclusions and nuclear clearance in amygdala, but only nuclear clearance in the hippocampus, cryptic exon incorporation could still be detected in the hippocampus. These data support the notion that the depletion of nuclear TDP-43 precedes its cytoplasmic aggregation and is widespread in AD, offering important mechanistic and therapeutic implications for this devastating illness of the elderly.

Abstract A8

Patient K.C.: neuropathology of a unique case of memory impairment

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Patient K.C. has been investigated by researchers for over 20 years after intracranial trauma from a motorcycle accident resulted in a unique profile of amnesia. K.C. suffered from severe anterograde amnesia, in both verbal and non-verbal domains. This was accompanied by a selective retrograde amnesia for

personal events experienced prior to the time of his injury (episodic memory), with relative preservation of memory for personal and world facts (semantic memory). This pattern of spared and impaired memory extended to spatial memory for large-scale environments and beyond memory to future imagining and decision-making. MRI showed widespread changes including diffuse atrophy, left PCA infarct, and left anterior frontal encephalomalacia. Notably, there was severe atrophy of the bilateral hippocampi, parahippocampal gyri, left amygdala, mammillary body, and anterior thalamus (after adjusting for generalized atrophy). We present neuropathological autopsy findings and clinicopathologic correlations in a case that has contributed greatly to our understanding of mechanisms of memory, especially the distinction between episodic and semantic memory.

Abstract A9

Neuropathological correlates of Corticobasal Syndrome

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Corticobasal syndrome (CBS) is characterized by asymmetric parkinsonism, apraxia, cortical sensory deficits, dystonia, myoclonus, and cognitive dysfunction. Although it was originally described as the clinical manifestation of corticobasal degeneration (CBD), it is now recognized that CBS may be the clinical presentation of a variety of neurodegenerative pathologic processes including, but not limited to, CBD, Alzheimer disease (AD) and frontotemporal lobar degeneration (FTLD). In order to evaluate the neuropathological correlates of CBS in our center, 37 retrospectively identified cases with clinical CBS and post-mortem examination were analyzed. CBD was the primary pathological diagnosis in only eight cases (22% of the total cohort), whereas the most common underlying pathology was AD with or without Lewy body disease (LBD) in 16 cases (43%). The remaining 35% of cases were found to have progressive supranuclear palsy (N = 5), FTLD-TDP (N = 3), LBD (N = 2), unclassifiable tauopathy (N = 1), mild developmental abnormality (N = 1) and neuronal intranuclear inclusion body disease (N = 1). Moreover, 27% of the CBS cases had other pathological findings in addition to the main neurodegenerative process, most often cerebrovascular disease and/or mild AD-related pathology. These findings confirm and illustrate the heterogeneous pathological substrate for CBS.

Abstract A10

Adult-onset progressive dementia and myoclonic epilepsy with polyglucosan bodies

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This 65 year-old left hand dominant male was referred for progressive cognitive decline with a working diagnosis of cortical basal degeneration versus Alzheimer's disease. The patient also had a 10-12 year history of spontaneous myoclonic jerks partially controlled with Valproic Acid. There were no reported sensory or bladder changes and no episodes of status epilepticus. Neuropsychological assessment was consistent with generalized cognitive impairment that suggested a widespread dementing illness with a MoCA of 8/30 which had deteriorated from 14/30 in the year prior. Other exam findings demonstrated difficulty with upward gaze, apraxia and a wide-based and unsteady gait. Electroencephalographic studies revealed dysrhythmia Grade IV, generalized spikes, polyspike and wave discharges, several of which were associated with myoclonic jerks, consistent with generalized epilepsy. MRI revealed generalized cerebral and cerebellar atrophy with ventriculomegaly.

Post-mortem examination failed to demonstrate significant neurofibrillary degenerative changes. Of note however, there were abundant polyglucosan bodies. These were most prominent within cerebellum, hippocampal CA4, cerebral white matter and subpial regions. Results from electron and confocal microscopy will be discussed as this pertains to neuronal localization as well as a comparison with age-matched controls and a case of childhood Lafora body disease.

Abstract A11

Progressive ataxia and palatal tremor: 2 autopsy cases of a novel tauopathy

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Sporadic Progressive Ataxia and Palatal Tremor (PAPT) is a rare syndrome characterized by symptomatic palatal tremor and slowly progressive cerebellar ataxia. To date, there has been only 1 autopsy report, which described a novel 4-repeat tauopathy with hypertrophic olivary degeneration and tau-positive inclusions in olivary neurons and dystrophic neuritic processes termed glomeruloid bodies. We report 2 further autopsy cases.

Case 1 is a 77-year-old man who presented with blurred vision and subsequently developed ataxia and gait instability. Dysarthria and palatal tremor appeared later. MRI showed T2 hyperintensity of the pons and bilateral inferior olives.

Case 2 is an 89-year-old man who presented with dysarthria and progressed to cerebellar ataxia and palatal tremor. 9 years into his disease course, his palatal tremor spontaneously resolved. MRI showed T2 hyperintensity in the bilateral olives, left midbrain, and right dentate nucleus.

Consistent findings in both cases included bilateral hypertrophic vacuolar olivary degeneration accompanied by tau-positive neuronal inclusions and glomeruloid bodies, along with tauopathy in the pons and midbrain. Cerebellar cortical degeneration was extensive, but involvement of the dentate was minimal. Tau and TDP-43 negative basophilic neuronal cytoplasmic inclusions in the olive and Purkinje cells were also a feature.