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 non-conserved 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

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