Session 4: Neurodegenerative Neuropathology

Abstract 9

Chronic traumatic encephalopathy (CTE) is absent from a European community-based aging cohort while cortical aging-related tau astrogliopathy (ARTAG) is highly prevalent

SL Forrest[1], JJ Kril[1], S Wagner[2], S Hönigschnabl[3], A Reiner[3], P Fischer[4], GG Kovacs[2,5]

[1]Discipline of Pathology, Faculty of Medicine and Health, University of Sydney, Australia; [2]Institute of Neurology, Medical University of Vienna; [3]Department of Pathology; [4]Department of Psychiatry, Danube Hospital, Austria; [5]University of Toronto and University Health Network, Toronto, Ontario, Canada

doi: 10.1017/cjn.2021.95

Chronic traumatic encephalopathy (CTE) and aging-related tau astrogliopathy (ARTAG) are characterised by tau-immunopositive neuronal and/or astrocytic inclusions, with overlapping cortical involvement and astrocytic inclusion morphology. This study determined the prevalence of CTE and cortical ARTAG in a European community-based population (n=310) and explored overlap of both pathological entities. Frontal, parietal and temporal cortices were assessed. No case fulfilling CTE criteria was found. However, isolated astroglial or neuronal tau pathologies were recognized in sulcal depths (<2%). One case without history of traumatic brain injury showed combined tau-immunoreactive features confined to frontal sulci without perivascular accumulation. Another 24 cases had single tau pathologies in cortical sulci. ARTAG was identified in 117 cases (38%), with a similar regional prevalence. Grey matter ARTAG was the most common followed by subpial, white matter and perivascular. The presence of any type of ARTAG was associated with having another type of ARTAG in the same region ($P<0.05$). In summary, cortical ARTAG in this population is common and contrasts the high prevalence of CTE in individuals with repeated mild traumatic brain injury.

LEARNING OBJECTIVES

This presentation will enable the learner to:
Classify tau-immunopositive astrocytic inclusions characteristic of ARTAG

1. Describe neuropathological components of CTE
2. Identify CTE and cortical ARTAG in a case series

Abstract 10

Nodding syndrome, an epidemic young-onset epilepsy-dementia complex in Uganda

MS Pollanen[1], S Onzivua[2]

[1]Department of Pathobiology and Laboratory Medicine, University of Toronto, Toronto, Ontario, Canada; [2]Department of Pathology, Mulago Referral Hospital, Kampala, Uganda

doi: 10.1017/cjn.2021.96

Nodding syndrome (NS) is an enigmatic recurrent epidemic neurological disease that affects children in East Africa. The illness begins with nodding of the head and grand mal seizures that may lead to death after several years. The most recent outbreaks of NS occurred in northern Uganda and South Sudan. We describe the clinicopathologic spectrum of NS in Uganda. Ten children or young adults with NS were studied at autopsy and the neuropathological findings correlated with the onset, duration and progression of their neurological illness. All cases had epilepsy with grand mal seizures. Three cases had a clinical course that was predominantly characterized by epilepsy. Seven patients had progressive frontotemporal dementia. Two of the patients with dementia also had progressive quadriparesis. In all cases, the brain revealed tau pathology. In cases with an epilepsy-predominate course, the tau pathology was largely limited to the anterior frontal lobes but cases with dementia had more widespread cortical and subcortical tau pathology. In some cases, the histologic pattern was reminiscent of progressive supranuclear palsy. There are some interesting parallels between NS and the amyotrophic lateral sclerosis/Parkinson-dementia complex (ALS/PDC). The similarities are the presence of geographical isolates of disease manifesting in indigenous populations with familial clusters but no clear heritability. Both disorders appear to be related to an unknown environmental factor and both diseases appear to be fading over time in the respective geographical locations. One of the major open questions is whether ALS occurs in NS. This question will be addressed in future clinical studies and postmortem examination of the spinal cord. We propose that NS is a unique epilepsy-dementia complex in East Africa.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Describe the clinicopathologic features of a nodding syndrome.
2. Compare the pathology of NS to ALS/PDC and related disease

Abstract 12

The Amygdala in Neurodegeneration

JT Joseph

Hotchkiss Brain Institute and University of Calgary, Calgary, Alberta

doi: 10.1017/cjn.2021.97

The amygdala is a key anatomic structure that has multiple different nuclei and is involved in several critical aspects of cognition and systemic functions. Several different neurodegenerative diseases have major pathological effects on distinct amygdala nuclei. This presentation will describe the classic and characteristic anatomic distributions in the amygdala of "pure" Alzheimer disease and "pure" Lewy body disease, as well as "normal aging". In addition, data will be presented on how these classic distributions are altered in either "mixed dementias" or in some atypical forms of neurodegeneration. Amygdala pathology will also be illustrated in several other neurodegenerative diseases. The implications of the differing anatomic distributions in different neurodegenerative diseases will be discussed.

LEARNING OBJECTIVES

This presentation will enable the learner to:
Recognize key anatomic divisions of the amygdala

1. Describe how different neurodegenerative diseases affect the amygdala
2. Consider how anatomic specificity of protein aggregation is important in the classification of neurodegenerative diseases

Abstract 13

The tissue proteome of dorsal root ganglia in Friedreich ataxia

AH Koeppen[1], AM Travis[1], J Qian[2], JE Mazurkiewicz[2], BB Gelman[3], S Pelech[4], C Sutter[4]

[1]VA Medical Center, Albany, NY, USA; [2]Albany Medical College; [3]University of Texas Medical Branch, Galveston, TX, USA; [4]Kinexus Bioinformatics Corp., Vancouver, BC, Canada and University of British Columbia

doi: 10.1017/cjn.2021.98

Dorsal root ganglia (DRG) at all levels of the spinal cord are a prominent target of Friedreich ataxia (FA). The lesions include hypoplasia of neurons, proliferation of satellite cells, infiltration by IBA- 1-reactive monocytes, and formation of residual nodules. Paucity and smallness of DRG neurons account for the lack of large myelinated axons in dorsal roots and sensory peripheral nerves. The lack of myelin in dorsal roots can be attributed to low levels of neuregulin 1 type III (NRG1[III]). Lysates of 13 DRG of genetically confirmed FA patients were analyzed by antibody microarray with 878 different validated antibodies that target structural and signaling proteins, and by Western blots. KIT and mTOR, two proteins involved in cellular proliferation, were significantly upregulated in the DRG of FA. KIT is a transmembrane receptor that dimerizes when it binds two molecules of stem cell factor (SCF) in its extracellular domain and becomes activated as protein tyrosine kinase. Immunohistochemistry with anti-KIT generated reaction product in satellite cells of normal DRG and prominent labeling of these cells in FA that co-localized with SCF on double- label immunofluorescence; SCF was present in S100-positive satellite cells rather than monocytes. Immunohistochemical reaction product of mTOR and other mTOR complex proteins, such as hamartin (TSC1), tuberin (TSC2), raptor (mTOR complex 1) and rictor (mTOR complex 2) was also present in satellite cells of normal DRG and DRG of FA. Antibodies to two downstream proteins that are considered to be indicators of mTOR activity, P70 S6K and 4E-binding protein 1, revealed no reaction product in DRG of FA. TSC1, TSC2, and mTOR are best known from their roles in tuberous sclerosis, but expression of these proteins, and KIT, in DRG may contribute to signaling cascades underlying the proliferation of satellite cells in FA.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Discuss cellular proliferation in the pathogenesis of the DRG lesion in Friedreich ataxia

CONFLICT OF INTEREST

AHK is a consultant to PTC Therapeutics of South Plainfield, NJ USA. SP and CS are majority owners of Kinexus.

Session 5: Neuropathology practice

Abstract 14

Canadian Association of Neuropathologists Workforce Survey, 2019

P Shannon

Mount Sinai Hospital, Toronto

doi: 10.1017/cjn.2021.99

To characterize the professional occupation of Canadian neuropathologists and estimate the future employment demands in neuropathologists, all the active members of the Canadian Association of Neuropathologists in Canada (n=53) were surveyed by E-mail, inquiring as to their estimated date of retirement, their current employment and practice profile, and as to any practice trends they had noticed. 49 members replied: all but one practice at medical school centers. 38 practice exclusively in neuropathology and three of these are employed at less than 75% of a full time equivalent. The remaining practices are mixed neuropathology and anatomical pathology, and one practices exclusively ophthalmic pathology. 35% reported significant neuropathology sub specialization (e.g. forensic, pediatric, neuromuscular). 42% reported greater than 10% of time dedicated to research (of these, median 30%) and 35% greater than 10% time spent in teaching, and 9% greater than 10% time in administration. Of the 49 surveyed, as of the spring of 2019, 14%(seven) of the full time neuropathologists can be expected to retire in the next 10 years, and 6% (three) with mixed AP/NP practices.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Understand the current spectrum of practice of Neuropathologists across Canada
2. Describe the patterns of employment and anticipated retirements of Canadian Neuropathologists