neuropathology practice and the access of different centres to these tests, we designed a survey that was sent to all members of the Canadian Association of Neuropathology member list in the fall of 2017. This survey asked a number of questions relating to the approach to glioma diagnosis, immunohistochemical/molecular test ordering patterns, in-house test availability, and need to send out for testing. In this presentation we will present preliminary results from this survey, with a focus on institutional testing capabilities. This provides a valuable resource that could ultimately need to a national database of immunohistochemical and molecular test availability for each neuropathology centre.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Review the key molecular markers in the diagnosis of adult gliomas and methods of testing for them
2. Discuss the effect that the 2016 WHO CNS tumor update has had on clinical practice in Canada

Abstract 14

Role of MacroH2A2 in the glioblastoma stem cell epigenome

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Glioblastoma is the most common primary malignant brain tumour in adults, and remains uniformly lethal. These tumours contain a subpopulation of glioblastoma stem cells (GSCs) that drive tumour recurrence and drug resistance. We find that MacroH2A2 is a histone variant that can stratify glioblastoma patients, with higher levels of this histone variant associated with better patient prognosis. Knockdown of macroH2A2 in GSCs is associated with increased self-renewal and an increased expression of stemness genes by RNA-seq. Our preliminary results suggest that macroH2A2 is a novel biomarker for glioblastoma and that macroH2A2 loss is a marker of GSC stemness and a poor prognostic marker in glioblastoma. This work identifies loss of macroH2A2 as a feature of GSCs and provides a framework for therapeutic modulation of this histone variant.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Explain the role of epigenetics in glioblastoma pathophysiology

Abstract 15

Cerebellar glioblastoma: a clinicopathologic series of 16 cases

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Due to their rareness, it is not known if the clinicopathological features of cerebellar glioblastomas (cGBMs) are different from supratentorial GBMs (sGBMs). We reviewed all 16 cases of cGBMs (total GBMs: 1350) at St. Michael's Hospital over 18 years and assessed their clinicopathologic features. The mean age at diagnosis was 57 years. The most common presentations were headache (56%) and gait instability (56%). The majority (81%) of cGBMs were hemispheric while 19% involved the midline. There was radiologic evidence of brainstem infiltration at presentation in one case. Radiologically, peritumoral edema (63%) and heterogeneous contrast enhancement (50%) were common. Histologically, cGBM showed leptomeningeal involvement in 10/12 of cases. Uncommon histologic variants included 3 giant cell GBMs, a gliosarcoma, and a tumor with Rosenthal fibres and eosinophilic granular bodies. IDH1 R132H mutation was detected in 3/14 cases, a rate much higher than sGBMs. Additionally, 7/11 tumors had widespread p53 immunopositivity suggestive of TP53 mutation which is in accordance with previous reports in the literature. Of 9 cases tested, none had histone H3 K27M or G34R/V mutation. In summary, cGBMs have unique features that distinguishes them from sGBMs.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Identify the clinicopathological features of cerebellar GBMs including major molecular alterations
2. Compare cerebellar and supratentorial GBMs and describe the distinguishing features of each type of tumor

Session 4: Infectious/Immune mediated Neuropathology and Neuromuscular Neuropathology

Abstract 16

Mycobacterium chimaera encephalitis following cardiac surgery in three adult immunocompetent patients: first detailed neuropathological report.

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Non-tuberculous mycobacterium encephalitis is rare. Since 2013, a global outbreak of Mycobacterium chimaera infection has been attributed to point-source contamination of heater cooler units used in cardiac surgery. Disseminated M. chimaera infection has presented many unique challenges, including non-specific clinical presentations with delays in diagnosis, and a high mortality rate among predominantly immunocompetent adults. Here, we describe three patients with fatal disseminated Mycobacterium chimaera infection showing initially non-specific, progressively worsening neurocognitive decline, including confusion, delirium, depression and apathy. Autopsy revealed widespread granulomatous encephalitis of the cerebrum, brain stem and spinal cord, along with granulomatous chorioretinitis. Cerebral involvement and differentiation between mycobacterial granulomas and microangiopathic changes can be assessed best on MRI with contrast enhancement. The prognosis of M. chimaera encephalitis appears to be very poor, but might be improved by increased awareness of this new syndrome and timely antimicrobial treatment.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Describe the clinical, radiological and neuropathological findings of Mycobacterium chimaera encephalitis
2. Be aware of this rare form of encephalitis, and explain its diagnosis, prognosis and management

Abstract 17

Clinical, neuropathological and molecular features of fatal human pegivirus-associated encephalitis.

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Flaviviruses include many viruses causing encephalitis, including West Nile encephalitis, St. Louis encephalitis, tick-borne encephalitis and Japanese encephalitis. Human pegivirus genotype-1 (HPgV-1) is a lesser known member of the Flaviviridae family and has been identified in human serum, cerebrospinal fluid and brain tissue. Here, we describe two adult patients with fatal HPgV-1-associated encephalitis. Neuroimaging revealed multifocal lesions, initially present in the periventricular and brain stem white matter, then one year later throughout the corona radiata bilaterally with marked involvement of the brainstem and cervical spinal cord. Phylogenetic analyses of HPgV-1 showed clustering of brain-derived sequences from both patients with other human pegiviruses. In both patients, a novel 87-nucleotide deletion in the viral NS2 gene was detected. The presence of positive and negative strand HPgV-1 RNA and viral antigens in both patients indicated viral persistence and replication in the CNS. Autopsy showed lymphocyte infiltration and gliosis predominantly in white matter of the brain and brain stem but, to a lesser extent, also in grey matter. Immunofluorescence revealed HPgV-1 NS5A antigen in lymphocytes as well as in astrocytes and oligodendrocytes. Thus, we hypothesize that the novel deletion in the NS2 coding region may have caused HPgV-1 neuroadaptation or might represent a yet unrecognized genotype of human pegivirus.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Describe the clinical and neuropathological features of fatal human pegivirus-associated encephalitis
2. Recognize the importance of molecular analysis in encephalitis cases with unknown etiology

Abstract 18

Absence of age-related neurodegenerative changes during SIV infection and treatment in aged macaques

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The advent of combined antiretroviral therapy (CART) has changed HIV infection from a lethal disease to a chronic infection. CART has substantially mitigated infection-associated immunosuppression, related opportunistic infections and HIV encephalitis, nevertheless a substantial percentage of infected individuals are afflicted with a spectrum of HIV-associated neurological disorders (HAND). As approximately 45% of HIV-infected subjects in developed countries are over the age of 50, it has been hypothesized that infection may exacerbate age related neurodegenerative processes. We used the nonhuman primate SIV infection model to test whether chronic infection of aged primates, with or without CART, is associated with accelerated age-related neurodegeneration. Two dozen aged macaques (average age 18 years at entry 20 years at the end) were divided into two groups, half infected with SICmac251 and the other half not. After 10 months, half of each of these groups were either treated or not with CART and followed for an additional 6 months. We previously reported the clinical and neurobehavioural outcome. Here we compared the molecular and histologic findings in the four groups. Using a broad spectrum of histological markers, we found no evidence in the macaques of neuropathological changes associated with aging in humans. While the number of animals is small and length of infection limited, this study does not support the hypothesis that lentiviral infection or