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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 gliaosis 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
treatment accelerates age-related neurodegenerative changes in the primate brain.

LEARNING OBJECTIVES
This presentation will enable the learner to:

1. Explore current theories on the pathogenesis of lentiviral-related neuropathology
2. Explain limitations of nonhuman primate models of age-related human brain changes

ABSTRACT 19

Immunohistochemical markers of reactive skeletal muscle fibres
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Although most patients undergo muscle biopsies to elucidate the cause of muscle symptoms (weakness, cramping, etc.), many muscle biopsies show relatively few specific alterations on routine staining. Immunohistochemical methods for muscle fibre typing and characterisation of inflammatory cell infiltrates are now well established but the value of other markers is less well documented. A preliminary study of other potentially useful immunohistochemical markers revealed that muscle biopsies in our hospital often contain CD56 and/or D2-40 positive myofibres. This study was extended to a series of 32 biopsies from adult patients (age 21–81, 12 males 20 females), 11 of which showed only minor changes on routine examination. Most cases contained CD56 positive mature fibres; D2-40 positive muscle fibres were more common in cases of inflammatory myopathy. Five cases with minor changes on routine examination showed CD56 and D2-40 staining of otherwise unremarkable myofibres, which might represent reactive changes.

LEARNING OBJECTIVES
This presentation will enable the learner to:

1. Describe patterns of immunohistochemical staining in reactive muscle fibres
2. Discuss the underlying physiology of reactive muscle fibres

SESSION 5: Quality Assurance in Neuropathology

ABSTRACT 20

Assessing autolyzed foetal brains
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Problem: Evaluating very soft foetal brains is problematic, since anatomic information is often lost when these collapse on a dissection board.

Methods: Present cases of very soft foetal brains photographed under water, discuss technical details on this technique, and indicate how these data can be used to evaluate the brains.

Results: Foetal brains from intrauterine foetal deaths and from foetal terminations that have a long death-to-delivery time are often very soft, even after fixation, and collapse under their own weight on a dissection board. To better evaluate these brains, they have been floated and photographed in water. When possible, the brain is photographed intact in ventral and dorsal views. After the brainstem with cerebellum is removed and hemispheres are separated, these are all photographed; hemispheres are imaged in both lateral and medial views. This technique records developmental data about cortical gyration, the presence of olfactory tracts/bulbs, corpus callosum posterior extension, cerebellum foliation, and brainstem, which can be compared to standard brain development references. Problems with this technique include fragmentation of autolyzed brain into water.

Discussions: Photography of very soft foetal brains under water allows evaluation of brains that normally collapse under their own weight. In cases too soft for meaningful dissection, these data often provide the only available brain developmental information.

LEARNING OBJECTIVES
This presentation will enable the learner to:

1. Photograph foetal brain under water
2. Evaluate key aspects of external examination using standard developmental literature