H21 A Brain Teaser: Two Atypical Meningoencephalitis Cases in Human Immunodeficiency Virus (HIV) Patients

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After attending this presentation, attendees will better understand the possible presentation of Neurological Immune Reconstitution Inflammatory Syndrome (Neuro IRIS) and appreciate the different atypical presentations of meningoencephalitis in HIV patients.

This presentation will impact the forensic science community by informing attendees of the differential diagnosis of lymphocytic meningoencephalitis, including unusual Central Nervous System (CNS) complications of HIV infection, and by describing approaches to conducting a work up of these cases at autopsy.

Two examples of a rare HIV complication, IRIS, are reported, which were diagnosed following an extensive autopsy. This presentation provides a case study of a rare complication with few reports in the literature.

IRIS is a paradoxical worsening of the patient's condition as a newly reconstituted immune system reacts to infection following initiation of Highly Active Anti-Retroviral Therapy (HAART). An overwhelming response involving T cells can result in an encephalitis as activated T cells infiltrate the brain to fight an underlying infection of the central nervous system (Neuro IRIS). Both IRIS and Neuro IRIS are associated with a breakdown of the blood-brain barrier.

The first patient was a 34-year-old black male inmate with a history of HIV infection and a plasma CD4+ lymphocyte count of 459/cmm who was not on HAART at the time of death. His clinical presentation entailed newly diagnosed schizophrenia one to two months prior to death, increasing disorientation, and profound terminal hypothermia with hypotension. He was treated for possible seizure and sepsis but died before a definitive diagnosis was made. At autopsy, the brain was edematous with bilateral uncal and tonsillar herniation. Microscopic examination revealed a diffuse, marked lymphoplasmacytic meningoencephalitis with non-specific features. Serologic testing on postmortem blood was negative for several arboviruses (including West Nile Virus), as well as Rabies virus and lymphocytic choriomeningitis viruses. Immunohistochemical staining for p24 antigen was diffusely positive; clusters of CD3+ and CD68+ cells were often found near positive-staining areas. The cause of Neuro IRIS in this case most likely represents a reaction to the HIV antigen itself.

The second patient was a 30-year-old Caucasian male inmate with a past medical history of AIDS diagnosed in 2010; he was started on HAART in 2013 and again upon re-incarceration in September of 2014. Recent blood work on 6/1/15 indicated an absolute CD4 of 143 and HIV viral load of 538 copies/ml. Approximately three weeks prior to his death on July 20, 2015, he began complaining of severe headaches, vomiting, and difficulty walking, and was admitted to the hospital. The Cerebrospinal Fluid (CSF) contained elevated protein and pleocytosis. At autopsy, there was marked cerebral edema with uncal herniation and a pronounced, diffuse lymphocytic meningoencephalitis with no visible viral inclusions or specific features. Postmortem Polymerase Chain Reaction (PCR) testing on frozen brain tissue by biofilm was negative for Eastern equine, Western equine, Venezuelan equine, cytomegalovirus,

enterovirus, Herpes simplex 1, *Varicella zoster*, and *Cryptococcus*. Of interest, PCR was positive for Human Herpes Virus 6 (HHV-6). Since the CNS is known to be a site of latent HHV6, the significance of this finding is unknown. By exclusion, the most likely cause of meningoencephalitis in this case was IRIS.

Clinical presentations of subacute meningitis can be subtle and pose a diagnostic challenge, particularly in HIV patients, where a range of opportunistic infections, HIV encephalitis, and neurologic IRIS are all diagnostic considerations.

Autopsy, IRIS, Meningoencephalitis