H104 Two Fatal Cases of Posterior Reversible Encephalopathy Syndrome (PRES)

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After attending this presentation, attendees will understand that PRES is a potentially fatal clinicoradiologic entity associated with a variety of risk factors. Few reports describing the neuropathology have been published. The information presented serves to increase awareness of this uncommon entity, its associated risk factors, and neuropathologic findings.

This presentation will impact the forensic science community by demonstrating the importance of a broad differential diagnosis in the combined setting of sudden natural death, peri-mortem neurologic symptoms, and relevant risk factors.

Introduction: PRES is defined by a constellation of clinical symptoms and characteristic radiologic findings of posterior cerebral white matter edema. PRES is associated with a growing list of risk factors including hypertension, immunosuppression, chemotherapy, and eclampsia. As the name reflects, the condition is usually transient (non-fatal); however, PRES may lead to progressive cerebral edema, infarcts, hemorrhage, and death in 15% of cases. Due to the low mortality rate, there are few reports describing the neuropathologic findings. Clinical, radiologic, and autopsy findings of two fatal cases of PRES are described.

Case 1: A 47-year-old female with past medical history of chronic obstructive pulmonary disease, migraines, and drug abuse presented to the emergency department with a two-day history of lethargy and progressive altered mental status. Admission systolic blood pressures were greater than 190mm Hg. A head Computed Tomography (CT) showed bilateral cerebral edema. A head Magnetic Resonance Imaging (MRI) without contrast revealed areas of increased signal involving the gray and white matter of the posterior parietal and occipital lobes. The findings were suggestive of PRES with a superimposed infarction. She was treated for hypertensive emergency that was difficult to manage. On day four, she developed bradycardia, hypotension, posturing, and dilated non-reactive pupils. A head CT revealed transtentorial herniation. Resuscitative efforts were unsuccessful. Autopsy findings of the brain included cerebral edema, most notably in the parietal and occipital regions, with bilateral uncal and tonsillar herniation. Microscopically, acute bilateral cerebral infarcts of the parietal and occipital lobes and parenchymal vasculopathy were identified. Additional findings at autopsy included granular kidneys and diffuse cardiomyocyte hypertrophy, consistent with hypertension.

Case 2: A 27-year-old immunosuppressed female, six months status post-bilateral lung transplantation for cystic fibrosis, was admitted for acute liver and renal failure. Serologic studies were negative for viral and autoimmune hepatitis; a liver biopsy was suggestive of drug-induced liver injury. On hospital day three, she developed altered mental status. A head CT showed signs of vasogenic edema and MRI showed PRES with cerebellar infarction. On day 16, she developed irregular respiration and a large intraparenchymal hemorrhage of the left parietal lobe. Hospital course was further complicated by gastrointestinal hemorrhage and pneumonia with respiratory failure. She was terminally extubated and died on day 21. Brain findings at autopsy included parenchymal hemorrhages in the left parietal and temporal lobes and right caudate nucleus in addition to multiple subacute infarcts in cerebellum

and cerebral cortex. Other autopsy findings included microangiopathic renal-glomerular injury suggestive of calcineurin-inhibitor toxicity.

Discussion: While PRES is increasingly recognized clinically, the true incidence is unknown and the pathophysiology remains controversial. The two current main hypotheses include disordered cerebral autoregulation and endothelial dysfunction. The end result of both mechanisms is blood-brain barrier dysfunction with vasogenic edema, particularly in regions supplied by the posterior circulation. Treatment involves removing the inciting factor and supportive measures. Clinical presentation is variable and may include headaches, visual disturbance, seizures, impaired consciousness, and focal neurologic signs. Due to the non-specific clinical manifestations, the differential diagnosis is broad, including status epilepticus, cerebrovascular accident, encephalitis, vasculitis, and cerebral venous-sinus thrombosis. The radiologic findings, which are a key factor diagnostically, are unlikely to be available in deaths occurring outside the hospital setting. It is important for medical examiners to be aware of risk factors and patterns of injury to suggest PRES as a contributing factor in the cause of death.

PRES, Cerebral Edema, Hypertension