H44 Intrauterine Liver Disease and Sudden Unexpected Infant Death: Causally-Related or Coincidence?

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After attending this presentation, attendees will understand the complexities of intrauterine liver diseases and specifically Gestational Alloimmune Liver Disease (GALD) in which transplacental maternal antibodies lead to fetal and neonatal liver disease with highly variable clinical and histopathologic features. Prior to recent understanding of the pathogenesis, liver transplantation was frequently required in order to save the lives of patients in whom the clinical diagnosis had been made antemortem.[1,2] Attendees will be introduced to the forensic significance of this and related intrauterine liver disease as mimics of abusive injury and will understand the importance of making a correct diagnosis.

This presentation will impact the forensic science community by informing attendees of recent advances in the understanding of intrauterine and neonatal liver disease by discussion of three cases, all presenting as sudden unexpected infant death in which fathers were charged or convicted of murder. The presentation will emphasize the clinical features of the disease and its histopathologic features at autopsy. It will discuss the differential diagnosis of gestational alloimmune liver disease in the face of sudden unexpected death in infancy and its role as a natural disease mimicking inflicted trauma. Forensic pathologists will learn of simple and inexpensive ways of confirming or excluding the disease at autopsy in cases of sudden unexpected infant death.

Studies of abusive head injury by investigators in various disciplines over the past decade have confirmed the presence of numerous mimics of abusive head trauma. These mimics include natural disease as well as accidental injury. The differentiation of abusive trauma from its mimics is increasingly important in terms of the financial and human costs to society of the litigation and incarceration of the innocent.

Gestational liver disease has only been studied intensively for the last two decades and by relatively few institutions in the United States and Europe. At the present time, the understanding is incomplete and much basic research needs to be done in various areas.

This presentation will discuss the details of a series of three autopsy-confirmed cases of intrauterine liver disease which were accompanied by unexpected death under unusual circumstances in the first three months of life. Legal proceedings in two of the cases resulted in convictions with lengthy prison terms; the third resulted in acquittal. After reviewing the first of the three cases, the sensitivity to this diagnosis was heightened and two other cases were seen in the subsequent two-year period. In two of the three patients, terminal cardiorespiratory arrest had precluded any clinical investigation and in the third case the clinicians did not entertain the diagnosis due to its protean clinical presentation, resulting in minimal investigation prior to autopsy. In different published series, the clinical course of the disease has varied from benign or virtually asymptomatic to rapidly lethal. The associated liver findings have also been highly variable, ranging from little or no clinical evidence of liver disease with essentially normal liver histology through advanced liver disease with hepatic failure and/or cirrhosis. Biochemical testing (liver function tests) are also highly variable and normal transaminase levels are common. Likewise, blood ammonia levels are variable.

Abnormalities of iron metabolism appear to be the most common feature and prior to a decade ago was widely referred to generically as Neonatal Hemochromatosis (NH). The histological hallmark of NH was typically regarded as accumulation of storage iron outside the reticuloendothelial system and in epithelial cells in a variety of organs; however, reticuloendothelial iron may be seen in this disease and was the key initial finding in one of these three cases. The basic criterion for the diagnosis remains the presence of stainable iron in one or more of various epithelial tissues including liver, pancreas, thyroid, adrenal, and minor salivary glands.

In cases of sudden unexpected death in infancy, there is typically inadequate time for clinical investigation and therefore the diagnosis must be made on the basis of autopsy findings. These findings typically require an index of suspicion but are generally easily confirmed if appropriate iron staining is done. This presentation will recommend routine iron staining of liver, pancreas, thyroid, and adrenal medulla in all infants under six months of age. Even when the correct diagnosis is made, it may not be possible to define a specific linkage between the disease and death in any given case, making assessment of "reasonable doubt" difficult. This difficulty notwithstanding, it is important for the trier of fact to be given all of the information generated at the autopsy.

References:

1. Gestational Alloimmune Liver Disease and Neonatal Hemochromatosis Whitington, PF *Seminars in Liver Disease* 2012 Vol. 32 325-332
2. Neonatal Hemochromatosis: Radiographical and Histological Signs Udell IW et al *Liver Transplantation* Vol. 11 No.8(August) , 2005: 998-1000

Liver Dease, Infant Death, Child Abuse