## H8 Pediatric Death by Macrophage-Activation Syndrome (MAS) Related to Epstein Barr Virus: The Role of Microbiological and Histological Postmortem Investigations

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After attending this presentation, attendees will be able to describe the impact of forensic science in cases of sudden pediatric death.

This presentation will impact the forensic science community by demonstrating the importance of immediate treatment in MAS to minimize the risks of sudden pediatric death.

In the context of immune-mediated diseases, MAS is a severe and potentially life-threatening complication of systemic inflammatory disorders. It may occur in response to an infection (often viral), malignancy, or a rheumatic disease. MAS typically appears in patients with Systemic-onset Juvenile Idiopathic Arthritis (SoJIA) and its adult equivalent, adult-onset Still's disease; it also is reported in other pediatric inflammatory disorders, including juvenile Systemic Lupus Erythematosus (SLE) and Kawasaki disease. It is a rare disorder. MAS expresses a close clinical resemblance to a group of histiocytic cell disorders collectively known as Hemophagocytic Lymphohistiocytosis (HLH). MAS is classified among the secondary, or acquired, forms of HLH. Primary HLH is a genetic disorder of immune regulation caused by mutations in genes encoding proteins required for the cytolytic activity exerted by NK cells and cytotoxic T cells. The clinical presentation of MAS is usually acute, may be dramatic, and is often difficult to distinguish from a severe sepsis. Typically, patients present fever, hepatosplenomegaly, lymphoadenopathy, profound depletion of all cellular blood elements, liver dysfunction, disseminated intravascular coagulation, and central nervous system dysfunction. Blood tests reveal: leukopenia, anemia, and thrombocytopenia; hyperbilirubinemia; high levels of Lactate Dehydrogenase (LDH), ferritin, and triglycerides; an increase in liver enzymes and cholestasis; normal or suddenly decreased Erythrocyte Sedimentation Rate (ESR); and sharply increased SCD25 and CD163. Coagulation is often altered, with elongation of the PT and PTT, hypofibrinogenemia, and the presence of fibrin degradation products (sharply increased D-dimer). In the field of forensic pathology, this postmortem diagnosis it is often difficult to detect; for this reason, cases sometimes remain unsolved. The treatment of MAS is not completely standardized. Steroids are considered the first-line therapy. Cyclosporine has demonstrated efficacy in non-responsive patients. The delay in diagnosis and multiorgan involvement are associated with a worse prognosis, so it is important that treatment is immediately instituted to prevent irreversible damage to the tissues and sudden pediatric death.

**Case Report:** A 2-year-old child was hospitalized for fever and vomiting. The child was pale and had dry skin. Nothing else was reported from the examination of the remaining systems. The hospital staff gave her antibiotics, antipyretics, and antiemetics. The results of chest and abdominal X-rays during the period of hospitalization were negative. A few hours after her admission, the child began to manifest mottled skin and bilious vomiting. She had kidney failure, absence of peripheral pulses, and loss of consciousness with convulsions and defecation. The child was treated with intubation, diazepam, and cortisone. Laboratory tests revealed lymph monocytosis, hyperglycemia, increased C-Reactive Protein (CRP) and ESR, and marked metabolic acidosis. Approximately six hours later, the first cardiac arrest occurred, but resuscitation was successful. Subsequently, two additional cardiac arrests ocurred, with a fatal outcome. After her death, an autopsy was performed. The microbiological data on postmortem samples from the lungs, pleural fluid, pericardial fluid, and cerebrospinal and ascitic fluid were negative for the detection of bacteria and yeasts. Microbiological investigation of the blood exhibited positivity for Epstein-Barr Virus (EBV) (Cytomegalovirus (CMV) and Mycoplasma pneumonia were negative). The postmortem histological examination revealed: labeled macrophage activation thymic cortical parenchyma; cardio-pulmonary thrombosis; pulmonary atelectasis; foci of interstitial pneumonia; follicular hyperplasia of lymphoid tissue associated with the intestinal and colon mucosa (Mucosa-Associated Lymphoid Tissue (MALT)); chronic hepatitis; and cerebral edema. The comparison of the clinical data with the autopsy data accompanied by microbiological investigations established that the MAS and Disseminated Intravascular Coagulation (DIC) in a child infected with EBV was the cause of death.

**Conclusions:** Cases of pediatric death with the absence of an antemortem diagnosis require a detailed analysis of antemortem clinical data with multidisciplinary collaboration with a pediatrician; it is necessary to conduct microbiological postmortem surveys on biological fluids in order to detect viruses and bacteria and to conduct histological investigations to explore in detail the thymus and lymphoid organs.

**Forensic Science, MAS, Pediatric Death**



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