G40 Hand, Foot, Mouth, ... And Medulla: Fatal Encephalitis in a Toddler Associated With Enterovirus 71 Infection

Rebecca Irvine, MD, Dept of Forensic Medicine, 50 Parramatta Road, Glebe, NSW 2037, AUSTRALIA; and Michael Rodriguez, MBBS, 50 Parramatta Road, Glebe 2037, AUSTRALIA*

After attending this presentation, attendees will understand the presentation, pathophysiology, and epidemiology of the emerging syndrome of Enterovirus 71-(EV 71) associated encephalitis in children.

This presentation will impact the forensic science community by elucidating the situations in which this condition should be considered and how identification at autopsy may be maximized. The significance of these cases to the public will be discussed.

A 17-month-old, previously healthy, female toddler presented to a Children's Hospital with fever, pallor, vomiting, poor perfusion, and shallow breathing. Initially tachycardic and self-ventilating, she abruptly developed bradycardia and deteriorated into cardiopulmonary arrest, from which she could not be resuscitated. During this brief terminal encounter, clinicians noted abnormal ocular findings, specifically ptosis, midline deviation, and nystagmus.

This child had been evaluated twice during the day preceding her death for suspected respiratory tract infection. No rashes or neurological findings were documented.

Gross autopsy findings included serous effusions, increased lung weight, and cerebral edema. The bladder was distended with urine. The lungs showed intra-alveolar edema and lymphocytic interstitial pneumonitis. Enterovirus was recovered from a lung swab. Examination of the fixed brain by a neuropathologist showed moderate symmetric brain swelling with dusky gray/brown discoloration, and congestion in the brainstem. Microscopy revealed meningoencephalitis, most severe in the caudal brainstem with focal necrosis, less severe in the cerebellate dentate nucleus, and relatively mild in the cerebrum (confined to the motor cortex, globus pallidus (inner segment), basal forebrain, hypothalamus, and inferior thalamus/subthalamus), typical of EV71 infection. No viral inclusions were identified.

The Enterovirus was subsequently sub-classified as EV 71. At least 3 children have died of EV 71-associated encephalitis in New South Wales this year, all identified following autopsy.

There is a clear association between Hand, Foot, and Mouth Disease (HFMD) and EV 71 and Coxsackie A virus 16, and a clear association between EV 71-associated HFMD and encephalitis. There is no strong evidence of a particular associated strain or recombinance between strains of EV or Coxsackie viruses.

HFMD is worldwide in distribution and outbreaks with associated encephalitis have been documented, although reports from Asia predominate. HFMD is a very common, highly infectious childhood disease with a highly variable presentation (non-specific, respiratory, or gastrointestinal); classically there is a vesicular rash on the hands and feet, or herpangina (vesicles within the mouth, often the posterior oropharynx) although the exanthema is often absent.

Possibly 6% of infected children will develop encephalitis. The prototypical case will be a child under three years of age with a brief, non-specific viral illness, with or without exanthema, in the summer or fall; deterioration will be rapid, with onset of any of a large variety of neurologic signs, although acute flaccid paralysis (sometimes monoplegia), myoclonic jerks, and cranial neuropathies are frequent. The mechanism of death is usually neurogenic pulmonary edema.

Forensic pathologists need be vigilant, as presentation may be non-specific and could be mistaken for Sudden Infant Death Syndrome (SIDS). Viral studies should be obtained, especially from the upper respiratory tract and rectum; cerebrospinal fluid is less reliable. Herpangina should be specifically sought, since the posterior oropharynx may be a "blind spot" in a routine autopsy. Ideally, the brain should be fixed and obviously examined with care, for it is the site of definitive pathology. If Enterovirus is recovered in the appropriate setting, the laboratory should be asked to sub-classify it. These cases are likely to be scrutinized by child mortality and public health authorities.

Although rare, these cases attract significant public interest and concern. It is unexpected in developed countries for children to die of an infectious disease, and in so rapid a fashion with dramatic neurologic signs; the presentation is ominously reminiscent of polio. The prodrome is indistinguishable from the usual frequent childhood viral illnesses. The public must invoke hygiene measures and isolation. Restriction from day care and support of children who survive with neurological impairment are economic burdens. Clinicians who see cases in the early stages may be considered culpable for a subsequent death. Trials of a promising vaccine are ongoing in China.

Enterovirus, Encephalitis, Children

 ** Presenting Author*