Mitochondrial medicine
a clinical guideline

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2.1 Leigh syndrome

Leigh syndrome or subacute necrotizing encephalopathy is named after the pathologist (Archibald Denis Leigh) who first described the neuropathology of this syndrome. The onset of symptoms is usually between ages 3 to 12 months but can occur in the neonatal period through adulthood. Signs include psychomotor retardation, floppiness, brainstem or extrapyramidal dysfunction, with or without lactic acidaemia. Additional clinical features include neurological, endocrine, renal or cardiac abnormalities or gastrointestinal problems may be present. Leigh syndrome is a progressive disease with in general a poor prognosis. Deterioration is variable over months to years or even decades, with episodes of rapid decline, often correlated with ‘minor’ infections. Death usually occurs within the first decade of life as a consequence of respiratory failure caused by brainstem dysfunction, with or without increasing muscle weakness.

Leigh syndrome has specific findings on MRI, namely symmetrical hyperintensities on T2 weighted images in the basal ganglia, brainstem, thalamus, diencephalon, cerebellum and spinal-cord. Postmortem pathological examination shows vacuolation of the neuropil and relative preservation of the neurons, associated with demyelination, gliosis and capillary proliferation. While the diagnostic gold standard is still based on neuropathology, clinical diagnosis can be made on the basis of medical history, physical examination, and radiological criteria.

Leigh disease can be caused by mutations in both mitochondrial and nuclear DNA. Many gene defects underlying Leigh disease are known.

Management includes education and support of the patient and his/her family. Daily caloric intake should be optimized, if necessary using tube feeding. Neurologic, ophthalmologic, and cardiologic evaluations at regular intervals to monitor progression and appearance of new symptoms are warranted. Seizures, dystonia, acidosis, cardiomyopathy and other complications should be treated appropriately.