Leigh Syndrome with Cytochrome C Oxidase Deficiency and Surf-1 Gene Mutations: MR Imaging Findings

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Purpose
To investigate brain MR findings in children with Leigh syndrome (LS) caused by cytochrome c oxidase (COX) defects, harboring verified mutations in the nuclear Surf-1 gene.

Materials & Methods
Brain MR studies performed in three LS patients with COX deficiency and mutations in the Surf-1 gene were reviewed retrospectively. There were two boys and one girl, aged 15 months to 3 years at presentation, who showed failure to thrive, neurodevelopmental regression, generalized muscle hypotonia, and lactic acidosis. Electrophysiologic studies revealed peripheral neuropathy in two cases. Isolated reduction of COX activity was demonstrated by histochemical and biochemical analysis. Surf-1 gene analysis identified pathogenetic mutations in all patients.

Results
MR imaging showed bilateral, symmetric signal alterations in the subthalamic nuclei, substantia nigra, and medullary pyramidal tracts in all cases. The periaqueductal gray matter and dentate nuclei were involved in two cases, and the posterior portion of the putamina in one. MR imaging also showed involvement of the mesencephalic interpeduncular nuclei, pallido-cortical, and nigro-cortical tracts in one case. The supratentorial white matter was consistently spared.

Conclusion
LS is a neurodegenerative disorder of infancy and childhood characterized by developmental delay or psychomotor regression, brainstem dysfunction, and lactic acidosis. It is a genetically heterogeneous disease caused by defects in enzymes involved in aerobic energy metabolism. Defects in COX play an important pathogenetic role in LS. Mutations in the nuclear Surf-1 gene, located on chromosome 9q34 and encoding a factor involved in the biogenesis of COX, have been identified recently in LS patients with COX deficiency, and are believed to play a causal role in the pathogenesis of this condition. Although symmetric signal alterations in the basal ganglia, brainstem, and cerebral white matter are the main MR findings in LS patients, correlation between MR features and biochemical/genetic defects is limited. Symmetric lesions of the subthalamic nuclei have been reported previously as an almost distinctive mark of LS with COX deficiency. Simultaneous, bilateral involvement of the subthalamic nuclei, substantia nigra, and medullary pyramidal tracts was the most consistent MR pattern in our genetically homogeneous series. We suggest that the detection of such pattern should lead to implement genetic studies intended to reveal the Surf-1 gene mutation. Signal abnormalities in the
mesencephalic interpeduncular nuclei, pallido-cortical, and nigro-cortical tracts represent other possible manifestations of brainstem involvement in these patients.

References