Leigh disease with brainstem involvement due to assembly factor NDUFAF2 defect.

Mitochondrial NADH: ubiquinone oxidoreductase (complex I) deficiency accounts for most defects in mitochondrial oxidative phosphorylation. Pathogenic mutations have been described in all 7 mitochondrial and 12 of the 38 nuclear encoded subunits as well as in assembly factors by interfering with the building of the mature enzyme complex within the inner mitochondrial membrane. We now describe a male patient with a novel homozygous stop mutation in the NDUFAF2 gene. The boy presented with severe apnoea and nystagmus. MRI showed brainstem lesions without involvement of basal ganglia and thalamus, plasma lactate was normal or close to normal. He died after a fulminant course within 2 months after the first crisis. Neuropathology verified Leigh disease. We give a synopsis with other reported patients. Within the clinical spectrum of Leigh disease, patients with mutations in NDUFAF2 present with a distinct clinical pattern with predominantly brainstem involvement on MRI. The diagnosis should not be missed in spite of the normal lactate and lack of thalamus and basal ganglia changes on brain MRI.