**Pigmentary degenerative maculopathy in a CYP2U1/SPG56 family**

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**Introduction:** SPG56 is an autosomal recessive form of Hereditary Spastic Paraplegia (HSP) caused by mutations in CYP2U1, a gene involved in lipid metabolism and mitochondrial function. Herein, we report three SPG56 patients with pigmentary degenerative maculopathy as a prominent clinical feature.

**Materials/Methods:** Patient 1 is a 50 year-old man, with progressive walking unsteadiness and progressive visual loss after age 30 years. His healthy consanguineous parents originated from a small village in Campania. He showed paraparetic gait, lower limbs spasticity and brisk tendon reflexes, bilateral Babinski sign (SPRS 8/52) and mild cerebellar signs. EMG/NCS disclosed a subclinical axonal motor and sensory polyneuropathy. MRI showed mild brainstem and cerebellar atrophy as well as a moderately thinned corpus callosum. His 46-year-old sister was similarly affected with onset after age 30 years. Patient 3 is their 42 year-old first cousin on both mother’s and father’s side.

After extensive genetic analyses (ARSACS, SPG7, SPG11, SPG15), a homozygous c.1168C>T (p.R390*) pathogenic mutation in the coding region of CYP2U1 was detected in all three patients, allowing a diagnosis of SPG56. As visual acuity of all patients was severely reduced (1/10 and 2/10, in patients 1 and 3 respectively), complete ophthalmologic evaluation, including (ocular fundus, OCT scan, PEV and PERG, was undertaken, which disclosed a pigmentary degenerative maculopathy.

**Discussion/Conclusion:** Mutations in CYP2U1 are associated with both pure and complicated forms of HSP. White matter lesions, basal ganglia calcifications, thin corpus callosum, mental retardation, infraclinical axonal motor and sensory neuropathy have been described. "Maculopathy" has been only found in one female patient in the original paper describing SPG56. This is the first formal report of pigmentary degenerative maculopathy associated with CYP2U1 mutation, which may reasonably be explained by the mitochondrial pathogenesis of the disorder.

**References**