Hereditary diffuse leukencephalopathy with spheroids: a microgliopathy due to CSF1 receptor impairment.

Abstract:
Hereditary diffuse leukencephalopathy with spheroids (HDLS) is a rare progressive form of leukodystrophy with variable clinical presentation and little known pathophysiology. Characteristic pathological features at brain biopsy or postmortem can support the diagnosis. The genetic basis of HDLS was elusive until 2011 when mutations in the colony-stimulating factor 1 receptor (CSF1R) gene were identified as the cause. Mutations in the CSF1R gene had previously been associated with tumor development, including hematological malignancies. We report three patients with HDLS who carried missense mutations in the CSF1R gene, two of them novel (p.L582P and p.V383L). Particularly in younger patients with rapid cognitive decline and/or leukencephalopathy of unknown origin, HDLS appears to be more common than previously thought. Various compounds acting on the CSF1 receptor are available from the treatment of hemato-oncological malignancies, so novel therapeutic approaches could be developed for this devastating condition.