Title: Hereditary leukoencephalopathy (hls) and csf1r heterogeneity

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Abstract
The leukodystrophies can present diagnostic challenges not least because of overlapping imaging and clinical phenotypes. We present an interesting patient with a novel CSF1R mutation. A 53-year-old Caucasian woman presented with a six-month history of left leg weakness, urinary incontinence and unprovoked falls. Within fifteen months she needed a four-wheeled walker to mobilise. Cognitive decline manifested as deteriorating episodic memory and progressive expressive dysphasia. Clinical examination identified left hand apraxia, a dystonic left ankle and spastic paraparesis. Clinical features and MRI, prompted genetic testing for Leukoencephalopathy with brainstem and spinal cord involvement with lactate elevation. This was negative. Subsequent whole exome sequencing revealed a novel CSF1R heterozygous c.1901T>G p. (Leu634Arg) mutation, indicative of Hereditary leukoencephalopathy with spheroids (HLS). HLS is rare, with fewer than 30 cases reported as of 2012. Autosomal dominant or sporadic, cases can present with mood and personality change. CSF1R is an emerging hotspot for discoveries of HLS-associated gene defects, with around 6 novel mutations reported in the last year. Their manifestations are protean and have been increasingly identified as a mimic for conditions ranging from CADASIL to extrapyramidal disorders. Our case highlights the diagnostic difficulty and the need for research into this leukodystrophy.