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.