Leukodystrophy	Age of onset	Gene	Pathophysiology	Suggestive clinical features	Suggestive MRI findings
Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP)	Adulthood	*CSF1R*	Abnormal microglia proliferation and survival	Spasticity Psychiatric symptoms	Frontal periventricular involvement Diffusion restriction Thinning of corpus callosum
Adult polyglucosan body disease (APBD)	Adulthood	*GBE1*	Abnormal glycogen brancher enzyme activity	Peripheral neuropathy Spasticity Cerebellar ataxia	Periventricular predominance Sparing of U-fibers Sparing of corpus callosum (early) Spinal cord atrophy
Vanishing white matter disease (VWM)	Adulthood	*eIF-2B*	Abnormal regulation of mRNA translation into proteins	Spasticity Cerebellar ataxia Psychiatric symptoms Amenorrhea	Sparing of the midline (early stages) Thinning of corpus callosum Cystic changes
Alexander disease	Adolescence to adulthood	*GFAP*	Glial fibrillary acidic protein aggregation in astrocytes	Cerebellar ataxia Bulbar dysfunction Palatal myoclonus Macrocephaly	Anterior predominance Contrast enhancement Brainstem involvement
Canavan disease	Adolescence to adulthood	*ASPA*	Abnormal aspartoacylase enzyme activity leading to buildup of N-acetylaspartic acid	Macrocephaly	Diffuse subcortical T2 hyperintensities extending into the internal and external capsules
X-linked adrenoleukodystrophy (X-ALD) and adrenomyeloneuropathy (AMN)	Childhood to adulthood	*ABCD1*	Abnormally high levels of very long chain fatty acids	Adrenal insufficiency Spasticity (particularly AMN) Psychiatric symptoms (X-ALD)	Parieto-occipital predominance (X-ALD) Contrast enhancement (X-ALD) Spinal cord atrophy (AMN)
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)	Childhood to adulthood	*NOTCH3*	Non-atherosclerotic vasculopathic changes of small arteries	Migraines Strokes and TIAs Psychiatric symptoms	Anterior temporal lobe involvement Diffusion restriction
Globoid cell leukodystrophy (Krabbe)	Childhood to adulthood	*GALC*	Deficient galactocerebrocidase enzyme leading to lipid accumulation	Peripheral neuropathy Spasticity Optic atrophy	Parieto-occipital predominance Involvement of basal ganglia and thalami Sparing of U-fibers
Metachromatic leukodystrophy (MLD)	Childhood to adulthood	*ARSA*	Abnormal arylsufatase A enzyme activity leading to buildup of sulfatides	Peripheral neuropathy Optic atrophy Psychiatric symptoms	Anterior predominance Sparing of U-fibers

Table e-2: Main types of leukodystrophies that can present in adulthood (Ahmed et al., 2014, Costello et al., 2009)