Some Newly Defined Forms of Leukodystrophies and Leukoencephalopathies

Modified after [1]

Disease	Genetics	Clinical Picture	Magnetic Resonance Imaging Result	Ref.
Mainly hypomyelination				
Hypomyelination and increased *N*-acetylaspartylglutamate		Early-onset nystagmus, seizures, resembling connatal PMD	Almost complete absence of myelin	[2]
PMD-like leukodystrophy with connexin defect	AR, connexin gene	PMD-like (nystagmus, spasticity)	Delayed myelination. Reversal of cortex/white matter signal ratio	[3]
Hypomyelination with atrophy of basal ganglia and cerebellum (HABC)		Onset 2 mo to 3 yr; delayed motor development followed by deterioration, spasticity, rigidity, ataxia, choreoathetosis, dystonia	Diffuse myelin deficiency, increased signal on T2, progressive atrophy putamen, head of caudate, cerebellum	[4, 5]
With formation of cysts				
Megalencephalic leukodystrophy with cysts (MLC)	AR, MLC1 gene	Megalencephaly, slowly progressive spasticity. High incidence in Asian Indians	Extensive white matter changes out of proportion to clinical picture, subcortical cystlike spaces in frontoparietal anterior temporal areas	[6-8]
Leukoencephalopathy with anterior temporal lobe cysts		Delayed initial development, spasticity, normocephaly or microcephaly, no obvious progression	Cystic lesions in anterior temporal lobes, periventricular demyelination	[9, 10]
Leukoencephalopathy, brain calcifications, cysts (LCC)		Onset early childhood, progressive dystonia, spasticity, ataxia	Diffuse leukodystrophy, sparing U fibers, calcifications in basal ganglia, thalamus, subcortical WM, interhemispheric cyst	[11]
Progressive cavitating leukoencephalopathy		Onset between 2 months and 3.5 years, followed by steady or intermittent deterioration	Patchy leukoencephalopathy with cavities, vascular permeability	[12]
Other prominent features				
Leukoecephalopathy with vanishing white matter (VWM)	AR, genes coding for translation initiation factor eIF2B	Episodes of deterioration following infections and minor head traumas, can result in coma	Diffuse cerebral leukoencephalopathy, areas of abnormal white matter have signal intensity close to that of CSF	[13, 14]
VWM-like leukodystrophy, dominant form	AD	Similar to VWM		[15]
Vacuolating glycine leukoencephalopathy	AR	Variant of nonketotic hyperglycinemia. Rapidly progressive neurological deterioration during first year of life. Pulmonary hypertension. High CSF/plasma glycine ratio. Defect of hepatic glycine cleavage system	Progressive extensive cerebral WM changes, sparing U-fibers	[16]
Leukoencephalopathy with brainstem and spinal cord involvement and elevated lactate	Probably AR	Onset in childhood, slowly progressive, variable mental deficits, pyramidal, cerebellar dysfunction	Extensive diffuse or spotty WM abnormalities, selective involvement pyramidal tract, sensory tracts, cerebellar peduncles, MRS shows increased lactate	[5, 17, 18]
Leukoencephalopathy with hydrocephalus	AD	Macrocephaly, nystagmus, spasticity, nonprogressive	Obstructive hydrocphalus caused by cerebellar enlargement, abnormal cerebellar WM, progresses to atrophy	[19]
Peroxisomal straight-chain acyl-CoA oxidase deficiency		Cranial dysmorphy, developmental regression in later infancy	Mostly cerebellar WM involved	[20]
Adult-onset autosomal dominant leukodystrophy	AD, Laminin B1 gene	Similar to chronic progressive multiple sclerosis		[21, 22]

AD, autosomal dominant; AR, autosomal recessive; MRS, magnetic resonance spectroscopy; PMD, Pelizaeus-Merzbacher disease; WM, white matter.

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