

Some Newly Defined Forms of Leukodystrophies and Leukoencephalopathies

Modified after [1]

| Disease | Genetics | Clinical Picture | Magnetic Resonance Imaging Result | Ref. |
|--|--|---|--|-------------|
| <i>Mainly hypomyelination</i> | | | | |
| 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] |
| <i>With formation of cysts</i> | | | | |
| 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] |
| <i>Other prominent features</i> | | | | |
| Leukoencephalopathy 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 hydrocephalus caused by cerebellar enlargement, abnormal cerebellar WM, progresses to atrophy | [19] |
| Peroxisomal straight-chain acyl-CoA oxidase deficiency | | Cranial dysmorphism, 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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