Table e-1. Common Infantile and Pediatric Leukodystrophies

	Pathophysiology	Diagnosis	Clinical manifestations
Krabbe disease* (globoid cell leukodystrophy)[e1]	Lysosomal storage disorder: Deficiency of the enzyme galactocerebrosidase	Autosomal recessive, biallelic variants in *GALC* gene	Irritability, limb spasticity, truncal hypotonia, absent reflexes, microcephaly
Alexander disease[e2]*	Dysmyelinating disorder with Rosenthal fibers within astrocytes	Autosomal dominant, de novo variants in *GFAP* gene (glial fibrillary acidic protein)	Megalencephaly, psychomotor regression; typically young school age but infantile forms described
Metachromatic leukodystrophy[e3]*	Lysosomal storage disorder: Deficiency of arylsulfatase A	Autosomal recessive, biallelic variants in *ARSA* gene; also detected by low enzyme activity or elevated urine sulfatides	Late infantile form with progressive gait problems (14-16 months)
Pelizaeus-Merzbacher disease[e4]*	Hypomyelinating disorder with axonal degeneration	X-linked pathogenic variant in *PLP1* gene**	Pendular nystagmus, head tremor, hypotonia and motor delays progressing to spasticity and ataxia, optic atrophy, seizures
X-linked Adrenoleukodustrophy[e5]*	Peroxisomal disorder: Abnormal function of protein within the peroxisomal membrane.	X-linked pathogenic variant in *ABCD1* gene**; now included on NBS for many states detected by elevated very long chain fatty acids	Boys (4-8 years of age) presenting with behavior problems and regression
Canavan disease[e6]*	Spongiform degeneration of the brain: Deficiency of aspartoacylase leading to increased *N*-acetylaspartic acid (NAA) causing demyelination	Autosomal recessive pathogenic variants in the *ASPA* gene; also detected by elevated NAA on MR spectroscopy or in urine	Normal development until 3-5 months of age, followed by lethargy, hypotonia, optic atrophy that progresses to spasticity, feeding difficulties, and seizures

*Listed in American Board of Psychiatry and Neurology (ABPN) Certification Examination Content Specifications

**X-linked disorders would be less likely in female patients

eReferences

e1. Orsini JJ, Escolar ML, Wasserstein MP, Caggana M. *Krabbe Disease*.; 2018.
e2. Srivastava S, Naidu S. *Alexander Disease*. University of Washington, Seattle; 2015.
e3. Gomez-Ospina N. *Arylsulfatase A Deficiency*. University of Washington, Seattle; 2017.
e4. Hobson GM, Kamholz J. *PLP1-Related Disorders*. University of Washington, Seattle; 2013.
e5. Raymond G V, Moser AB, Fatemi A. X-Linked Adrenoleukodystrophy. GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1315/. Published February 15, 2018. Accessed June 26, 2019.
e6. Matalon R, Delgado L, Michals-Matalon K. *Canavan Disease*. University of Washington, Seattle; 2018.