**Supplementary table 2: Comparison of clinical features between adult-onset and childhood-onset vanishing white matter disease from previous studies**

|  |  |  |  |
| --- | --- | --- | --- |
| **Author/year/country** | **Adult-onset** | **Childhood-onset** | **Remarks** |
| **Fogli et al., 2004,1 France** | **n=2**  **CF: Both had only motor manifestations**  **Genes: *eIF2B5*** | **n=81**  **CF: motor manifestations (n=76), episodic worsening (n=34), cognitive and behavioral features (n=4), headache (n=1)**  **Genes: *eIF2B2*, *eIF2B3*, *eIF2B4*, *eIF2B5*** | **Risk of rapid disease evolution and death was higher in patients with younger age at onset** |
| **Ohlenbusch et al.,2 2005, Germany** | **n=1**  **CF: motor signs, cognitive signs**  **Genes: *eIF2B2*** | **n=14**  **CF: motor signs (n=11), cognitive signs (n=4), episodic worsening (n=9)**  **Genes: *eIF2B1*, *eIF2B2*, *eIF2B3*, *eIF2B4*, *eIF2B5*** |  |
| **Labauge et al., 2009,3 France** | **n=16**  **CF: Cerebellar ataxia (n=9), cognitive decline (n=8), ovarian failure (n=8), spastic paraplegia or tetraplegia (n=7), seizures (n=7), stress induced worsening (n=6), psychiatric symptoms (n=2), subcortical gait (n=1)**  **Genes: *eIF2B2*, *eIF2B5*** | **-** |  |
| **Robinson et al., 2014,4 Canada** | **n=1**  **CF: migraine, ataxia, hemiparesthesia, encephalopathy, episodic worsening (pregnancy triggered)**  **Genes: *eIF2B3*** | **n=4**  **CF: spasticity (n=4), ataxia (n=4), episodic worsening (n=3), cognitive changes (n=1), headache (n=1)**  **Genes: *eIF2B2*, *eIF2B3*, *eIF2B5*** |  |
| **Turon-Vilas et al., 2014,5 Spain** | **-** | **n=21**  **Spasticity (n=21), ataxia (n=16), seizures (n=9), cognitive impairment (n=12), hemiparesis (n=1), dystonia (n=1), ptosis (n=1), optic atrophy (n=4), macrocephaly (n=3), episodic deterioration (n=21)**  **Genes (n=16): *eIF2B3*, *eIF2B4*, *eIF2B5*** |  |
| **Zhang et al., 2015,6 China** | **-** | **n=34**  **CF: Progressive motor deterioration (n=34), episodic aggravation (n=24), seizures (n=16)**  **Genes: *eIF2B1*, *eIF2B2*, *eIF2B3*, *eIF2B4*, *eIF2B5*** |  |
| **Hamilton et al., 2018,7 multicenter** | **n=38**  **CF: episodic worsening (n=17)**  **Genes: *eIF2B3*, *eIF2B5*** | **n=258**  **CF: episodic worsening (n=195)**  **Genes: *eIF2B2*, *eIF2B3*, *eIF2B5*** | **Age at onset was an important factor determining the disease course, time to loss of ambulation, and mortality.** |
| **Gungor et al., 2020,8 Turkey** | **-** | **n=11**  **CF: Gait disturbance (n=5), seizures (n=2), developmental delay (n=2), speech disturbance (n=1), dystonia (n=1)**  **Genes: *eIF2B1*, *eIF2B3*, *eIF2B4*, *eIF2B5*** |  |
| **Bindu et al., 2020,9 India** | **-** | **n=5**  **CF: episodic regression/ encephalopathy (n=5), seizures (n=5), spasticity & ataxia (n=3)**  **Genes: *eIF2B2*, *eIF2B3*, *eIF2B4*** |  |

‘CF’: clinical features

1Fogli A, Schiffmann R, Bertini E, Ughetto S, Combes P, Eymard-Pierre E, Kaneski CR, Pineda M, Troncoso M, Uziel G, Surtees R, Pugin D, Chaunu MP, Rodriguez D, Boespflug-Tanguy O. The effect of genotype on the natural history of eIF2B-related leukodystrophies. Neurology. 2004 May 11;62(9):1509-17.

2Ohlenbusch A, Henneke M, Brockmann K, Goerg M, Hanefeld F, Kohlschütter A, Gärtner J. Identification of ten novel mutations in patients with eIF2B-related disorders. Hum Mutat. 2005 Apr;25(4):411.

3Labauge P, Horzinski L, Ayrignac X, et al. Natural history of adult-onset eIF2B-related disorders: a multi-centric survey of 16 cases. Brain. 2009;132(Pt 8):2161-2169.

4Robinson MÈ, Rossignol E, Brais B, Rouleau G, Arbour JF, Bernard G. Vanishing white matter disease in French-Canadian patients from Quebec. Pediatr Neurol. 2014 Aug;51(2):225-32.

5Turón-Viñas E, Pineda M, Cusí V, et al. Vanishing white matter disease in a spanish population. J Cent Nerv Syst Dis. 2014;6:59-68.

6Zhang H, Dai L, Chen N, Zang L, Leng X, Du L, Wang J, Jiang Y, Zhang F, Wu X, Wu Y. Fifteen novel EIF2B1-5 mutations identified in Chinese children with leukoencephalopathy with vanishing white matter and a long term follow-up. PLoS One. 2015 Mar 11;10(3):e0118001.

7Hamilton EMC, van der Lei HDW, Vermeulen G, et al. Natural History of Vanishing White Matter. Ann Neurol. 2018;84(2):274-288.

8Güngör G, Güngör O, Çakmaklı S, et al. Vanishing white matter disease with different faces. Childs Nerv Syst. 2020;36(2):353-361.

9Parayil Sankaran B, Nagappa M, Chiplunkar S, Kothari S, Govindaraj P, Sinha S, Taly AB. Leukodystrophies and Genetic Leukoencephalopathies in Children Specified by Exome Sequencing in an Expanded Gene Panel. J Child Neurol. 2020 Jun;35(7):433-441