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Clinical Pictures in Pelizaeus-Merzbacher Disease: A Report of a Case

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Pelizaeus-Merzbacher disease (PMD) is a rare (1.45 in 100,000 live births in Japan[1]) X-linked disease characterized by developmental defects in the myelin sheath formation, which deeply affects the central nervous system. PMD is caused by abnormalities in the proteolipid protein 1 (PLP1) gene, which is responsible for the differentiation and myelination of oligodendrocytes[2]. Clinical findings are hypotonia, nystagmus and delayed development of motor skills, and the prognosis is dismal in later life[3].

Case

A 5-month-old boy was referred to our hospital due to delayed head control and nystagmus. Family history showed no significant hereditary diseases or neuromuscular disorders. He was born at 40 weeks and 6 days of gestation, and weighed 2,910 g. No abnormalities, including hypotonia or congenital nystagmus, were presented on delivery, and no fetal distress or abnormal findings on congenital metabolic-disorder mass screening were indicated. On referral, he showed nodding of the head, eye tracking inability, and hyper-extensiveness of the joints, although he was able to smile spontaneously, babble actively, and respond to sound. He showed no deformities, including abnormality of countenance, abnormal reflexes, or tremor. Laboratory examination results were normal for the lactic acid/pyruvic acid ratio, and tests for metabolism of amino acid, organic acid, sugar, blood gas, urine vanillylmandelic acid, and urine homovanillic acid were also normal. Ophthalmological examination also showed no abnormalities. Magnetic resonance imagining (MRI) of the brain at 7 months of age (**Fig. 1**) showed hypomyelination of the white matter, but there was no progression of the myelination thereafter. Genetic analysis by fluorescence in situ hybridization showed duplication of the PLP1 gene (**Fig. 2**).

Conclusion

Differential diagnosis of hypomyelination includes: 1) PMD, 2) spastic paraplegia type 2 (SPG2), 3) hypomyelination with atrophy of the basal ganglia and cerebrum, 4) 18q- syndrome, 5) 11q- syndrome (Jacobsen syndrome), and 6) hypomyelination with congenital cataracts. MRI findings indicating PMD are: 1) diffuse pattern of hypomyelination, 2) increased signal intensity on T2-weighted or fluid-attenuated inversion recovery (FLAIR) scans in affected white matter regions in the cerebral hemispheres, cerebellum and brainstem, 3) thinning of the corpus callosum, and 4) atrophy of the cerebral hemispheres[4].

Conflict of Interest: The authors declare that they have no conflict of interest.

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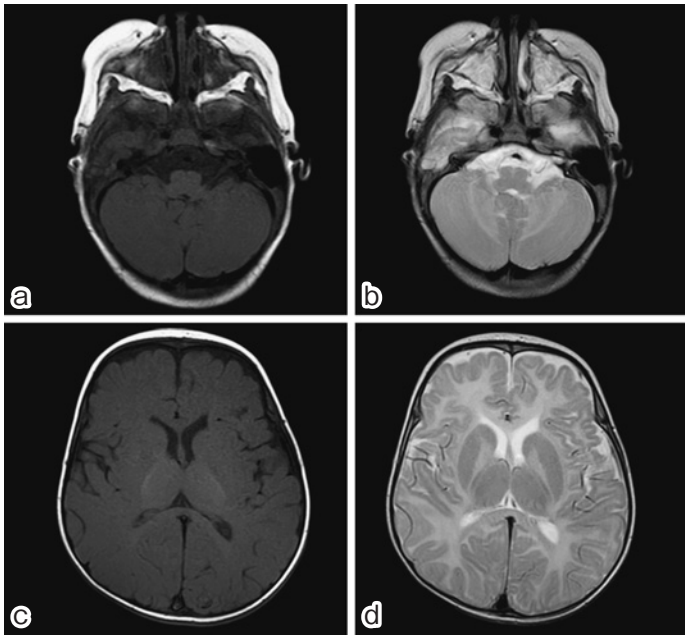

Fig. 1

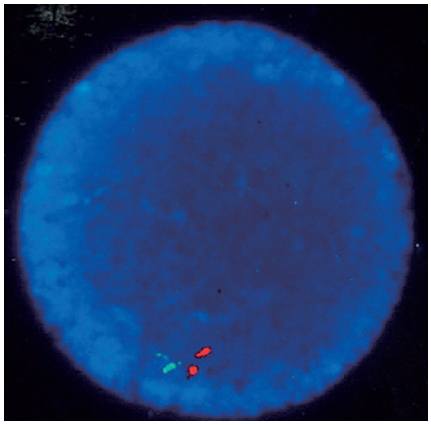

Fig. 2

Fig. 1a–d MRI findings at 7 months of age

Loss of contrast intensity signals on T1-weighted MRI and high intensity signals on T2-weighted MRI suggested hypomyelination.

a T1-weighted MRI findings at 7 months of age show diminished contrast between the cortex and the white matter.

b T2-weighted MRI findings at 7 months of age in the same slice as in Fig. 1a.

The abnormal high intensity signal of T2-weighted MRI indicates hypomyelination.

c T1-weighted MRI findings at 7 months of age

The loss of contrast between the cortex and the white matter intensity signal on T1-weighted MRI suggests hypomyelination.

d T2-weighted MRI findings at 7 months of age in the same slice as in Fig. 1c.

The abnormal high intensity signal of T2-weighted MRI indicates hypomyelination.

Fig. 2 Interphase FISH assay of the patient

Duplication of PLP1 genes was observed. Using BAC clone RP11-832L2, which involves PLP1 gene (red spots), and control BAC clone, CTD-2270O5 (green spot), which is located 2 Mb distant from PLP1 in Xq22.2

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