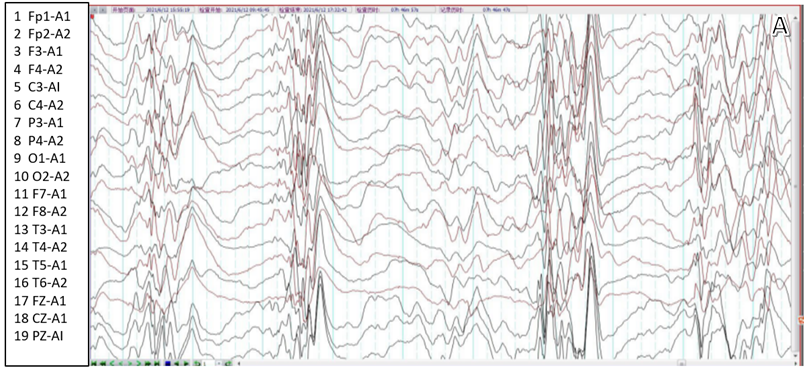
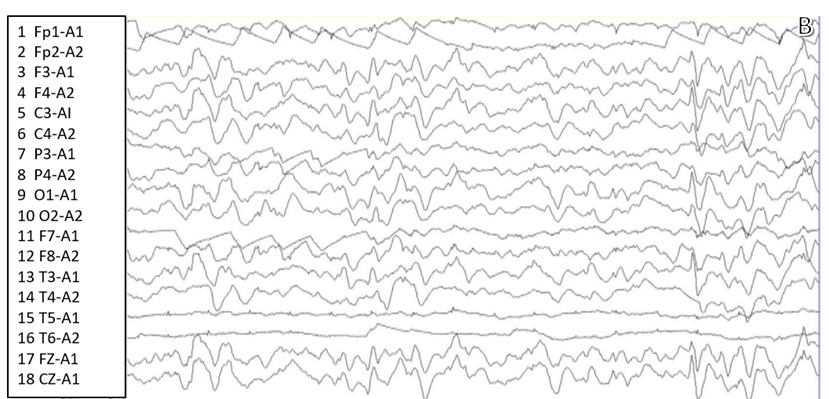
Supplementary data

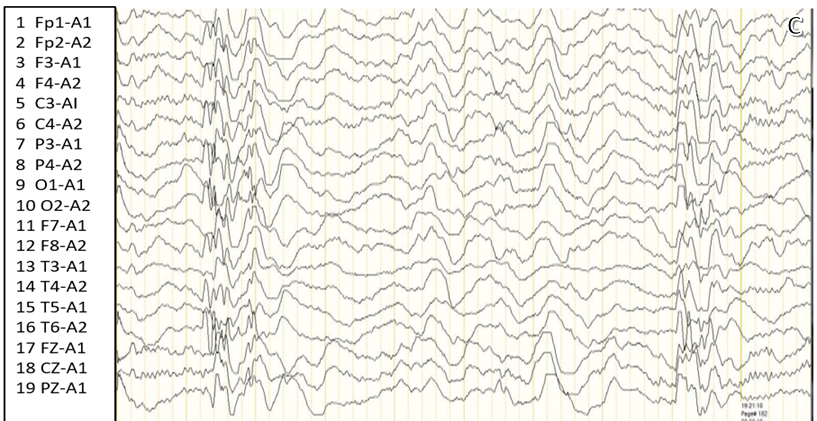
**Table ： the features of 14 patients suffered from West syndrome with MACF1 mutations.**

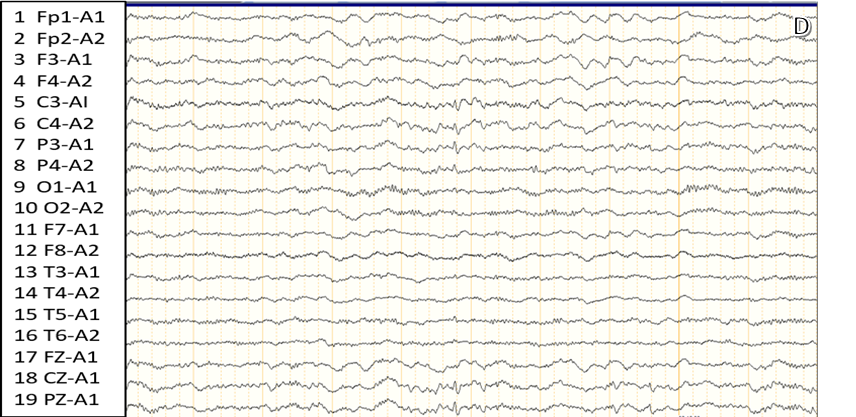
|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Case [Reference] | | Seizure onset | sex | head circumstance (SD) | weight (SD) | height (SD) | brain MR | seizure types | developmental delay | Muscle tension | Protein variants |
| 1 | Dobyns et al.(2018) **[1]** | 5 months | female | 50.5cm(0) | 13.7kg(-1.7) | 105.0cm(-0.5) | lissencephaly with brainstem malformation | ISS | global | poor | p.Cys5177Phe (GENEBANK:NM\_012090.5) |
| 2 | Dobyns et al.(2018) **[1]** | 6 months | male | 53.0cm(+0.7) | 28.0kg(+1.0) | 128.0cm(0) | lissencephaly with brainstem malformation | ISS,LGS | global | poor | p.Cys5177Phe (GENEBANK:NM\_012090.5) |
| 3 | Dobyns et al.(2018) **[1]** | 3 months | female | 45.5cm(-1.0) | 13.5kg(+1.7) | 103.0cm(-1.0) | lissencephaly with brainstem malformation | SE,LGS | global | poor | p.Asp5228Tyr (GENEBANK:NM\_012090.5) |
| 4 | Dobyns et al.(2018) **[1]** | 3 months | male | 47.0cm(+0.5) | 14.0kg(-3.0) | 116.0cm(-1.0) | lissencephaly with brainstem malformation | MYO | global | poor | p.Asp5228Tyr (GENEBANK:NM\_012090.5) |
| 5 | Dobyns et al.(2018) **[1]** | 7 months | female | 49.5cm(-4.0) | 32.5kg(-3.0) | 150.0cm(-2.0) | lissencephaly with brainstem malformation | FSIA,LGS | global | poor | p.Cys5230Phe (GENEBANK:NM\_012090.5) |
| 6 | Dobyns et al.(2018) **[1]** | 5 months | female | 47.7cm(-5.0) | 29.0kg(-4.0) | 137.0cm(-4.0) | lissencephaly with brainstem malformation | FSIA,FTCS,GTCS | global | poor | p.Cys5230Phe (GENEBANK:NM\_012090.5) |
| 7 | Dobyns et al.(2018) **[1]** | 6 months | male | ND | 22.0kg(-0.4) | 50.0cm(-2.0) | lissencephaly with brainstem malformation | probable GTCS | global | poor | p.Cys5230Gly (GENEBANK:NM\_012090.5) |
| 8 | Dobyns et al.(2018) **[1]** | 5 years | female | 47.2cm(-0.4) | 10.0kg(-1.6) | 82.5cm(-1.6) | lissencephaly with brainstem malformation | MYO,GTCS | global | normal | **\***deletion |
| 9 | Dobyns et al.(2018) **[1]** | 4 years,3 months | female | 51.3cm(0) | 20.4kg(+0.7) | 107.9cm(-0.1) | lissencephaly with brainstem malformation | FSIA,GTCS | mild | normal | p.Gly4706Arg (GENEBANK:NM\_012090.5) |
| 10 | Bölsterli et al.(2021) **[2]** | < 1 year | female | ND | ND | ND | pachygyria with brainstem malformation | ISS | global | ND | p.Asp5228Tyr (GENEBANK:ND) |
| 11 | Lulu Kang et al.(2020) **[3]** | 1 year | male | ND | ND | ND | white matter dysplasia | ND | global | poor | p.Thr506Ile&p.Ile3885Thr (GENEBANK:ND) |
| 12 | Cox et al.(2019) **[4]** | ND | female | ND | ND | ND | ND | ISS | ND | ND | p.Rrg4344Gln&p.Val3535Phe (GENEBANK:ND) |
| 13 | Cox et al.(2019) **[4]** | ND | female | ND | ND | ND | ND | ISS | ND | ND | p.Ala3264Ser&p.Phe5885Leu (GENEBANK:ND) |
| 14 | Present patient | 5 months | male | 43.0cm(-0.8) | 8.5kg(+0.2) | 66.0cm(-1.4) | pachygyria and lissencephaly | ISS | moderate | normal | p.Met5089Thr (GENEBANK:NM\_012090.5) |

FSIA, focal seizure with impaired awareness; FTCS, focal tonic-clonic seizure; GT, gastrostomy tube; GTCS, generalized tonic-clonic seizure; ISS, infantile spasm; LGS, Lennox-Gastaut epilepsy syndrome with atonic, tonic, tonic-clonic, and myoclonic seizures; MYO, myoclonic seizure; ND, no data available; SD, standard deviation;**\***Deletion of exons 58–89 (p.Ala3540\_Arg5192; GenBank: NM\_012090.5)









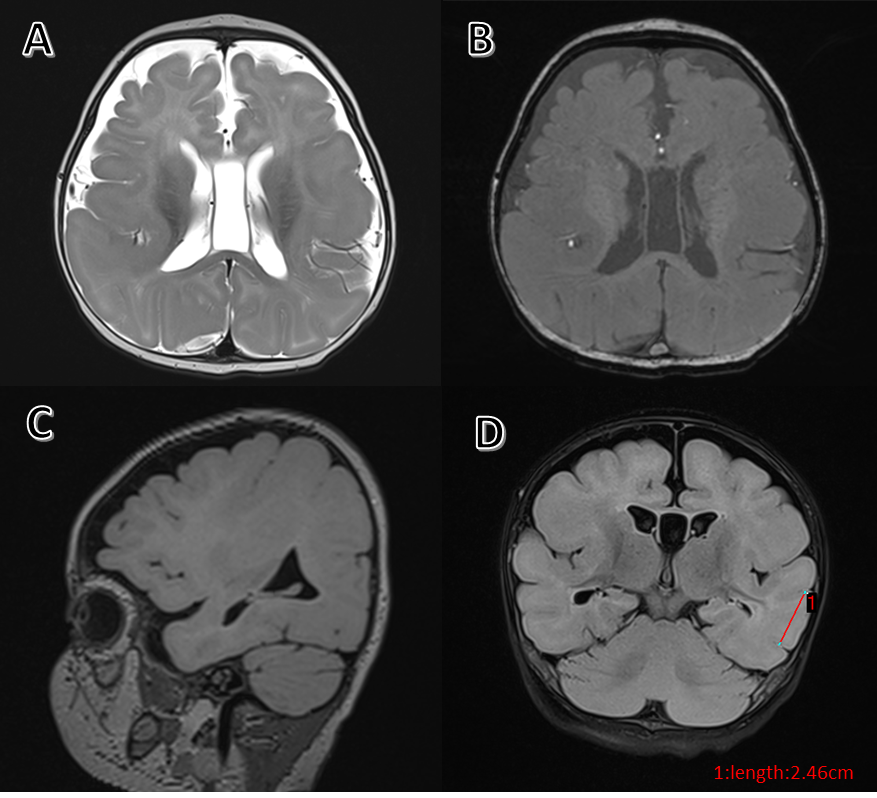
**Fig.1.** Video-electroencephalogram ﬁndings.

***Panel A*** Hypsarrhythmia was observed in the whole brain area with increased slow background waves in waking and sleeping periods.

***Panel B*** Re-examination of VEEG showed scattered spikes and slow waves of low-medium amplitude in the whole brain area at both periods of waking and sleeping. No obvious hypsarrhythmia was found.

***Panel C*** Hypsarrhythmia recurred in the whole brain area at both periods of waking and sleeping.

***Panel D*** After adding Vigabatrin, no obvious epileptiform wave was found in VEEG during the waking period. Few low-medium amplitude sharp waves were scattered in bilateral central and parietal areas during sleep.



**Fig.2.** ***Panels A–D***: Magnetic Resonance Imaging scans. (A) Axial T2-weighted imaging; (B) Axial T1-weighted imaging; (C) Sagittal T2 dark-fluid imaging; (D) Coronal T2-weighted imaging. The MRI scans revealed pachygyria and lissencephaly: posterior > anterior gradient.

**References**

[1] Dobyns, W.B., et al., *MACF1 Mutations Encoding Highly Conserved Zinc-Binding Residues of the GAR Domain Cause Defects in Neuronal Migration and Axon Guidance.* Am J Hum Genet, 2018. **103**(6): p. 1009-1021.

[2] Bolsterli, B.K., et al., *Lissencephaly with Brainstem Hypoplasia and Dysplasia: Think MACF1.* Neuropediatrics, 2021. **52**(3): p. 227.

[3] Kang, L., et al., *Mutations of MACF1, Encoding Microtubule-Actin Crosslinking-Factor 1, Cause Spectraplakinopathy.* Front Neurol, 2019. **10**: p. 1335.

[4] Cox, A.J., et al., *In trans variant calling reveals enrichment for compound heterozygous variants in genes involved in neuronal development and growth.* Genet Res (Camb), 2019. **101**: p. e8.

[5] Ka, M., J.J. Moffat, and W.Y. Kim, *MACF1 Controls Migration and Positioning of Cortical GABAergic Interneurons in Mice.* Cereb Cortex, 2017. **27**(12): p. 5525-5538.