|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | P1  Siekierska et al. 2016 (2) | P2  Siekierska e al. 2016 (2) | P1  Al-Mehmadi et al. 2016 (3) | P2  Al-Mehmadi et al. 2016 (3) | P3  Al-Mehmadi et al. 2016 (3) | P1  Guella et al. 2016 (6) | P2  Guella et al. 2016 (6) | P1  Shi et al. 2017 (7) | Our patient |
| Genetic alteration | *FGF12,*  p.R52H, de novo | *FGF12,*  p.R52H, de novo | *FGF12,*  p.R52H, de novo | *FGF12,*  p.R52H, de novo | *FGF12,*  p.R52H, de novo | *FGF12,*  p.R52H, de novo | *FGF12,*  p.R52H, de novo | duplication involving exons 1-4 of *FGF12* gene, de novo | duplication involving exons 1-4 of *FGF12* gene, de novo |
| Current age and sex | Died age 7 years, female | Died age 3.5 years, male | 3 years, male | 16 years, female (DDD patient 251978) | 18 years, female | 11 months, female | 15 years, female | 8 years, male | 7 years, female |
| Age at first seizure | 2 weeks | 4weeks | 2 days | 6 weeks | 2 days | 3 days | 2 days | 3 years (viral infection) | 4years |
| Status epilepticus | Frequent | Frequent | Frequent | Frequent | Frequent | Not reported | Not reported | Not reported | NCSE at age 6 and 7 years. |
| Seizure type | Tonic seizures | Tonic seizures | GTC; right facial twitching | Myoclonic; GTC; partial motor seizures, lip-smacking, left facial twitching | Partial motor seizures with retained consciousness; left versive seizures followed by GTC | Tonic and focal seizures | Tonic seizures, generalized stiffening evolving to intermittent stiffening and twitching of the limbs. At age 4 years: focal seizures with impaired awareness, possibly evolving to bilateral tonic-clonic seizures. | Tonic clonic, brief tonic with vocalisation, complex partial seizures with repeated blinking | Generalized tonic and tonic-clonic seizures. Before hospital admission at the age of 7 years up to 6 times per day. |
| Interictal EEG findings | High-voltage slow activity with multifocal epileptiform discharges | High-voltage slow activity with multifocal epileptiform discharges | High-voltage slow activity with multifocal epileptiform discharges | Slow background with bilateral, right more than left, epileptiform discharges | Slow background with bilateral, right more than left, epileptiform discharges | Multifocal spikes, EEG at 10 m: normal | Mild background slowing and left frontotemporal spikes. | Not reported | Slow background with multifocal epileptic discharges |
| Ictal EEG findings | Generalized high-voltage spike, sharp wave and spike waves followed by long suppression of background |  | Onset of high-amplitude 1.5-2 Hz rhythmic activity over right posterior head region with secondary generalization |  |  | Left and right frontal seizures occurring from sleep | Suppression of the background and multifocal spikes | Severe suppression of background activity with paroxysmal bursts | Severe suppression of background activity with paroxysmal bursts during NCSE |
| Developmental delay/intellectual disability | Severe psychomotor retardation, nonverbal | Severe psychomotor retardation | Severe global developmental delay, nonverbal | Severe global developmental delay and ID, single words | Moderate ID, possible autism spectrum disorder | Normal development at age of 11 m | Developmental delay with 1 year. Regression at times of increased seizure frequency, moderate ID and autism at age of 15 years | Normal development until 3 years of age.  Regression with begin of seizures, profound ID | Normal development until 4 years of age.  Stagnation since onset of seizures. Transient loss of speech, ambulation, and tube feeding following NCSE. Severe ID |
| Cerebellar involvement | Cerebellar atrophy, ataxia | Cerebellar atrophy, ataxia | To date uninvolved | Episodic cerebellar ataxia from age 7 years, cerebellar atrophy on MRI from age 8 years | Mild cerebellar atrophy appearing in adolescence | none | none | Mild cerebellar atrophy, ataxia | Transient ataxia following NCSE |
| Neurologic examination/ additional abnormalities | Hypotonia, microcephaly, cerebral visual impairment | Hypotonia, microcephaly, poor visual contact | Diffuse hypotonia with head lag, cortical visual impairment | Not reported | Normal tone, slightly hyperreflexic, heel cord tightness with spastic circumductive gait | Mild hypotonia, normal head circumference (85th percentile) | Normal head circumference | Not reported | Normal head circumference, normal gait, motor apraxia, hypacusis, poor visual contact |
| Concomitant morbidities | Feeding difficulties | Feeding difficulties | Constipation and vomiting; feeding difficulties that necessitate tube feeding | Severe chronic constipation | Signs of autonomic dysfunction: hypohidrosis, reduced lacrimation; chronic constipation | Not reported | Not reported | Tube feeding and sleeping disorders after severe seizures | Transient tube feeding and sleeping disorders after NCSE |
| MRI findings | Cerebellar atrophy at age 6 years | Cerebellar atrophy at age 3 years | Cortical atrophy between 2 months and 2 years | Cerebellar atrophy at age 8 years | Bilateral mesial temporal sclerosis, more marked on the right; prominence of cerebellar folia | 4 days: normal | 2weeks and 2 years: normal (incidental finding: Chiari I malformation) | Mild cerebral and cerebellar atrophy at age 8 years | No abnormalities at age 7 years |
| Therapies | AED regimen included phenytoin | AED regimen included phenytoin | Levetiracetam, phenobarbital, ketogenic diet | Phenytoin, perampanel, VNS | Phenytoin, pregabalin, perampanel, VNS | Phenytoin and topiramate on day 20 (reduction to 1-3 seizures/month) + carbamazepine at week 6 (seizure free since 5 months of age) | Rufinamide at age 8 years added to lamotrigine | Phenytoin (supression of seizures but still cognitive decline) | Seizure free interval (6months) under levetiracetam +phenytoin (discontinued because of potential side effects) |

Table e-1: adapted from Al-Mehmadi et al. 2016 (3)

Comparison of the phenotype of patients with p.R52H point mutation and exon 1-4 tandem duplication affecting *FGF12.*

Abbreviations: AED (antiepileptic drug), GTC (generalized tonic-clonic), NCSE (non-convulsive status epilepticus), VNS (vagal nerve stimulation), DDD (Deciphering Developmental Disorders), *FGF12* p.R52H (NM\_021032, [GRCh37] 192053223C>T, p.R114H in A-isoform, p.R52H in B-isoform)