Table e-1. Phenotypes of patients with diagnostic variants.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Gene | Sex | Age of onset | Age at last exam | Ataxia | Intellectual disability | Seizures | Spasticity | Peripheral neuropathy | Abnormality of eye movements | First signs and symptoms | Other signs and symptoms | Abnormality of the brain on MRI (age imaged) | Disease, phenotype MIM number if applicable | Management possibilities |
| P19 | *ATP1A3* | M | Infantile | 27 y | + | - | - | - | - | - | hypotonia and ataxia-athetosis following febrile infection | ataxia worsens with infections, hypotonia, areflexia, pes cavus, athetosis, intermittent Babinski sign, hearing aid at the age of 1 | - (8 y) | ATP1A3-related disease |  |
| P18 | *ATP1A3* | M | Infantile | 20 y | + | - | + | - | - | - | seizure, hypotonia and ataxia following febrile infection | ataxia worsens with infections, reduced tendon reflexes, hypotonia, elevated hepatic transaminase | - (12 y) | ATP1A3-related disease |  |
| P4 | *BCSL1* | M | Neonatal | 10 y | + | + | + | - | - | - | hypoglycemia, poor weight gain | neonatal elevated hepatic transaminase, elevated lactate, microcephaly, areflexia, sensorineural hearing loss | small volume of thalami (7 y) | Leigh syndrome, BCS1L, #256000 |  |
| P17 | *CACNA1A* | M | Infantile | 5 y | + | - | + | - | - | - | motor delay |  | - (2 y) | CACNA1A-related slowly progressive ataxia | Treatment trial with acetazolamide or 4-aminopyridine. Most evidence concerning treatment is for episodic ataxia 2, but benefit from acetazolamide in the chronic presentation has also been reported e1 |
| P20 | *CASK* | F | Infantile | 5 y | + | + | - | - | - | strabismus | deceleration of head growth | hypotonia, motor delay, speech delay, abnormal facial shape | pontocerebellar hypoplasia (4 y) | Mental retardation and microcephaly with pontine and cerebellar hypoplasia, #300749 |  |
| P13 | *CLN5* | M | Childhood | 10 y | + | + | + | - | - | - | visual impairment | developmental regression (cognitive decline), chorioretinal degeneration | cerebellar atrophy (7 y) | Neuronal ceroid lipofuscinosis-5, #256731 |  |
| P2 | *COQ8A* | M | Childhood | 25 y | + | - | - | - | - | nystagmus, abnormality of saccadic eye movements | poor gross motor coordination |  | cerebellar atrophy (12 y) | Primary coenzyme Q10 deficiency-4, ATX‐ADCK3, #612016 | Treatment trial with CoQ10. The effect of CoQ10 supplementation in COQ10D4 is inconsistente2 |
| P21 | *EBF3* | F | Infantile | 5 y | + | - | - | - | - | - | motor delay | hypotonia | cerebellar dysplasia (2 y) | Hypotonia, ataxia, and delayed development syndrome, #617330 |  |
| P9 | *EBF3* | F | Infantile | 12 y | + | - | - | - | - | strabismus | asymmetrical movement of upper limbs | hypotonia | cerebellar atrophy/hypoplasia (10 y) | Hypotonia, ataxia, and delayed development syndrome, #617330 |  |
| P8 | *EBF3* | F | Infantile | 4 y | + | - | - | + | - | strabismus | hypotonia | pes planus | - (4 y) | Hypotonia, ataxia, and delayed development syndrome, #617330 |  |
| P10 | *EBF3* | F | Childhood | 9 y | + | - | - | - | - | strabismus | motor delay |  | - (5 y) | Hypotonia, ataxia, and delayed development syndrome, #617330 |  |
| P7 | *GPAA1* | M | Infantile | 32 y | + | + | + | - | - | nystagmus, abducens palsy | seizure hypotonia | optic atrophy | cerebellar and brainstem atrophy (31 y) | Glycosylphosphatidylinositol biosynthesis defect-15, #617810 | Treatment trial with vitamin B6e3 |
| P3 | *HIBCH* | M | Childhood | 10 y | + | - | - | - | - | - | language delay | episodic ataxia, dystonia and weakness | vermis atrophy, basal ganglia abnormality (T2 hyperintensity and restricted diffusion in the globus pallidus) (9 y) | 3-hydroxyisobutryl-CoA hydrolase deficiency, HIBCH, #250620 | Treatment trial with valine restriction, vitamin/cofactor supplementation?e4 |
| P6 | *ITPR1* | F | Congenital | 3 y | + | - | - | - | - | nystagmus | aniridia | aniridia, intestinal malrotation and volvulus | cerebellar atrophy (2 y) | Gillespie syndrome, #206700 |  |
| P5 | *ITPR1* | M | Infantile | 13 y | + | + | - | - | - | nystagmus, strabismus | nystagmus | mild hepatic steatosis | cerebellar atrophy (9 y) | Spinocerebellar ataxia-29, #117360 |  |
| P14 | *NKX2-1* | M | Infantile | 19 y | + | - | - | - | - | - | motor delay | choreoathetosis, hypotonia | -, (8 y) | Benign hereditary chorea, CHOR-NKX2-1, #118700 | Screening for hypothyroidism and pulmonary alterations |
| P16 | *PTRH2* | F | Infantile | 4 y | + | + | - | + | + | - | motor delay | microcephaly, hypotonia, hypothyroidism, pancreatic exocrine insufficiency, sensorineural hearing impairment | cerebellar atrophy (2 y) | Infantile-onset multisystem neurologic, endocrine, and pancreatic disease, ATX‐PTRH2, #616263 | Screening for hypothyroidism and insufficiency of the exocrine pancreas |
| P1 | *SLC2A1* | M | Infantile | 2 y | + | - | + | - | - | - | motor delay | hypotonia | - (11 m) | GLUT1 deficiency syndrome - 1, #606777 | Treatment with ketogenic diet |
| P22 | *SLC2A1* | F | Childhood | 22 y | + | + | + | - | - | - | seizure | paroxysmal dyskinesia, developmental regression (cognitive decline) | - (13 y) | GLUT1 deficiency syndrome - 2, #612126 | Treatment with ketogenic diet |
| P15 | *STUB1* | M | Childhood | 18 y | + | - | - | - | - | nystagmus | poor gross motor coordination |  | cerebellar atrophy (12 y) | Autosomal recessive spinocerebellar ataxia-16, ATX‐STUB1, #615768 |  |
| P12 | *TCTN1* | M | Congenital | 2 y | + | + | + | - | - | nystagmus | malformations | hypotonia, hydrocephalus, hypospadias, polydactyly, talipes equinovarus, micrognathia, short palpebral fissure, abnormal shape of the occiput | missing vermis, molar tooth sign, abnormality of the posterior cranial fossa (4 m) | Joubert syndrome-13, TCTN1, #614173 |  |
| P11 | *TPP1* | M | Childhood | 6 y | + | + | + | + | - | - | seizure | severe developmental regression (cognitive decline), dystonia, myoclonus | cerebellar atrophy (3 y) | Neuronal ceroid lipofuscinosis-2, ATX/MYC‐TPP1, #204500 | Treatment with cerliponase alfa; gene therapy trials ongoinge5 |

For some patients, the signs and symptoms did not completely match the phenotypes reported in OMIM but are on the phenotypic continuum. When possible, the International Parkinson and Movement Disorder Society Task Force on Classification and Nomenclature of Genetic Movement Disorders recommended nomenclature is included in the “Disease”-column. In the case of young children or progressive disease, intellectual disability may later be diagnosed. Onset: congenital (at birth), neonatal (birth-28 days), infantile (28 days - 1 year), childhood (1-5 years). MIM number, phenotype entry in Online Mendelian Inheritance in Man (OMIM), https://omim.org/; m, months; MRI, magnetic resonance imaging; y, year(s).