**eTable 1:** Summary of genetic and clinical findings.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Family ID** | **Family history** | **Age of onset** | **Gene** | **Variant** | **Allele frequency** | **HGMD/ dbSNP reference** | **ACMG classification** | **Molecular finding** | **Median motor NCV** | **Skeletal deformities** | **Additional features** |
| **1** | **isolated** | 11-20 years | - | - | - | - | - | Unsolved | 36.9 m/s | pes cavus, scoliosis, hammer toes | - |
| **2** | **isolated** | DMM | - | - | - | - | - | Unsolved | 60 m/s | - | - |
| **3** | **isolated** | 2-10 years | - | - | - | - | - | Unsolved | 3.7 m/s | pes cavus | tremor |
| **4** | **2 affected sibs** | 21-40 years | MME (NM\_000902.3) | homozygous; c.531del; p.Lys177Asnfs\*15 | NP | - | pathogenic | Novel allele in known gene | 44.8 m/s | pes cavus | tremor |
| **5** | **isolated** | 2-10 years | GDAP1 (NM\_018972.2) | homozygous; c.786del; p.Phe263Leufs\*22 | NP | CD023843 | pathogenic | Recurrent mutation | IE | pes cavus, scoliosis | - |
| **6** | **isolated** | 2-10 years | MFN2 (NM\_014874.3) | heterozygous; c.1090C>T; p.Arg364Trp | NP | CM060340 | pathogenic | Recurrent mutation | IE | pes cavus, hammer toes | - |
| **7** | **2 affected cousins** | 2-10 years | SH3TC2 (NM\_024577.3) | homozygous; c.1586G>A; p.Arg529His | 0.0000283 | rs80338923 | likely pathogenic | Novel allele in known gene | 22 m/s | pes cavus, scoliosis | sensory ataxia |
| **8** | **isolated** | 11-20 years | HINT1 (NM\_005340.5) | homozygous; c.99del; p.Phe33Leufs\*22 | NP | - | pathogenic | Novel allele in known gene | 50 m/s | - | neuromyotonia |
| **9** | **isolated** | 2-10 years | GDAP1 (NM\_018972.2) | homozygous; c.174\_176delinsTGTG; p.Pro59Valfs\*4 | NP | CX083408 | pathogenic | Recurrent mutation | IE | pes cavus | tremor, sensory ataxia |
| **10** | **2 affected sibs** | >40 years | - | - | - | - | - | Unsolved | 38,8 m/s | pes cavus, hammer toes | sensory ataxia |
| **11** | **isolated** | at birth | MFN2 (NM\_014874.3) | homozygous; c.271G>T; p.Val91Leu | NP | - | likely pathogenic | Novel allele in known gene | 16,7 m/s | claw hands | - |
| **12** | **isolated** | 2-10 years | GDAP1 (NM\_018972.2) | homozygous; c.786del; p.Phe263Leufs\*22 | NP | CD023843 | pathogenic | Recurrent mutation | 48.1 m/s | pes cavus | - |
| **13** | **3 affected individuals** | 2-10 years | - | - | - | - | - | Unsolved | 55 m/s | pes cavus | - |
| **14** | **isolated** | at birth | EGR2 (NM\_000399.3) | heterozygous; c.1142G>A; p.Arg381His | NP | CM004043 | pathogenic | Recurrent mutation | IE | pes planus | - |
| **15** | **isolated** | at birth | SPG7 (NM\_003119.2) | homozygous; c.454A>G; p.Met152Val | 0.00006721 | rs146186857 | VUS | Novel allele in known gene | 26.6 m/s | pes cavus, scoliosis | tremor |
| **16** | **2 affected sibs** | 20 years | SH3TC2 (NM\_024577.3) | compound heterozygous; c.2642A>G; p.Asn881Ser and c.1586G>A; p.Arg529His | 0.00002123 and 0.00002830 | CM064263 and rs80338923 | likely pathogenic | Recurrent mutation | 32 m/s | pes cavus | - |
| **17** | **4 affected individuals** | 21-40 years | GJB1 (NM\_001097642.2) | heterozygous; c.47A>T; p.His16Leu | NP | CM095432 | pathogenic | Recurrent mutation | 29 m/s | pes cavus | - |
| **18** | **isolated** | 2-10 years | - | - | - | - | - | Unsolved | 19.8 m/s | pes cavus, hammer toes | - |
| **19** | **4 affected individuals** | 11-20 years | - | - | - | - | - | Unsolved | 57.8 m/s | pes cavus | - |
| **20** | **2 affected sibs** | at birth | PRX (NM\_181882.2) | homozygous; c.1102C>T; p.Arg368Ter | NP | CM011005 | pathogenic | Recurrent mutation | IE | pes cavus, scoliosis | tremor, sensory ataxia, hearing loss, cerebellar dysfunction, cataract |
| **21** | **isolated** | DMM | - | - | - | - | - | Unsolved | 16 m/s | pes cavus, hammer toes | - |
| **22** | **2 affected sibs** | 11-20 years | - | - | - | - | - | Unsolved | 19 m/s | pes cavus | tremor |
| **23** | **isolated** | 2-10 years | NDRG1 (NM\_001135242.1) | homozygous; c.237C>A; p.Tyr79Ter | NP | rs199928197 | pathogenic | Novel allele in known gene | 11.7 m/s | pes planus | - |
| **24** | **3 affected sibs** | DMM | FXN (NM\_000144.4) | homozygous; c.493C>T; p.Arg165Cys | NP | rs138034837 | pathogenic | Candidate gene† | IE | scoliosis | nystagmus |
| **25** | **2 affected sibs** | DMM | NEFL (NM\_006158.3) | homozygous; c.54C>A; p.Tyr18Ter | 0.000004363 | - | likely pathogenic | Novel allele in known gene | IE | pes cavus, scoliosis, hammer toes | - |
| **26** | **2 affected sibs** | at birth | GDAP1 (NM\_018972.2) | homozygous; c.786del; p.Phe263Leufs\*22 | NP | CD023843 | pathogenic | Recurrent mutation | IE | scoliosis | vocal cord involvement |
| **27** | **5 affected individuals** | 11-20 years | SH3TC2 (NM\_024577.3) | homozygous; c.1178-1G>A | NP | CS064451 | pathogenic | Recurrent mutation | IE | - | hearing loss |
| **28** | **isolated** | DMM | - | - | - | - | - | Unsolved | 13.3 m/s | pes cavus, hammer toes, kyphoscoliosis | vocal cord involvement, tremor, sensory ataxia |
| **29** | **isolated** | 2-10 years | AP5Z1 (NM\_014855.3) | homozygous; c.1568G>A; p.Arg523His | 0.000038 | rs370116509 | VUS | Novel allele in known gene | 44 m/s | - | mild spasticity |
| **30** | **2 affected sibs** | at birth | GDAP1 (NM\_018972.2) | homozygous; c.112C>T; p.Gln38Ter | NP | - | pathogenic | Novel allele in known gene | N/A | - | - |
| **31** | **isolated** | 2-10 years | C12ORF65 (NM\_152269.4) | homozygous; c.18\_21del; Leu6Phefs\*7 | NP | - | likely pathogenic | Novel allele in known gene | 51.9 m/s | pes cavus, hammer toes | pyramidal signs |
| **32** | **2 affected sibs** | 11-20 years | MFN2 (NM\_014874.3) | heterozygous; c.1085C>T; p.Thr362Met | 0.00003181 | CM062856 | pathogenic | Recurrent mutation | 56 m/s | pes cavus | - |
| **33** | **isolated** | DMM | - | - | - | - | - | Unsolved | 42.2 m/s | pes cavus, hammer toes | sensory ataxia |
| **34** | **3 affected couisins** | 2-10 years | SH3TC2 (NM\_024577.3) | homozygous; c.1894\_1897delinsAAA; p.Glu632Lysfs\*13 | NP | CX117975 | pathogenic | Recurrent mutation | 32.8 m/s | - | - |
| **35** | **isolated** | DMM | - | - | - | - | - | Unsolved | 26.8 m/s | pes cavus, hammer toes | tremor |
| **36** | **2 affected sibs** | 2-10 years | SH3TC2 (NM\_024577.3) | homozygous; c.54dup; p.Lys19Ter | NP | - | pathogenic | Novel allele in known gene | demyelinating | - | - |
| **37** | **isolated** | DMM | SBF2 (NM\_030962.3) | homozygous; c.2549T>C; p.Met850Thr | NP | - | VUS | Novel allele in known gene | 14 m/s | - | tremor |
| **38** | **2 affected sibs** | 2-10 years | - | - | - | - | - | Unsolved | 40.3 m/s | - | - |
| **39** | **isolated** | 2-10 years | SEPTIN11 (NM\_018243.2) | homozygous; c.265dup; p.Glu89Glyfs\*12 | NP | - | GUS | Candidate gene | 47.1 m/s | - | cerebellar ataxia, hypertrophic cardiomyopathy |
| **40** | **isolated** | DMM | PRX (NM\_181882.2) | homozygous; c.3208C>T; p.Arg1070Ter | 0.000007958 | CM044034 | pathogenic | Recurrent mutation | 4 m/s | - | sensory ataxia |
| **41** | **3 affected sibs** | 2-10 years | - | - | - | - | - | Unsolved | 46 m/s | pes cavus | - |
| **42** | **2 affected sibs** | DMM | GDAP1 (NM\_018972.2) | homozygous; c.786del; p.Phe263Leufs\*22 | NP | CD023843 | pathogenic | Recurrent mutation | IE | pes cavus | - |
| **43** | **3 affected individuals** | DMM | MPZ (NM\_000530.6) | heterozygous; c.362A>G; p.Asp121Gly | NP | - | VUS | Novel allele in known gene | 14.7 m/s | scoliosis | - |
| **44** | **2 affected sibs** | 2-10 years | - | - | - | - | - | Unsolved | 5.6 m/s | scoliosis | - |
| **45** | **2 affected sibs** | DMM | SH3TC2 (NM\_024577.3) | homozygous; c.1894\_1897delinsAAA; p.Glu632Lysfs\*13 | NP | CX117975 | pathogenic | Recurrent mutation | 13.3 m/s | scoliosis | - |
| **46** | **isolated** | at birth | SACS (NM\_014363.4) | homozygous; c.2182C>T; p.Arg728Ter | 0.00001597 | CM087685 | pathogenic | Recurrent mutation | 30 m/s | pes cavus, hammer toes | tremor, mild spasticity, pyramidal signs, cerebellar ataxia |
| **47** | **isolated** | 2-10 years | - | - | - | - | - | Unsolved | 54.5 m/s | - | sensory ataxia |
| **48** | **isolated** | 11-20 years | MPV17 (NM\_002437.4) | homozygous; c.122G>A; p.Arg41Gln | 0.00002475 | CM1510714 | pathogenic | Recurrent mutation | 58 m/s | pes cavus | - |
| **49** | **isolated** | 11-20 years | HINT1 (NM\_005340.5) | homozygous; c.368G>A; p.Trp123Ter | NP | CM128652 | pathogenic | Recurrent mutation | 48 m/s | pes cavus | neuromyotonia, intellectual disability |
| **50** | **2 affected sibs** | 2-10 years | GDAP1 (NM\_018972.2) | homozygous; c.458C>T; p.Pro153Leu | 0.00001591 | CM077286 | pathogenic | Recurrent mutation | 46 m/s | pes cavus | - |
| **51** | **10 affected individuals** | 2-10 years | GJB1 (NM\_001097642.2) | hemizygous; c.518G>T; p.Cys173Phe | NP | CM070941 | pathogenic | Recurrent mutation | 36.6 m/s | pes cavus, hammer toes | - |
| **52** | **isolated** | 2-10 years | MFN2 (NM\_014874.3) | heterozygous; c.1090C>T; p.Arg364Trp | NP | CM060340 | pathogenic | Recurrent mutation | IE | pes cavus | - |
| **53** | **isolated** | 2-10 years | MFN2 (NM\_014874.3) | heterozygous; c.310C>T; p.Arg104Trp | NP | CM083543 | pathogenic | Recurrent mutation | IE | pes cavus | - |
| **54** | **2 affected cousins** | 21-40 years | - | - | - | - | - | Unsolved | 29.6 m/s | pes cavus | short stature |
| **55** | **2 other individuals with HSP** | 2-10 years | - | - | - | - | - | Unsolved | 37.3 m/s | - | visual impairment |
| **56** | **isolated** | 2-10 years | - | - | - | - | - | Unsolved | 15.9 m/s | - | - |

†Reported in 24. N/A: not available. IE: inexcitable. DMM: delayed motor milestones. NCV: nerve conduction velocity. NP: not present in databases. VUS: variant of unknown significance. GUS: gene of unknown significance.