A rare case of autosomal recessive spastic paraplegia with learning difficulties, optic atrophy and neuropathy (SPG55).

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Objectives

Hereditary spastic paraplegia are extremely heterogeneous neurodegenerative conditions in clinical and genetic aspects, often misinterpreted due to varied clinical spectrum. Our case presented at young age with nystagmus, unsteadiness of her gait with progression to tip toes walking. Patients had metabolic investigation and brain MRI in keeping with mitochondrial disorder SURF1.

Methods

We report a case of 13-year-old girl, previously fit and well presented at 2-3 years of age with deteriorating vision and developed horizontal nystagmus at 4 years of age.

Thereafter she was noticed to have unsteadiness on her feet with a clinical progression to tiptoe walking by her 7th birthday.

She was a product of consanguineous marriage (distantly related) and there was history of paternal uncle who died at 19 years having suffered from gait abnormality from 7 years of age.

On examination, she had pes caves high stepping gait and in-toeing of gait.

Upper limb examination was normal, however in lower limb examination power was 3/5, in both lower limbs, with particular weakness of dorsiflexion of her ankles with brisk deep tendon reflexes and up- going plantar.

She had vertical and horizontal nystagmus with normal eye movements and no other cranial nerve deficits. There is no other significant family history of note.

Her diagnostic work up showed normal metabolic investigation including variants in a hereditary ataxia panel and a 27 gene Leigh disease panel did not identify pathogenic variants.

She had radiological evidence of optic atrophy with predominantly mid-brain focus of high signal SURF1 mutation considered due to Charcot-Marie-Tooth like symptoms (peripheral neuropathy).Her echocardiography and ECG was reported to be unremarkable. Whole genome sequencing was requested under the neurogenetics team review.

Result

Whole genome sequencing done showed frameshift variant (c.264dupC; p(Ser89LeufsTer14)) in both copies of the MTRFR (C12orf65) gene were consistent with a diagnosis of autosomal recessive spastic paraplegia with optic atrophy and neuropathy, which was also called spastic paraplegia, type 55 (SPG55).

Discussion:

HSP pathology and clinical manifestations slowly progress with higher challenges to diagnose early. In addition to the disease period's difficulty, the proband's genotype, age, and the complicating clinical manifestation aids to HSP severity.

Other features of SPG55 included variable degree of developmental delay and/or learning difficulties, subtle MRI brain scan findings and reduced levels of respiratory complexes I and IV in muscle from affected individuals.

Conclusion:

Mitochondrial DNA for oxidative phosphorylation mitoribosomes (SPG55/C12ORF65) are found at 12q24.31 and these genes mutations are linked with peripheral neuropathies, optic zone atrophy, cognitive disabilities, and pyramidal characteristics .

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