Parkinsonism and Related Disorders 58 (2019) 74–78

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Short communication

Identifying *SYNE1* ataxia and extending the mutational spectrum in Korea

Ji Sun Kim[a,b,1], Ah Reum Kim[c,d,1], Jinyoung Youn[a,b], Chung Lee[c], Nam-Soon Kim[e,f], Woong-Yang Park[c,g], Jong Kyu Park[h], Nayoung K.D. Kim[c], Jin Whan Cho[a,b,*]

[a] Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
[b] Neuroscience Center, Samsung Medical Center, Seoul, South Korea
[c] Samsung Genome Institute, Samsung Medical Center, Seoul, South Korea
[d] Medical Research Institute, School of Medicine, Sungkyunkwan University, Seoul, South Korea
[e] Research Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon, South Korea
[f] Department of Functional Genomics, KRIBB School of Bioscience, Korea University of Science and Technology (UST), Daejeon, South Korea
[g] Department of Molecular Cell Biology, Sungkyunkwan University School of Medicine, Suwon, South Korea
[h] Department of Neurology, Soonchunhyang University Hospital, Soonchunhyang University School of Medicine, Gumi, South Korea

ARTICLE INFO

Keywords:
SYNE1
Ataxia
Next generation sequencing
Whole exome sequencing

ABSTRACT

Introduction: Recent advances in next generation sequencing technologies have uncovered the genetic background of various diseases. The mutations in the *SYNE1* gene was previously identified as a potential cause of pure cerebellar ataxia. Although autosomal recessive ataxias are slightly more frequent than autosomal dominant forms worldwide, autosomal recessive forms are extremely rare in Korea. In this study, we aimed to identify *SYNE1*-associated ataxia by whole exome sequencing in a Korean sample, and to review the prevalence of *SYNE1* in non-French-Canadians.

Methods: Patients with suspected cerebellar ataxia who visited movement disorders clinic from March 2014 to December 2017 were clinically screened. After excluding cases with acquired causes and common genetic causes in Korea, including spinocerebellar ataxia and dentatorubral-pallidoluysian atrophy, 63 undiagnosed subjects were screened for *SYNE1* mutations by next generation sequencing methods.

Results: We identified four novel mutations (one splicing, one truncating, and two missense mutations) distributed throughout the *SYNE1* gene in two patients. The phenotype was mainly pure cerebellar ataxia in both cases. However, axonal neuropathy, mild frontal dysfunction, and autonomic dysfunction were also revealed. The age of disease onset was relatively late and the disease course was only mildly progressive.

Conclusion: Our results indicate that *SYNE1* mutations are not an uncommon cause of recessive ataxia with additional clinical features in the Korean population. The results of this study should alert neurologists to request *SYNE1* testing to aid the diagnosis of undetermined adult-onset ataxia in Korean patients.

1. Introduction

Hereditary cerebellar ataxias are a clinically, pathologically, and etiologically heterogeneous group of disorders. Clinical diagnostic workup is therefore complex and can be challenging. The prevalence of different forms of ataxias varies by geographic region, and ethnicity and region need to be considered in the diagnostic strategy. Although autosomal recessive ataxias are slightly more frequent worldwide than autosomal dominant ataxias, with an estimated prevalence of 5 in 100,000, recessive forms are extremely rare in Korea. For example, Friedreich ataxia (FRDA) is the most prevalent genetic ataxia in Caucasians, but there have been no genetically confirmed reports in the Korean population [1].

Recent advances in next generation sequencing (NGS) technologies have helped to unravel the biological bases of genetic ataxias and uncover new genetic causes. In 2007, synaptic nuclear envelope protein 1 (*SYNE1*) gene was first reported as a cause of pure cerebellar ataxia in patients originating from the Quebec region of Beauce and Bas-St-Laurent, Canada [2]. The condition was termed autosomal recessive cerebellar ataxia type 8 (SCAR8), also referred to as autosomal recessive cerebellar ataxia type 1 (ARCA1) or recessive ataxia of Beauce (MIM 610743). *SYNE1*-related autosomal recessive ataxias have mainly

* Corresponding author. Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50, Irwon-Dong, Gangnam-Gu, Seoul, 135-710, South Korea.
E-mail address: jinwhan.cho@samsung.com (J.W. Cho).
[1] Ji Sun Kim and Ah Reum Kim contributed equally to this work.

https://doi.org/10.1016/j.parkreldis.2018.08.009
Received 3 May 2018; Received in revised form 7 August 2018; Accepted 13 August 2018

been observed in Quebec, Canada. However, recent investigations have identified *SYNE1*-related ataxias in patients originating from Brazil, Japan, Turkey, Saudi Arabia and England [3–6]. In this study, we aimed to identify *SYNE1* ataxia through whole exome sequencing in a Korean sample, and to review reports of *SYNE1* in non-French-Canadians.

2. Materials and methods

2.1. Patients

Patients who visited our Movement Disorders Clinic from March 2014 to December 2017 were clinically screened and examined as having suspected cerebellar ataxia. We performed the following tests to detect acquired ataxias in patients whose progression was acute or subacute: thyroid function, levels of vitamin B12 and E, serology for syphilis and HIV, autoimmune antibodies, tumor markers, paraneoplastic antibodies, and brain magnetic resonance imaging (MRI). Patients were evaluated according to Korean ataxia genetic screening protocols for disorders including spinocerebellar ataxias (SCA1, 2, 3, 6, 7, 8 and 17) and dentatorubral-pallidoluysian atrophy (DRPLA) if they had 1) positive family history compatible with dominant inheritance, 2) young age of onset (age of onset < 30), or 3) additional neurologic clues. More specific genetic tests were performed in selected patients who were suspected as having specific subtypes of genetic ataxic disorder (e.g., patients with polyneuropathy or myopathy, telangiectasia, xanthoma, cognitive decline, oculomotor apraxia, or abnormal findings upon fundus examination). After that, 63 undiagnosed ataxic patients were selected. Consanguineous background was not detected. The existence of similar cases among siblings or family members was observed in 7 patients from 5 families, and 56 patients denied family histories of ataxia. All of the patients were negative upon genetic screening for FRDA. Whenever possible, affected siblings and other family members were also analyzed. Blood samples were obtained for all patients who gave informed consent to take part in the study, which was approved by the Institutional Review Board of Samsung Medical Center, Seoul, Korea. In cases of family members who could not visit the hospital, we sent Oragene kits (DNA self-collection kit, DNAGenotek, Canada) and they returned saliva samples.

2.2. Genetic screening using next-generation sequencing

Genomic DNA was extracted from peripheral blood or saliva samples for each proband and their family, using a QIAamp DNA Mini Kit (Qiagen, Hilden, Germany). Subjects were screened for *SYNE1* mutations by the following next-generation sequencing methods. We used whole exome sequencing by the Samsung Genome Institute (SGI; Samsung Medical Center, Seoul 06351, South Korea), for which the raw data of 63 patients were filtered for nonsynonymous SNV in coding regions and splice site regions with sufficient read depth ($> = 10\times$) and genotype quality ($> = 99$) in the first step. Second, the number of variants was narrowed down according to minor allele frequency (MAF) with the cutoff set at < 1% based on the following population databases: 1000 Genomes Project (1000G, http://www.internationalgenome.org/), Exome Sequencing Project 6500 (ESP6500, http://evs.gs.washington.edu/EVS/), and ExAC (http://exac.broadinstitute.org/). For the remaining variants, we also considered the relationship between allele frequency and ethnicity by reviewing the Korean Reference Genome Database (KRGDB, http://152.99.75.168/KRGDB/menuPages/firstInfo.jsp), Korean Variant Archive (KOVA) [7], and our in-house database containing 192 unrelated Korean control WES. Third, through the examination of inheritance patterns by pedigree analysis, we considered the potential configurations for autosomal recessive or *de novo* mutations in autosomal dominant genes that are associated with known clinical phenotypes. Finally, to identify strong candidates among these variants, we performed direct Sanger sequencing in affected individuals and their parents or unaffected siblings when available to confirm segregation or mutation phase for compound heterozygous or *de novo* mutations. To estimate the potential for pathogenicity among novel variants, we evaluated variants under the ACMG guidelines for germline variants with *in-silico* analysis using SIFT (http://sift.jcvi.org/) and polyphen2 (http://genetics.bwh.harvard.edu/pph2/), evolutionary conservation by examining GERP++ scores in the UCSC genome browser (http://genome.ucsc.edu) of amino acid changes, and splice site prediction using the ESE finder (http://rulai.cshl.edu/cgi-bin/tools/ESE3/esefinder.cgi?process=home) and BDGP (http://www.fruitfly.org/seq_tools/splice.html) tools.

2.3. Review about reports of SYNE1

Literature was obtained using the electronic databases PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) and searched keywords included *SYNE1*. We selected clinical reports of SYNE1 mutation in non-French-Canadians.

3. Results

A total of 63 patients were analyzed and four novel variants were detected in two patients using the in-house basic filtering for WES, as described above.

In Case 1, a splice site variant c.26153+1G > A and a stop gain variant p. Q1741X of *SYNE1* (NM_182961) were detected as final candidates as compound heterozygotes, which were validated by Sanger sequencing. For these variants, we confirmed the phase of the *in-trans* allele using data for two siblings (II-2 and II-3) because their parents were deceased (Fig. 1-A). In Case 2, two missense variants, p. I2995V and p. E5112D, were detected as final causal candidate variants as compound heterozygotes, and were also validated by Sanger sequencing. For these variants, we confirmed the phase of the *in-trans* allele by examining parental data (I-3 and I-7) as the carrier and a sibling (II-4) as the wild type of the genotypes (Fig. 1-B).

For three variants in the coding region, we investigated orthologs by aligning amino acids of *SYNE1* of human to zebrafish. Though these variants were not highly conserved, they were observed in mammals (Fig. 1-C). Additionally, we confirmed that all four variants were in the 'spectrin repeat-spectrin alpha actinin' domain (Fig. 1-D).

3.1. Case I

The index case is a 56-year-old man who visited our clinic at the age of 42 with progressively worsening dysarthria and dysphagia. He had started to slur his speech at age 39 and felt imbalanced while walking. He had no family history of similar symptoms. Neurologic examination revealed subtle limb ataxia and his International Cooperative Ataxia Rating Scale (ICARS) score was 3. His reflexes were normal and there was no clinical or electrophysiologic evidence of neuropathy. Autonomic function tests were normal. Neuropsychological studies showed good attention and normal psychomotor speed, but mild retrieval dysfunction and frontal/executive dysfunction. MRI of the brain revealed global atrophy of the cerebellum (Supplemental Materials). Videonystagmography revealed apogeotropic type nystagmus during the head rolling test. The severity of these symptoms hardly progressed in following years and the patient could still walk independently at his last visit at the age of 56. In his neurological exam at the last visit, we observed subtle limb and gait ataxia. He complained of nocturia, residual urine sensation, and sexual dysfunction.

3.2. Case II

The index case is a 46-year-old man who visited our clinic at the age of 42 with progressive gait imbalance. He first noticed that his body swayed while skating at the age of 39. He complained of signs of

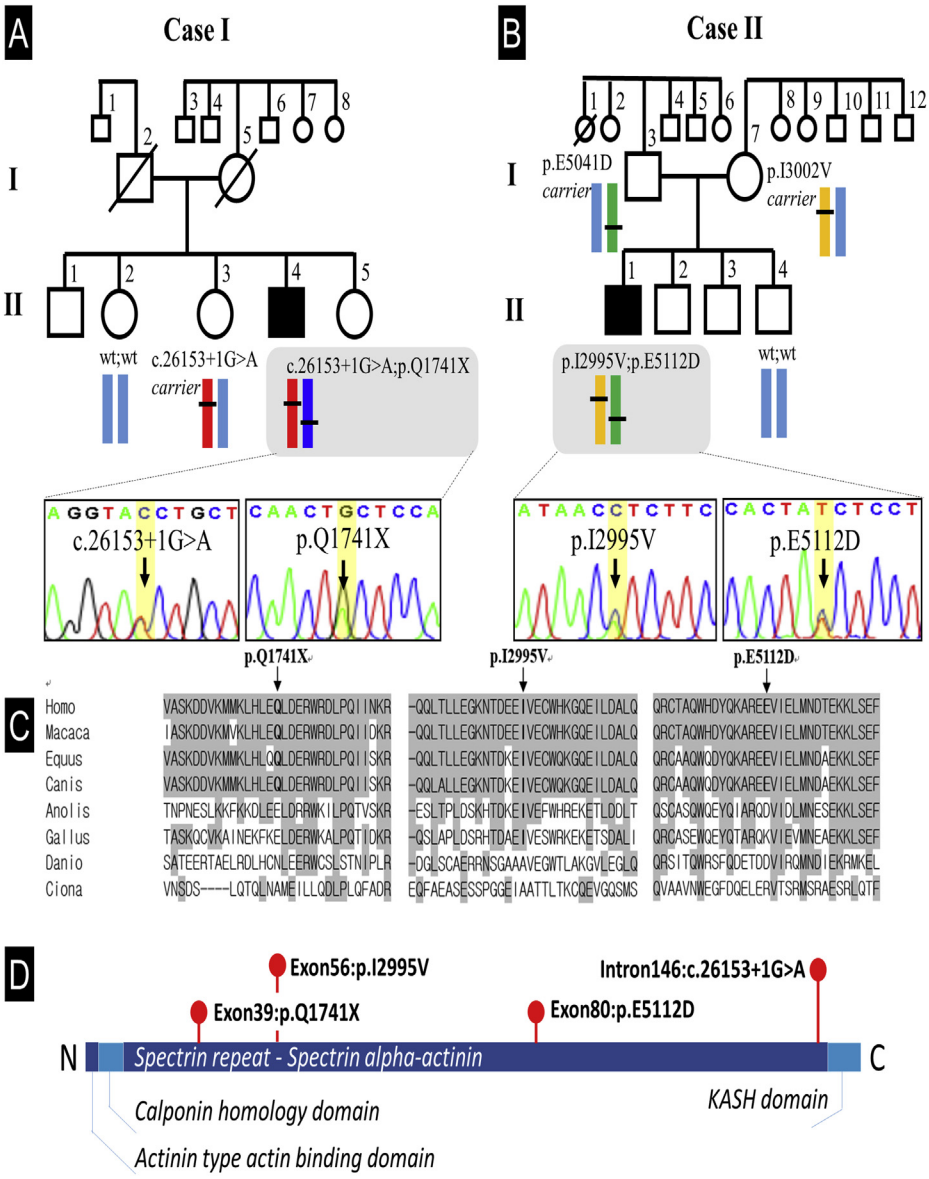

Fig. 1. (A, B) Pedigrees and Sanger sequencing traces of the two SYNE1 families. Both were confirmed with in trans configuration underlying the autosomal recessive inheritance pattern. The penetrance results were identified with each alleles from their parents or siblings, as we mentioned in detail. (C) The diagram for orthologs shows alignments of amino acid sequences from coding regions among various species. One truncating variant and two missense variants are conserved in mammals, but not in nonmammal species, such as zebrafish (Danio rerio). In other words, the GERP scores are lower than those of the essential amino acids, which are highly conserved. Abbreviations: Homo, Homo sapiens (human); Macaca, Macaca mulatta (rhesus macaque); Equus, Equus caballus (horse); Canis, Canis lupus familiaris (dog); Anolis, Anolis carolinensis (green anole); Gallus, Gallus gallus (chicken); Danio, Danio rerio (zebrafish); Ciona, Ciona intestinalis (vase tunicate). (D) Domain for the four variants analyzed in this study. All the variants are in the 'spectrin repeat-spectrin alpha-actinin' domain. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

autonomic dysfunction including urinary frequency, sexual dysfunction, and orthostatic dizziness. Initial neurologic examination revealed dysmetria, dysdiadochokinesia in both hands, saccadic slowing, gaze-evoked nystagmus, and side pocket nystagmus (ICARS score: 12). Deep tendon reflexes were decreased and a nerve conduction study revealed sensory polyneuropathy of axonal type. Autonomic function tests showed mild parasympathetic dysfunction. Brain MRI revealed global atrophy of the cerebellum and 18 F-fludeoxyglucose-positron emission tomography showed marked hypometabolism in the cerebellum (Supplemental Materials). The severity of these symptoms mildly progressed, but he still could walk independently at his last visit at the age of 46. His last neurological exam results were as follows: Mini Mental State Examination score was 27, Montreal Cognitive Assessment score was 24, ICARS was 30, BDI was 17, and Barthel index of activities of daily living was 20.

3.3. Reports of SYNE1 in non-French-Canadians

A total of 164 articles were identified based on the literature search. Among them, 7 articles were clinical reports outside of French-Canadian population. Those are summarized in Table 1. The mean age of onset in previous cases was 25.7 years, and the phenotypes include motor neuron disease, pyramidal sign, cognitive dysfunction, dysphagia, neuropathy, and various oculomotor findings as well as pure ataxia. In our cases, average age of onset was late (39 years of age) and disease progression was extremely slow in comparison with previous reports. Case I revealed mild frontal and autonomic dysfunction, and Case II showed axonal sensory polyneuropathy.

4. Discussion

SYNE1 mutations have been observed mainly in Quebec, Canada, where it is the third most common hereditary ataxia and occurs primarily in cases of relatively pure cerebellar ataxia. However, two recent large cohort studies of non-French-Canadians revealed that *SYNE1* mutations are not uncommon outside of the French-Canadian founder population, and that they commonly present as multisystemic neurodegenerative disease [8,9]. Additional identifications of *SYNE1* mutations in other countries extended the ethnic diversity and phenotypic spectrum underlying *SYNE1*.

We demonstrate that *SYNE1* mutations are not uncommon in the Korean population. In this study, we identified four novel mutations (1 splicing, 1 truncating, and 2 missense mutations) in two patients. To minimize coincidence of this large gene, we first excluded synonymous

Table 1
Previous cases of SYNE1 mutation in non-FC populations.

Cases	Ethnicity	AAO	Mutation	Onset symptom	Additional features	Progression course
Noreau et al. [4]	France	NA	c.10753_10757delCCAAG; p.R3432Vfs*4	Gait ataxia and dysarthria	Pure ataxia	NA
	Brazil	NA	c.4335C > T; p.Q1300X	Gait ataxia and dysarthria	Pure ataxia	NA
Izumi et al. [10]	Japan	6	c.22456_22457insG; p.R7486fs7488X	Running difficulty	Pure ataxia	NA
		36	c.C10789T; p.R3597X	Gait ataxia	Pure ataxia	NA
		27	c.13600_13601insA; p.Y4534fs4539X	Gait ataxia	motor neuron disease	NA
Yucesan et al. [5]	Turkey	26	c.13086delC; p.H4362EfsX2	Dysarthria	upper motor neuron sign	Ambulatory state after 13 years
		23	c.13086delC; p.H4362EfsX2	Dysarthria	upper motor neuron sign	NA
		26	c.13086delC; p.H4362EfsX2	Gait ataxia and dysarthria	Pure ataxia	NA
		21	c.13086delC; p.H4362EfsX2	Gait ataxia and dysarthria	Pure ataxia	NA
Yoshinaga et al. [11]	Japan	22	c.6843del; p.Q2282Sfs*3	Dysarthria	Pure ataxia	SARA 26
		30	c.6843del; p.Q2282Sfs*3	Gait ataxia	Pure ataxia	SARA 35 unable to walk
		30	c.6843del; p.Q2282Sfs*3	Gait ataxia and dysarthria	Pure ataxia	Unable to walk at 40
Algahtani et al. [3]	Saudi	24	c.14091 GNT; p.M4697I,	Gait ataxia	Ataxia mimicking multiple sclerosis	Wheelchair bound in 2 years
		22	c17483CNG; p.T5828R	Gait ataxia	Ataxia mimicking multiple sclerosis	Bedridden in 1 year
Wiethoff et al. [6]	England	40	c.14091 GNT; p.M4697I,	Gait ataxia	mild cognitive dysfunction	Ambulatory state after 25 years
		32	c17483CNG; p.T5828R	Gait ataxia and dysarthria	mild cognitive dysfunction	Ambulatory state after 17 years
	Turkey	18	c.1849G > T; p.E617X,	Gait ataxia and dysarthria	pyramidal sign mild cognitive dysfunction	Bedridden in 16 year
	Sri Lanka	22	c.18431G > A; p.W6144X	Gait ataxia	axonal neuropathy mild cognitive dysfunction	Ambulatory state after 16 years
Gama et al. [12]	Brazil	37	c.1849G > T; p.E617X,	Axial and limb ataxia	dysphagia	NA
		24	c.18431G > A; p.W6144X	Axial ataxia	Pure ataxia	NA
		23	c.19897C > T; p.Q6633X	Axial ataxia	Pure ataxia	NA
		16	c.13429C > T; p.Q4477X	Axial and limb ataxia	lower motor neuron sign saccadic slowing	NA

variants of the *SYNE1* gene from possible candidates by performing a segregation study. We also screened the borders of exons for splicing site variants. Therefore, we were able narrow down the sample to identify final variants for analysis in each family. In Case 1, a stop gain variant p. Q1741X and a splice site variant c.26153 + 1G > A were detected as final candidates as compound heterozygotes. For the nonsense variant, the 1741th residue of glutamine amino acid was terminated by one nucleotide substitution of exon39 in the coding region. This variant lead to a premature stop codon explaining the lack of the KASH domain in Spectrin repeat-containing nuclear envelope protein 1 (nesprin 1). Furthermore, this variant was evaluated as a variant of uncertain significance (VUS) and was considered 'likely pathogenic' based on the ACMG guidelines. For the splice site variants, scores decreased from 0.13 to 0.01 on the BDGP and from 7.69 to −3.3 on the ESE finder. These findings strongly suggest that the variant has pathogenic potential. Additionally, it is evaluated as 'pathogenic' based on the ACMG guidelines. In Case 2, two missense variants of *SYNE1*, p. I2995V and p. E5112D, were detected. Because our predictions of pathogenicity for both variants were 'tolerated' by SITF and considered 'benign' by Polyphen2, it remains uncertain that they are causative variants. We considered that the variations could represent phenotype expansions unlike typical SCAR8 ataxia.

These four variants were absent in non-Korean population databases. However, two missense variants, p. I2995V and p. E5112D, were detected in the Korean population database, KRGDB (http://152.99.75.168/KRGDB/menuPages/intro.jsp). The minor allele frequencies of these variants were 0.001 and 0.0004, respectively. For the three variants in the coding region, conservation of orthologs was confirmed in mammals, but not in protoplasts such as zebrafish (Fig. 1-C).

5. Conclusions

Our results provide the first insights into the identification of *SYNE1* mutations underlying undetermined ataxias in Korean patients. We extended the ethnic, phenotypic, and mutational spectrum of *SYNE1* associated cerebellar ataxia. Our results should alert neurologists to request *SYNE1* testing for cases of undetermined adult-onset ataxia in the Korean population.

Conflicts of interest

No potential conflicts of interest relevant to this article are reported.

Author's roles

1. Research project: A. Conception, B. Organization, C. Execution.
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique.
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

Ji Sun Kim, MD: 1ABC, 2AB and 3AB
Ah Reum Kim, PhD: 1BC, 3AB
Jinyoung Youn, MD: 1 B.
Chung Lee, PhD: 1C.
Woong-Yang Park, MD, PhD: 1AB
Jong Kyu Park, MD: 1BC
Nayoung K. D. Kim, PhD: 1BC
Jin Whan Cho, MD, PhD: 1ABC, 2BC and 3 B.

Financial disclosure

J.S.K., A.R.K, J.Y.Y., C.L. W.Y. P., J.K.P., N.K.K. and J.W.C report no

disclosures.

Acknowledgments

This work was supported by the KRIBB Research Initiative Program and by the Basic Science Research Program of the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (NRF-2014M3C9A2064619). This work was also supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT, Ministry of Science and ICT) (NRF-2017R1A2B4005276). The funding body had no role in study design, data collection, or analysis, decision to publish, or preparation of the manuscript. [10–12].

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.parkreldis.2018.08.009.

References

[1] J.S. Kim, J.W. Cho, Hereditary cerebellar ataxias: a Korean perspective, J Mov Disord 8 (2015) 67–75.
[2] F. Gros-Louis, N. Dupre, P. Dion, M.A. Fox, S. Laurent, S. Verreault, J.R. Sanes, J.P. Bouchard, G.A. Rouleau, Mutations in SYNE1 lead to a newly discovered form of autosomal recessive cerebellar ataxia, Nat. Genet. 39 (2007) 80–85.
[3] H. Algahtani, Y. Marzouk, R. Algahtani, S. Salman, B. Shirah, Autosomal Recessive Cerebellar Ataxia type 1 mimicking multiple sclerosis: a report of two siblings with a novel mutation in SYNE1 gene in a Saudi family, J. Neurol. Sci. 372 (2017) 97–100.
[4] A. Noreau, C.V. Bourassa, A. Szuto, A. Levert, S. Dobrzeniecka, J. Gauthier, S. Forlani, A. Durr, M. Anheim, G. Stevanin, A. Brice, J.P. Bouchard, P.A. Dion, N. Dupre, G.A. Rouleau, SYNE1 mutations in autosomal recessive cerebellar ataxia, JAMA Neurol 70 (2013) 1296-1231.
[5] E. Yucesan, S.A. Ugur Iseri, B. Bilgic, Z. Gormez, B. Bakir Gungor, A. Sarac, O. Ozdemir, M. Sagiroglu, H. Gurvit, H. Hanagasi, U. Ozbek, SYNE1 related cerebellar ataxia presents with variable phenotypes in a consanguineous family from Turkey, Neurol. Sci. 38 (2017) 2203–2207.
[6] S. Wiethoff, J. Hersheson, C. Bettencourt, N.W. Wood, H. Houlden, Heterogeneity in clinical features and disease severity in ataxia-associated SYNE1 mutations, J. Neurol. 263 (2016) 1503–1510.
[7] S. Lee, J. Seo, J. Park, J.Y. Nam, A. Choi, J.S. Ignatius, R.D. Bjornson, J.H. Chae, I.J. Jang, S. Lee, W.Y. Park, D. Baek, M. Choi, Korean Variant Archive (KOVA): a reference database of genetic variations in the Korean population, Sci. Rep. 7 (2017) 4287.
[8] M. Synofzik, K. Smets, M. Mallaret, D. Di Bella, C. Gallenmuller, J. Baets, M. Schulze, S. Magri, E. Sarto, M. Mustafa, T. Deconinck, T. Haack, S. Zuchner, M. Gonzalez, D. Timmann, C. Stendel, T. Klopstock, A. Durr, C. Tranchant, M. Sturm, W. Hamza, L. Nanetti, C. Mariotti, M. Koenig, L. Schols, R. Schule, P. de Jonghe, M. Anheim, F. Taroni, P. Bauer, SYNE1 ataxia is a common recessive ataxia with major non-cerebellar features: a large multi-centre study, Brain 139 (2016) 1378–1393.
[9] I. Mademan, F. Harmuth, I. Giordano, D. Timmann, S. Magri, T. Deconinck, J. Claassen, D. Jokisch, G. Genc, D. Di Bella, S. Romito, R. Schule, S. Zuchner, F. Taroni, T. Klockgether, L. Schols, P. De Jonghe, P. Bauer, E. Consortium, J. Baets, M. Synofzik, Multisystemic SYNE1 ataxia: confirming the high frequency and extending the mutational and phenotypic spectrum, Brain 139 (2016) e46.
[10] Yuishin Izumi, R. Miyamoto, H. Morino, A. Yoshizawa, K. Nishinaka, F. Udaka, M. Kameyama, H. Maruyama, H. Kawakami, Cerebellar ataxia with SYNE1 mutation accompanying motor neuron disease, Neurology 80 (2013) 600–601.
[11] T. Yoshinaga, K. Nakamura, M. Ishikawa, T. Yamaguchi, K. Takano, K. Wakui, T. Kosho, K. Yoshida, Y. Fukushima, Y. Sekijima, A novel frameshift mutation of SYNE1 in a Japanese family with autosomal recessive cerebellar ataxia type 8, Hum Genome Var 4 (2017) 17052.
[12] M.T. Gama, G. Houle, A. Noreau, A. Dionne-Laporte, P.A. Dion, G.A. Rouleau, O.G. Barsottini, J.L. Pedroso, SYNE1 mutations cause autosomal-recessive ataxia with retained reflexes in Brazilian patients, Mov. Disord. 31 (2016) 1754–1756.