ANDES PEDIATRICA
REVISTA CHILENA DE PEDIATRÍA
www.scielo.cl

Andes pediatr. 2026;97(2):282-290
DOI: 10.32641/andespediatr.v97i2.5770

CLINICAL CASE

Charcot-Marie-Tooth disease type 4J and autosomal recessive spinocerebellar ataxia type 20 in a girl: coexistence of two rare disorders

Enfermedad de Charcot-Marie-Tooth tipo 4J y ataxia espinocerebelosa autosómica recesiva tipo 20 en una niña: coexistencia de dos enfermedades poco frecuentes

Daniela Avila-Smirnow[a,b], Javier Martini[c], Aida Bertoli-Avella[c], Tania Otero Rodriguez[c], Guillermo Lay-Son[d,e]

[a]Sección de Neurología Pediátrica, División de Pediatría, Escuela de Medicina, Pontificia Universidad Católica de Chile. Santiago, Chile.
[b]Unidad de Neurología, Servicio de Pediatría, Complejo Asistencial Dr. Sótero del Río. Santiago, Chile.
[c]CENTOGENE GmbH. Rostock, Germany.
[d]Sección de Genética, División de Pediatría, Escuela de Medicina, Pontificia Universidad Católica de Chile. Santiago, Chile.
[e]Unidad de Genética, Servicio de Pediatría, Complejo Asistencial Dr. Sótero del Río. Santiago, Chile.

Received: May 29, 2025; Approved: December 29, 2025

What do we know about the subject matter of this study?

CMT4J is a hereditary demyelinating polyneuropathy that begins in the second decade of life. SCAR20 is a spinocerebellar ataxia that manifests with ataxic gait or absence of ambulation, cognitive impairment, and dysmorphisms that become evident in the third year of life.

What does this study contribute to what is already known?

We present the first reported case of CMT4J and SCAR20 in the Latin American population and the first to report a dual diagnosis. Symptoms began in the first months of life, combining characteristics of both diseases, such as absence of gait and speech, cerebellar atrophy, and polyneuropathy. Phenotypic characterization guided the syndromic diagnosis, and whole-exome sequencing identified associated pathogenic variants in FIG4 and likely pathogenic variants in SNX14. In children of consanguineous parents, the probability of more than one autosomal recessive disease is higher than in the general population; therefore, whole exome sequencing is particularly useful in these cases.

Correspondence:
Daniela Avila-Smirnow
davila@uc.cl

Edited by:
Carolina Heresi Venegas

How to cite this article: Andes pediatr. 2026;97(2):282-290. DOI: 10.32641/andespediatr.v97i2.5770

Abstract

Charcot-Marie-Tooth disease type 4J (CMT4J) and autosomal recessive spinocerebellar ataxia type 20 (SCAR20) are rare autosomal recessive disorders that, to our knowledge, have not been previously reported in the Latin American population. **Objective**: To present the case of a patient of Chilean descent with a dual clinical and genetic diagnosis of CMT4J and SCAR20. **Clinical Case**: The patient was born to healthy consanguineous parents with congenital hypotonia and a swallowing disorder. At 2 years of age, dystonia, areflexia, predominantly distal muscle weakness, and sensorineural hearing loss were observed. Additional tests revealed demyelinating polyneuropathy and cerebellar atrophy. At the last evaluation (6 years), she had a coarse facial appearance, did not speak, could sit independently, but was unable to walk. A whole-exome sequencing (WES) identified a homozygous pathogenic variant in FIG4 and another likely pathogenic variant in SNX14, establishing a dual diagnosis of CMT4J and SCAR20. The patient's symptoms overlapped with those of patients with CMT4J and SCAR20. **Conclusions**: This case underscores the importance of performing adequate phenotypic characterization before ordering WES, especially in cases with nonspecific or combined clinical presentations, in order to obtain an accurate genetic diagnosis and provide personalized medical care.

Keywords:
Charcot-Marie-Tooth Disease;
Ataxia;
Hearing Loss;
Spinocerebellar Ataxia;
Whole-Exome Sequencing

Introduction

Dual diagnoses of two genetic disorders are uncommon. However, the identification of genetic findings responsible for more than one condition in the same patient has increased with the implementation of genome-wide molecular techniques[1,2]. In this context, the coexistence of autosomal recessive diseases may be higher in children of consanguineous parents. Recognizing the presence of more than one genetic disease in the same patient helps to understand cases in which phenotypes are unexpected or overlapping, allowing for better prognostic assessment and adaptation of the medical management for the affected patient.

Hereditary neuropathies can be classified into two main groups: primary and secondary neuropathies. In primary neuropathies, there is usually selective peripheral nerve involved. On the other hand, in secondary neuropathies, a multisystemic disease presents with neuropathy as one of its symptoms. Hereditary sensory-motor neuropathies or Charcot-Marie-Tooth (CMT) disease are primary neuropathies[3]. CMT disease is a heterogeneous group of neuropathies characterized by muscle weakness and atrophy (predominantly distal, hyporeflexia, and pes cavus), with an estimated prevalence of 40/100,000, and has been linked to more than 130 genes[2]. There are several classifications of CMT. One of the best-known classifications divides CMT into autosomal dominant demyelinating CMT (CMT1), axonal CMT (CMT2), autosomal recessive demyelinating CMT (CMT4), intermediate CMT, and X-linked CMT (CMTX). CMT1 is the most common subtype, accounting for 41% of all CMT cases, and is mainly associated with *PMP22* gene duplications. On the other hand, several genes have been involved in CMT4, including *FIG4*, which is associated with type 4J CMT and accounts for less than 0.5% of CMT cases (CMT4J)[2,4-8].

Spinocerebellar ataxia (SCA) is a heterogeneous group of hereditary diseases characterized by cerebellar ataxia and spinal cord neuronal loss. SCA subtypes are numbered according to the order in which they were described. Clinically, SCAs are characterized by a lack of coordination and dysarthria. The prevalence of SCA is 3/100,000, with regional variations[9]. SCAR20 is a rare autosomal recessive SCA characterized by ataxia, dysmorphism, and intellectual disability[10-14].

In this report, we describe the case of a girl born to healthy consanguineous parents with demyelinating neuropathy and central nervous system involvement. Whole exome sequencing (WES) allowed for the dual diagnosis of CMT4J and SCAR20, both of which are autosomal recessive disorders. Patient's mother signed written informed consent, following the institutional guidelines.

The objective is to describe the dual diagnosis of CMT4J and SCAR20, which has not been previously reported in international literature.

Clinical Case

The patient, currently a 6-year-old girl, is the daughter of consanguineous parents, first cousins, from Santiago, Chile. The pregnancy was monitored, and there were no ultrasound abnormalities. The patient was born at term without complications, weighing 3.8 kg and measuring 49 cm in length. Head circumference and Apgar scores were not recorded. No otoacoustic emission testing was performed at birth.

During the first two years of life, the patient was followed at another hospital for a swallowing disorder, with adequate weight gain. She had three episodes of aspiration pneumonia associated with such a swallowing disorder. She required hospitalization for oxygen therapy, but mechanical ventilation was not used. During this time, she presented global psychomotor developmental delay, hypotonic syndrome, chronic lung damage, and oxygen dependence. A gastrostomy was performed using the Nissen technique. During her last hospitalization due to pneumonia at 9 months of age, she was referred for evaluation in the Neurology and Genetics unit at the hospital, where she was being followed at the time. An electroencephalogram was performed and was normal, but no neuroimaging or genetic studies were available at that time.

Figure 1. Patient with CMT4J and SCA20. **A.** At 5 years of age: mild facial dysmorphic features, including broad lateral eyebrows, telecanthus, epicanthus, a thick nasal tip, and thick lips with a tent-shaped open mouth. **B.** At 7 years of age: progression of the previously described dysmorphic features, with a coarser facial appearance. **C.** At 5 years of age: bilateral foot drop, pes cavus, and distal muscle atrophy. **D.** At 7 years of age: the patient achieved independent sitting, her highest motor milestone to date. *CMT4J: Charcot–Marie–Tooth disease type 4J; SCA20: spinocerebellar ataxia type 20.*

At 2 years of age, follow-up was initiated at our neuromuscular clinic due to hypotonia and global psychomotor developmental delay. The initial examination revealed that the patient was able to fix her gaze but did not respond to sounds. Motor examination showed generalized hypotonia, predominantly distal and axial, with proximal strength graded as M4+/5 and distal strength as M4/5 in all four extremities according to the Medical Research Council scale. She lacked head control and had generalized areflexia. Hearing tests revealed severe bilateral sensorineural hearing loss at 2 years of age, which remained in the same range at a follow-up at 4 years of age. Hearing aids were prescribed, but she did not use them consistently, so it was not possible to assess their effectiveness. The patient developed persistent hypotonia and hyporeflexia, and choreoathetotic movements were observed during follow-up (Figure 1).

Complete blood count, blood ammonia, blood lactate, liver function tests, renal function tests, and total creatine kinase were performed and were normal. A peripheral electrophysiological study was performed at 2 years of age, revealing signs of hereditary demyelinating polyneuropathy. Cerebral MRI revealed subtle signal alteration in the bilateral periventricular and deep frontoparietal white matter on T2/FLAIR sequences, with a nonspecific appearance, as well as atrophic changes in the superior aspect of both cerebellar hemispheres and the vermis, with widening of the interfolial spaces (Figure 2). Based on these findings, a white matter disease with central and peripheral demyelinating involvement was initially suspected. Electrophysiological tests were repeated at 4 years of age, confirming these findings and showing that they remained stable compared to the previous evaluation.

Given the clinical phenotype, which includes intellectual disability, polyneuropathy, sensorineural hearing loss, and choreoathetosis, a diagnostic entity involving the central and peripheral nervous systems, including the *FITM2*, *AP1S1*, and *AP1B1* genes was initially suspected. These genes were not covered by the commercial genetic panels available at

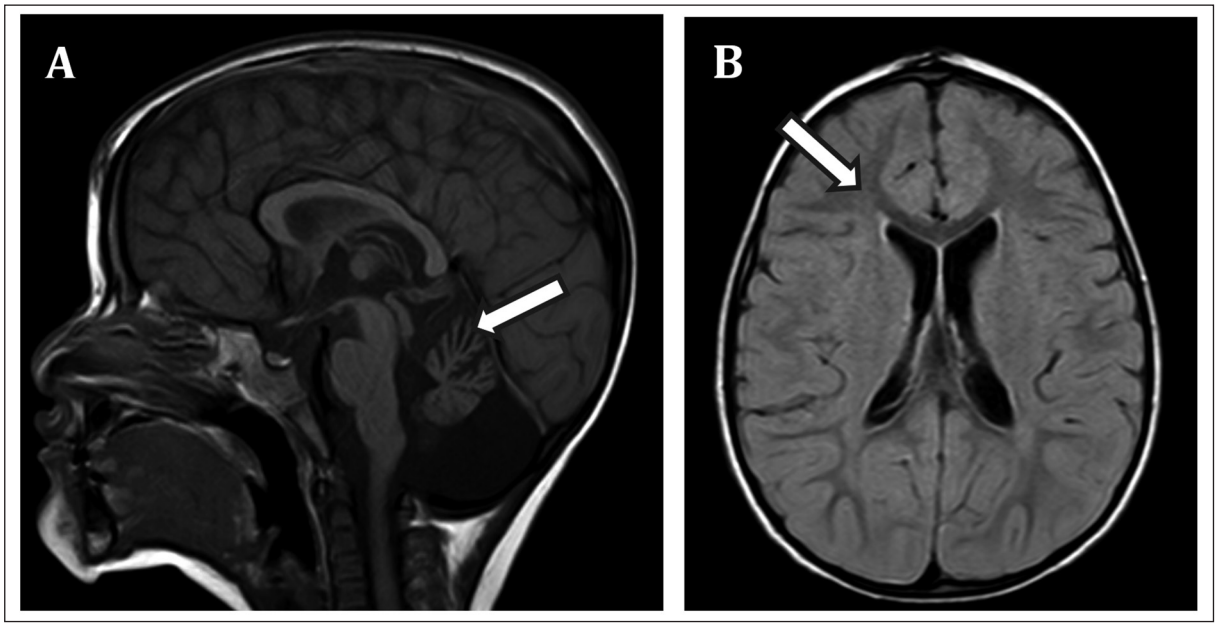

Figure 2. Brain magnetic resonance imaging showing atrophy of the superior aspect of both cerebellar hemispheres and the vermis, with mild widening of the interfolial spaces on sagittal T1-weighted images **(A)**. Mild signal abnormalities in the bilateral periventricular and deep frontoparietal white matter on axial T2/FLAIR sequences, considered nonspecific **(B)**.

our institution, so WES was requested, focusing on the genes mentioned above (CENTOGENE laboratory). The genetic study and its correlation with the phenotype showed that the patient was a carrier of a dual pathology. The genes initially considered when proposing a diagnostic unit did not show pathogenic variants in the WES. In contrast, two genes that did present variants were consistent with the observed phenotype. WES detected the pathogenic homozygous variant in *FIG4* (NM_014845.6:c.122T>C, p.(Ile41Thr)) and the likely pathogenic variant in *SNX14* (NM_153816.6:c.2379C>G, p.(Tyr793*)). It is important to note that although the *FITM2*, *AP1S1*, and *AP1B1* genes share similarities with our patient's clinical picture, they are all associated with skin involvement (ichthyosis or dry skin), which is not present in this case. *FITM2* is also related to chronic enteropathy, diarrhea, and malabsorption, while *AP1B1* is associated with keratitis, manifestations that were also not observed. Likewise, the dysmorphisms observed in our patient have not been described in relation to any of these three genes. Finally, ataxia, which was not evident in the early years due to the inability to sit up, is also not part of the clinical spectrum of *FITM2*, *AP1S1*, or *AP1B1*.

The *FIG4*:p.Ile41Thr variant is well known and has been reported as pathogenic according to the criteria of the American College of Medical Genetics and Genomics[15] based on its identification in multiple patients, both in compound heterozygosity and in homozygosity, co-segregating with the CMT4J phenotype (PM3_vs)[6]. It is present at low frequency in the general population, with no homozygotes reported (gnomAD: 0.0010) (PM2_p). Functional studies indicate that it is a hypomorphic allele (PS3_p), and the aggregated REVEL score (0.855) predicts a deleterious effect (PP3_m)[15]. Only two patients presented homozygosity for this variant. They also had progressive demyelinating polyneuropathy, but with onset between the ages of 9 and 11, with preserved gait and no cognitive impairment[4,16]. In one of them, cerebral white matter involvement was also observed on T2/FLAIR[16].

The *SNX14*:p.(Tyr793*) variant is classified as probably pathogenic. The criteria contributing to this classification include that it is a null variant in a gene whose loss of function is a known disease mechanism (PVS1_vs) and has a very low frequency in the population, with no reported homozygotes (gnomAD: 0.000004) (PM2_p).

The first gene is related to CMT4J with autosomal recessive inheritance, while the second is related to the diagnosis of SCAR20, also autosomal recessive. These diagnoses are consistent with the clinical presentation of this patient. As both genes are located on the long arm of chromosome 6: (*SNX14* [6q14.3] and *FIG4* [6q21]), WES data were evaluated to determine the possibility that the patient inherited a large genetic segment with absence of heterozygosity (AOH) from both consanguineous parents. WES data showed one or more regions of homozygosity on chromosome 6, but

guinity. In particular, the largest segment (47.1 Mb) was located on chromosome 6q12q22.1 (arr[GRCh37] 6q12q22.1(67749352_114838326)x2 hmz), which includes *FIG4* and *SNX14*.

The patient has gradually achieved new motor milestones in psychomotor development. She currently has profound intellectual disability, is in a multidisciplinary rehabilitation program at a specialized center, attends school with special education support, and uses hearing aids. During follow-up, dysmorphic features that were not evident at the onset of the clinical presentation were identified, such as laterally broad eyebrows, telecanthus, epicanthus, a broad nasal tip, and full lips with a tented open mouth, beginning at age 5. Subsequently, the patient's facial features have become coarser. She does not produce any meaningful words and communicates minimally through sign language, although she understands some simple instructions.

The patient achieved independent sitting at age 4 and was able to stand with the use of orthoses at age 6. She has not yet developed a gait and mobilizes using a wheelchair. Ataxia manifested as delayed and unstable sitting, absence of independent standing, and absence of gait. The weakness associated with neuropathy may have contributed to a lesser extent to the observed motor delay. Although scales such as the Scale for the Assessment and Rating of Ataxia (SARA) and the International Cooperative Ataxia Rating Scale (ICARS) allow quantification of the degree of ataxia, they were not applied in this patient because they are difficult to use in nonverbal or nonambulatory patients, as they require a certain degree of cooperation and understanding of instructions. Dystonia has been very mild; therefore, the use of antidystonic medications has not been necessary. The patient is dependent on activities of daily living such as eating, dressing, and personal hygiene. The MRI study has not been repeated, as this patient requires sedation, and no neurological deterioration has been observed clinically.

The patient's phenotype and genotype information was uploaded to LOVD. (https://databases.lovd.nl/shared/individuals/00441138).

Discussion

We report the case of a patient with a dual diagnosis of two rare diseases, CMT4J and SCAR20. To our knowledge, this is the first reported case of the coexistence of these diseases in a patient. Cases of dual diagnosis of neuromuscular diseases concurrent with another disease have been reported previously. Some examples include CMT1A in combination with other diseases, such as Kennedy's disease, facioscapulohumeral dystrophy, and myotonia congenita[17].

CMT4J is a rare autosomal recessive hereditary demyelinating neuropathy[18-21] with approximately 50 reported cases. The first report described only peripheral involvement[5]. Subsequently, numerous cases with central involvement have been described[16,22-24], including white matter abnormalities (40%), intellectual disability (38%), cerebellar atrophy (28%), parkinsonism (19%), dystonia (6%), and sensorineural hearing loss (6%) (Table 1). All of these signs, except for parkinsonism, were detected in our patient. However, she also had marked language delay and facial dysmorphia, which have not been reported in CMT4J. It is speculated that patients with CMT4J and central nervous system involvement have a second pathogenic variant in another gene, as did our patient. However, to our knowledge, the case reported here is the first in which the association of CMT4J with a second genetic disease has been identified. The alterations previously described in white matter are diverse, including periventricular hyperintensity on T2/FLAIR, as in the patient described here[18], and in other locations (basal ganglia, brainstem, and spinal cord)[16]. A degree of cerebral hypomyelination has also been described, ranging from severe to mild[23]. The patient's dystonias affected the limbs, as described in a case in the literature in patients with CMT4J[24]. In other cases, focal dystonia of the face and neck has been described[18]. Absence of ambulation is uncommon in patients with CMT4J; however, cases have been described in which the onset occurred within the first two years of life, and walking was never achieved, with the c.506A>C, p.Tyr169Ser variant present in homozygosity[24].

SCAR20 is another rare disease, with approximately 35 cases reported[25]. On average, it presents at 2.5 years of age and is characterized by a dysmorphic face with coarse features (100%), intellectual disability (94%), cerebellar atrophy (94%), absence of speech (68%), ataxia (82%), absence of ambulation (44%), and sensorineural hearing loss (34%) (Table 2). In the patient described here, the dysmorphic features are similar to those reported in other patients with SCAR20. As detailed in Table 2, absence of speech is common in SCAR20 and can therefore be attributed solely to that pathology, although hearing loss may also have contributed to some extent. The absence of ambulation is also common in patients with SCAR20, which presents with significant ataxia; thus, in our patient, the absence of ambulation appears to be a manifestation of ataxia rather than CMT4J, in which walking is usually maintained.

The age of CMT4J onset varies widely, from newborns[4] to 66 years of age[18]. In 16/47 reported cases, onset occurred during the first 2 years of life. However, the patient's variant has been reported in homozygos-

Table 1. Characterization of 47 reported cases of CMT4J.

N, Origin (ref)	Onset NP year, median	NP demyelinating, %	Cognitive impairment, %	Parkinsonism, %	Dystonia, %	Brain MRI	Sensory neural Hypoacusis, %	Visual signs	Ambulant, %
5, Germany, Turkey[18]	30	100	60	60	20	Brain and cerebellar atrophy, WMI	60	Optic atrophy, cataracts	100
1, Spain[19]	14	100	0	100	0	Normal	0	0	100
2, US[20]	12	100	50	100	0	Brain atrophy	0	0	100
11, US[4]	12	100	18	0	0	WMI	0	0	100
1, US[16]	11	100	no	0	0	WMI	0	Optic neuritis	100
5, US[5,6]	11	100	0	0	0	Normal	0	No	100
1, Canada, Montreal[22]	12	100	0	0	0	ND	0	No	100
7, US, Asia[23]	0.5	100	100	0	14	Cerebellar atrophy, WMI, ventriculomegaly	0	Strabismus, maculopathy, optic atrophy	72
3, Pakistan[24]	0.5	100	100	0	67	WMI, HOD, hyperintensities, cerebellar atrophy	0	No	0
2, Britain[21]	11	100	0	0	0	SD	0	No	100
1, Grece[8]	50	100	No	Si	No	Normal	No	Anisocoria strabismus, diplopia	100
8, Australia[7]	28	100	25	38	0	Brain and cerebellar atrophy	0		100
Mean	13.5								
N°		40	18	9	3	19	3	10	40
Percentage		100%	38%	19%	6%	76%	6%	21%	85%

N, number; Ref, reference; NP, neuropathy; MRI, magnetic resonance imaging; WMI, white matter involvement; ND, no data; hypertrophic olivary degeneration, HOD.

ity in only two previous cases, with a milder phenotype[4,16]. It is possible to suggest that the earlier onset phenotype observed in our patient can be explained by the association with SCAR20.

The described dysmorphisms, absence of speech, and inability to walk independently, which are characteristics of SCAR20 combined with those of CMT4J, perfectly explain the complex phenotype of our patient, who presents a combined phenotype.

WES allowed us to identify two rare diseases with a combined phenotype. A known advantage of WES and genome sequencing (GS) is the unbiased evaluation of genes performed during these analyses. Given the rarity of both diseases, WES identified both conditions accurately, quickly, and cost-effectively, resulting in adjustments to the management of personalized patient support. Dual diagnoses have been consistently reported since WES/GS became part of the genetic diagnostic offering, in 1-2% of patients evaluated[26]. As expected, the rate of dual diagnoses is higher in consanguineous families for whom there is a higher probability of two or more recessive diseases, as presented by the patient in this report.

Longitudinal follow-up is essential in patients with neuromuscular diseases, as it allows the identification of useful phenotypic clues for the search for a specific etiological diagnosis and for phenotype-genotype correlation. In addition, systematic evaluation favors

Table 2. Characterization of 35 reported cases of SCAR20

N, Origin (ref)	Age at onset, years	Epilepsy %	Cognitive impairment %	Absent speech %	Brain MRI	Sensory Neural Hypoacusis, %	Ambulant %	Ataxia
1, India[12]	0	100	100	100	Cerebellar atrophy	0	100	100
1, India[14]	12	0	100	100	Cerebellar atrophy	0	100	100
1, Portugal[13]	0,2	50	100	100	Cerebellar atrophy	50	0	SD
7, Portugal, Turkey[10]	12	0	100	85	Cerebellar atrophy, narrow pons	71	57	57
22, UAE, Egipto, Yemen, Pakistán, Turkey[11]	2.2	36	100	64	Cerebellar and brain atrophy, white matter involvement	22	73	100
2, Oman[25]	1.6	0	100	0	Cerebellar atrophy, white matter involvement	50	50	50
Mean	4.3							
N		10	35	24	34	12	18	29
Percentage		28%	94%	68%	94%	34%	56%	82%

N, number; Ref, reference; MRI, magnetic resonance imaging; ND, no data; UAE, United Arab Emirates.

the implementation of more personalized therapeutic interventions and contributes to generating relevant clinical and scientific evidence.

This case illustrates the importance of performing a comprehensive clinical characterization before requesting an exome study, as this allows for the precise definition of Human Phenotype Ontology (HPO) terms. An adequate phenotypic description optimizes genotype-phenotype correlation and improves the diagnostic performance of genetic analysis.

Conclusions

In cases with complex phenotypes, a detailed description of clinical signs is necessary to guide the interpretation of WES/GS. This case with a dual diagnosis of CMT4J and SCAR20 highlights the importance of considering WES/GS as a first-line test in patients with complex, highly heterogeneous, and/or atypical phenotypes, especially if the parents are consanguineous, as there is a possibility that more than one gene may explain the patient's clinical presentation.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the parents (tutors) of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Javier Martini, Tania Otero Rodriguez, and Aida Bertoli-Avella are employees of CENTOGENE GmbH (Rostock, Germany).

Financial Disclosure

Authors state that no economic support has been associated with the present study.

References

1. Lal D, Neubauer BA, Toliat MR, et al. Increased Probability of Co-Occurrence of Two Rare Diseases in Consanguineous Families and Resolution of a Complex Phenotype by Next Generation Sequencing. PLoS One. 2016 Jan 20;11(1):e0146040. doi: 10.1371/journal.pone.0146040. PMID: 26789268; PMCID: PMC4720433.
2. Record CJ, Pipis M, Skorupinska M, et al. Whole genome sequencing increases the diagnostic rate in Charcot-Marie-Tooth disease. Brain. 2024 Sep 3;147(9):3144-56. doi: 10.1093/brain/awae064. PMID: 38481354; PMCID: PMC11370804.
3. Magy L, Mathis S, Le Masson G, Goizet C, Tazir M, Vallat JM. Updating the classification of inherited neuropathies: Results of an international survey. Neurology. 2018 Mar 6;90(10):e870-6. doi: 10.1212/WNL.0000000000005074. Epub 2018 Feb 2. PMID: 29429969.
4. Hu B, McCollum M, Ravi V, et al. Myelin abnormality in Charcot-Marie-Tooth type 4J recapitulates features of acquired demyelination. Ann Neurol. 2018 Apr;83(4):756-70. doi: 10.1002/ana.25198. Epub 2018 Mar 30. PMID: 29518270; PMCID: PMC5912982.
5. Chow CY, Zhang Y, Dowling JJ, et al. Mutation of FIG4 causes neurodegeneration in the pale tremor mouse and patients with CMT4J. Nature. 2007 Jul 5;448(7149):68-72. doi: 10.1038/nature05876. Epub 2007 Jun 17. PMID: 17572665; PMCID: PMC2271033.
6. Zhang X, Chow CY, Sahenk Z, Shy ME, Meisler MH, Li J. Mutation of FIG4 causes a rapidly progressive, asymmetric neuronal degeneration. Brain. 2008 Aug;131(Pt 8):1990-2001. doi: 10.1093/brain/awn114. Epub 2008 Jun 12. PMID: 18556664; PMCID: PMC2724900.
7. Nicholson G, Lenk GM, Reddel SW, et al. Distinctive genetic and clinical features of CMT4J: a severe neuropathy caused by mutations in the PI(3,5)P_2 phosphatase FIG4. Brain. 2011 Jul;134(Pt 7):1959-71. doi: 10.1093/brain/awr148. PMID: 21705420; PMCID: PMC3122378.
8. Michaelidou K, Tsiverdis I, Erimaki S, et al. Whole exome sequencing establishes diagnosis of Charcot-Marie-Tooth 4J, 1C, and X1 subtypes. Mol Genet Genomic Med. 2020 Apr;8(4):e1141. doi: 10.1002/mgg3.1141. Epub 2020 Feb 5. PMID: 32022442; PMCID: PMC7196464.
9. Sullivan R, Yau WY, O'Connor E, Houlden H. Spinocerebellar ataxia: an update. J Neurol. 2019 Feb;266(2):533-44. doi: 10.1007/s00415-018-9076-4. Epub 2018 Oct 3. PMID: 30284037; PMCID: PMC6373366.
10. Thomas AC, Williams H, Setó-Salvia N, et al. Mutations in SNX14 cause a distinctive autosomal-recessive cerebellar ataxia and intellectual disability syndrome. Am J Hum Genet. 2014 Nov 6;95(5):611-21. doi: 10.1016/j.ajhg.2014.10.007. Epub 2014 Nov 6. Erratum in: Am J Hum Genet. 2015 Jun 4;96(6):1008-9. PMID: 25439728; PMCID: PMC4225633.
11. Akizu N, Cantagrel V, Zaki MS, et al. Biallelic mutations in SNX14 cause a syndromic form of cerebellar atrophy and lysosome-autophagosome dysfunction. Nat Genet. 2015 May;47(5):528-34. doi: 10.1038/ng.3256. Epub 2015 Apr 6. PMID: 25848753; PMCID: PMC4414867.
12. Sait H, Moirangthem A, Agrawal V, Phadke SR. Autosomal recessive spinocerebellar ataxia-20 due to a novel SNX14 variant in an Indian girl. Am J Med Genet A. 2022 Jun;188(6):1909-14. doi: 10.1002/ajmg.a.62701. Epub 2022 Feb 23. PMID: 35195341.
13. Maia N, Soares G, Silva C, et al. Two Compound Heterozygous Variants in *SNX14* Cause Stereotypies and Dystonia in Autosomal Recessive Spinocerebellar Ataxia 20. Front Genet. 2020 Sep 24;11:1038. doi: 10.3389/fgene.2020.01038. PMID: 33193593; PMCID: PMC7543990.
14. Shukla A, Upadhyai P, Shah J, Neethukrishna K, Bielas S, Girisha KM. Autosomal recessive spinocerebellar ataxia 20: Report of a new patient and review of literature. Eur J Med Genet. 2017 Feb;60(2):118-23. doi: 10.1016/j.ejmg.2016.11.006. Epub 2016 Nov 29. PMID: 27913285; PMCID: PMC5241222.
15. Richards S, Aziz N, Bale S, et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-24. doi: 10.1038/gim.2015.30. Epub 2015 Mar 5. PMID: 25741868; PMCID: PMC4544753.
16. Lewis HS, Willis E, Veerapandiyan A. Charcot-Marie-Tooth Disease Type 4J and Multiple Sclerosis. J Clin Neuromuscul Dis. 2019 Dec;21(2):117-8. doi: 10.1097/CND.0000000000000258. PMID: 31743256.
17. Ardissone A, Brugnoni R, Gandioli C, et al. Double-trouble in pediatric neurology: myotonia congenita combined with charcot-marie-tooth disease type 1a. Muscle Nerve. 2014 Jul;50(1):145-7. doi: 10.1002/mus.24205. Epub 2014 May 5. PMID: 24515601.
18. Zimmermann M, Schuster S, Boesch S, et al. FIG4 mutations leading to parkinsonism and a phenotypical continuum between CMT4J and Yunis Varón syndrome. Parkinsonism Relat Disord. 2020 May;74:6-11. doi: 10.1016/j.parkreldis.2020.03.021. Epub 2020 Mar 28. PMID: 32268254.
19. Posada IJ, Domínguez-González C. CMT4J, parkinsonism and a new FIG4 mutation. Parkinsonism Relat Disord. 2020 Dec;81:82-3. doi: 10.1016/j.parkreldis.2020.10.011. Epub 2020 Oct 17. PMID: 33096303.
20. Orengo JP, Khemani P, Day JW, Li J, Siskind CE. Charcot Marie Tooth disease type 4J with complex central nervous system features. Ann Clin Transl Neurol. 2018 Jan 22;5(2):222-5. doi: 10.1002/acn3.525. PMID: 29468183; PMCID: PMC5817837.
21. Menezes MP, Waddell L, Lenk GM, et al. Whole exome sequencing identifies three recessive FIG4 mutations in an apparently dominant pedigree with Charcot-Marie-Tooth disease. Neuromuscul Disord. 2014 Aug;24(8):666-70. doi: 10.1016/j.nmd.2014.04.010. Epub 2014 May 4. PMID: 24878229; PMCID: PMC4096049.
22. Gentil BJ, O'Ferrall E, Chalk C, Santana LF, Durham HD, Massie R. A New Mutation in FIG4 Causes a Severe Form of CMT4J Involving TRPV4 in the Pathogenic Cascade. J Neuropathol Exp Neurol. 2017 Sep 1;76(9):789-99. doi: 10.1093/jnen/nlx062. PMID: 28859335; PMCID: PMC6251583.
23. Lenk GM, Berry IR, Stutterd CA, et al; Broad Center for Mendelian Genomics; White SM, Christodoulou J, Skibina O, Ruddle J, Tan TY, Leventer RJ, Livingston JH, Meisler MH. Cerebral hypomyelination associated with biallelic variants of FIG4. Hum Mutat. 2019 May;40(5):619-30. doi: 10.1002/humu.23720. Epub 2019 Feb 28. PMID: 30740813; PMCID: PMC6467804.
24. Wright GC, Brown R, Grayton H, et al. Clinical and radiological characterization of novel FIG4-related combined system disease with neuropathy. Clin Genet. 2020 Aug;98(2):147-54. doi: 10.1111/cge.13771. Epub 2020 Jun 10. PMID: 32385905.
25. Al-Hashmi N, Mohammed M, Al-Kathir S, Al-Yarubi N, Scott P.

Exome Sequencing Identifies a Novel Sorting Nexin 14 Gene Mutation Causing Cerebellar Atrophy and Intellectual Disability. Case Rep Genet. 2018 Oct 24;2018:6737938. doi: 10.1155/2018/6737938. PMID: 30473892; PMCID: PMC6220403.

26. Bertoli-Avella AM, Beetz C, Ameziane N, et al. Successful application of genome sequencing in a diagnostic setting: 1007 index cases from a clinically heterogeneous cohort. Eur J Hum Genet. 2021 Jan;29(1):141-53. doi: 10.1038/s41431-020-00713-9. Epub 2020 Aug 28. PMID: 32860008; PMCID: PMC7852664.