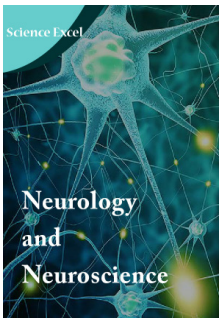
Neurology & Neuroscience

Original Article



Distal Hereditary Motor Neuropathy With SIGMAR 1 Mutation: 2 Cases at Fann University Hospital, Dakar, Senegal

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- Received Date: 01 Aug 2025
- Accepted Date: 05 Sep 2025
- Publication Date: 08 Sep 2025

Keywords

Distal Hereditary Motor Neuropathy; dHMN; SIGMAR1; Dakar; Senegal.

Abstract

Introduction: *Distal hereditary motor neuropathies (dHMN) constitute a rare heterogeneous group of disorders characterized by degeneration of the motor component of peripheral nerves. Their clinical and electrophysiological presentation is very variable due to the genetic heterogeneity of these latter. Among the rare autosomal recessive forms of dHMN, mutations in the SIGMAR1 gene have recently been described and are responsible for variable phenotypes. Below, we describe the clinical, electrophysiological, and genetic features of two patients with dHMN linked to a mutation in the SIGMAR1 gene.*

Observations: *The two patients, aged 15 and 19 at consultation, exhibited distal limb weakness beginning at ages 9 and 10, with progressive worsening that initially affected the lower limbs and later involved the upper limbs. The second patient had a first-degree consanguinity. Clinical examination revealed pes cavus in the first patient and equinovarus feet (in the second). Both showed distal motor deficits in the lower limbs without sensory involvement.*

Neurography showed very reduced or nearly absent motor response amplitudes in both cases, with preserved sensory potentials. Needle EMG revealed a pattern of chronic denervation

Our two patients benefited from a whole exome sequencing from the DNA extracted from whole blood and the same genetic variant (variant c.580C>T) was identified homozygotically in the SIGMAR1 gene (genomic position 9:34635721 based on the reference genome version GRCh37). Given the autosomal recessive mode of transmission, genetic counseling was offered to affected families, informing them of the 25% risk of transmitting the causal mutation to their offspring.

Conclusion: *dHMN is a rare condition, and cases caused specifically by mutations in the SIGMAR 1 gene are even more uncommon. Since only a few patients with this mutation have been described in scientific literature, it is difficult to know exactly what phenotypes are linked to it. To improve our understanding, it xould be helpful to conduct more genetic studies and identify additional cases, which would add valuable information to what is already known.*

Introduction

Hereditary peripheral neuropathies are degenerative diseases of the peripheral nerves genetically transmitted in an autosomal dominant, recessive or X-linked mode. Their overall prevalence is not very well known but would be estimated at 1/5000 [1]. We distinguish among hereditary peripheral neuropathies, pure hereditary peripheral neuropathies (neuropathy being the main if not the only expression of the pathology) and neuropathies in the context of systemic hereditary conditions [2]. In the subgroup of pure hereditary neuropathies, we find among others: motor and sensory hereditary neuropathies or Charcot-Marie-Tooth disease (CMT), distal hereditary motor neuropathies or dHMN (distal Hereditary Motor Neurophathy) and hereditary sensory and autonomic neuropathies [3]. While diseases belonging to the CMT group are the most common, since they represent about 40% of chronic neuropathies of genetic origin (prevalence from 4.7 to 36 per 100,000), those belonging to the group of distal motor hereditary neuropathies are much rarer and less studied [4].

Distal hereditary motor neuropathies (dHMN) also known as spinal amyotrophies are a diverse group of disorders charcterized by degeneration of the motor part of peripheral nerves. Their estimated prevalence is about 2.14 per 100,000 people [5]. They are defined

Citation: Diop-Sene MS, Ngoule M-O[1], Senghor HVF, et al. Distal Motor Neuropathy With SIGMAR 1 Mutation: 2 Cases, Fann Hospital, Dakar. Neurol Neurosci. 2025;6(7):035.

by a pure motor neuropathic clinical presentation, confirmed by electrophysiological and anatomical studies [6]. They usually appear in chilhood or adolescence and tend to progress slowly. The clinical, neurophysiological, and progression variability of dHMN is rooted in their genetic diversity. Indeed, to date, about 30 responsible genes have been identified with autosomal dominant, recessive and X-linked transmission [5]. But, despite these findings, about 60 to 70% of dHMN cases remain genetically uncharacterized [7]. Among the rare autosomal recessive forms of dHMN, mutations in the SIGMAR1 gene (Sigma non-opioid intracellullar receptor-1) have recently been described and are responsible for variable phenotypes of motor neuropathy often associated with damage to the upper motoneurons. Due to the scarcity and heterogeneity of dHMN, and the low number of reported cases of mutations in the SIGMAR1 gene, we describe two cases of patients with dHMN associated with the same mutation in the SIGMAR1 gene.

Presentation of the Observations

Observation 1

AIt was a 15-year-old teenager, Senegalese, of Peuhl ethnicity, 4th child of a non-consanguineous couple. She has been presenting since the age of 9 with a walking disorder progressively worsening over several years, associated after an unspecified period with progressive weakness in both hands. Moreover, she did not present any cognitive disorders, dyspnea, dysphagia, or epileptic seizures. The psychomotor development was normal; patient's medical history was unremarkable. Similar neurological deficit was found in a brother of our patient's mother (of the same father but from a different mother) (Figure 1).

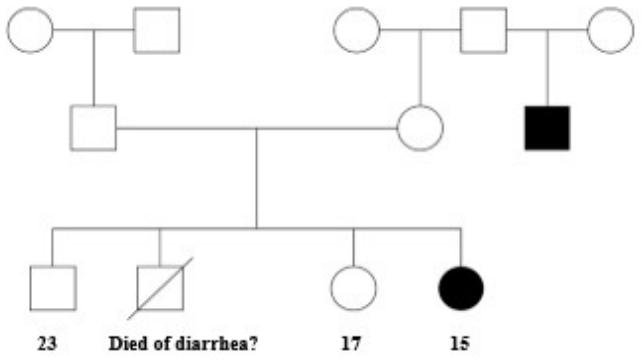

Figure 1: *Patient 1 Family Tree*

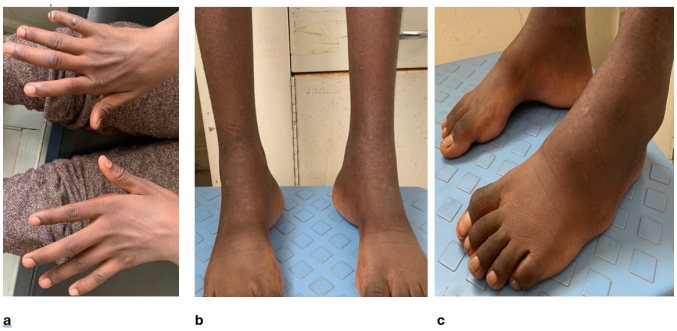

Figure 2: *Distal amyotrophy of : a: a- Dorsal interosseous; b: Lower limbs muscles; c: Pes cavus*

Table 1*: Muscular Evaluation of Patient 1 According to the Medical Research Council (MRC) Score*

MUSCLE GROUP	RIGHT	LEFT
FACE AND NECK		
Orbicularis and facial muscles	5	5
Neck flexors	5	5
Neck extensors	5	5
UPPER LIMBS		
Shoulder abduction (deltoid)	5	5
Elbow flexion (biceps)	5	5
Elbow extension (triceps)	5	5
Wrist flexion	5	5
Wrist extension	5	5
Finger extension	4	4
Finger abduction (1st dorsal interosseous and ADM)	4	4
Thumb abduction	2	2
LOWER LIMBS		
Hip flexion (iliopsoas)	5	5
Knee extension (quadriceps)	5	5
Knee flexion (hamstrings)	5	5
Ankle dorsiflexion (tibialis anterior)	1	1
Ankle plantarflexion (triceps surae)	5	5

The neurological examination highlighted a distal and symmetrical motor deficit of the 4 limbs associated with distal amyotrophy of the lower and upper limbs and pes cavus (Figure 2). Details on the assessment of segmental muscle strength are given in Table 1. The achillean osteotendinous reflexes were abolished, but other reflexes were normal. No sign of damage to the pyramidal tract was found. Walking was possible without assistance, with limitations for running and jumping. Examination of the different modalities of sensitivity, cranial nerves and cerebellar functions was normal. No cognitive deficit, dysautonomic disorders or fasciculations were found.

Electroneuromyography (ENMG) was performed. The nerve conduction studies demonstrate several abnormalities. The peroneal and posterior tibial nerves motor potentials

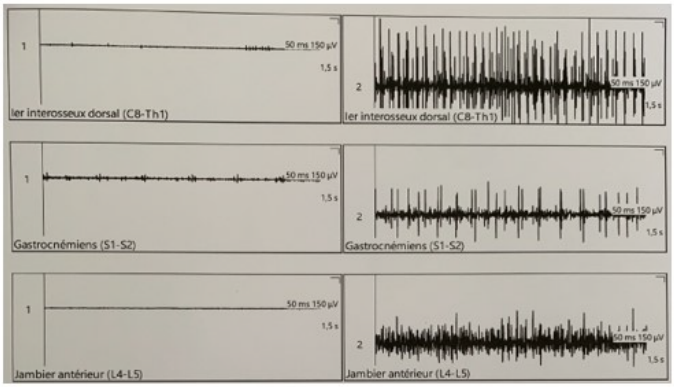

Figure 3: *Patient 1 EMG needle*

***Table 2**: Motor Parameters of Patient 1 at Neurography*

NERVES TESTED	AMPLI-TUDES (µV)	VCM (m/s)	INCR SURFAC-ES (%)	LD (ms)
Median nerve, right				
Wrist	0.7	-	-	4.0
Elbow crease	0.6	40.6	-23.7	10.4
Median nerve, left				
Wrist	0.4	-	-	3.8
Elbow crease	0.4	60.4	+41.3	7.9
Ulnar nerve, right				
Wrist	0.5	-	-	2.8
Below elbow	0.3	42.2	-55.4	8.8
Ulnar nerve, left				
Wrist	0.6	-	-	4.0
Below elbow	0.6	66.7	+83.0	7.6
Fibular nerve, right				
Ankle	0.0	-	-	-
Fibular head	0.0	-	-	-
Popliteal fossa	0.2	-	-	-
Fibular nerve, left				
Ankle	0.0	-	-	-
Fibular head	0.0	-	-	-
Popliteal fossa	0.2	-	-	-

***Table 3**: Sensory Parameters of Patient 1 at Neurography*

NERVES TESTED	AMPLI-TUDES (mV)	VCS (m/s)	SURFACES (µV×s)
Median (thumb)			
Right	37.2	75.8	19.4
Left	40.2	74.3	21.0
Ulnar (5th finger)			
Right	16.0	65.2	9.6
Left	22.3	57.7	13.3
Musculocutaneous nerve, leg			
Right	14.8	83.3	9.8
Left	12.2	70.3	18.8
Sural			
Right	9.2	59.8	5.6
Left	10.8	54.3	7.8

were absent. Amplitudes of motors potentials of median and ulnar nerves were very reduced, with preservation of motor conduction velocities in the upper limbs (Table 2). Sensory parameters were normal in all four limbs (Table 3).

On needle electomyography (EMG) fibrillation potentials were observed at rest on the medial gastrocnemus and the right dorsal interosseous muscles (Figure 3). No biological or radiological assessment has been carried out.

In view of the clinical arguments (age of onset, mode of installation and evolution, predominance of motor deficit in distal, absence of sensory signs) and electrophysiological (normality of sensitive parameters and severe alterations of motor amplitudes), the diagnosis of axonal and distal motor hereditary neuropathy of the 4 limbs was evoked. In order to identify the possible genetic abnormality involved in the genesis of the disease, a whole exome sequencing (WES) from DNA extracted from whole blood was performed (RefSeq: NM_005866.4). A genetic variant (variant c.580C>T) was identified homozygotically in the SIGMAR1 gene (genomic position 9:34635721 based on the reference genome version GRCh37). Variant c.580C>T is a single nucleotide substitution of a Cytosine for a Thymine (exon 4), resulting in an amino acid shift at position 194 of the protein from Glutamine to a premature stop codon (p.Gln194Ter). The genetic analysis of other family members could not be carried out. The finding of this variation in the SIGMAR1 gene made the diagnosis of distal hereditary motor neuropathy even more likely. Genetic counseling was offered to the affected families, informing them of the 25% risk of transmitting the causal mutation to their offspring.

Observation 2

Patient 2 aged 19 years, Guinean, of Peuhl ethnicity, 2nd child of a first-degree consanguineal couple (Figure 4). There was no previous history of similar neurological impairment in the family. Prenatal and natal antecedents are unknown. Since the age of 10, she presents a weakness in the distal extremities of installation and progressive worsening, starting with the lower limbs and reaching the upper limbs after a few years of

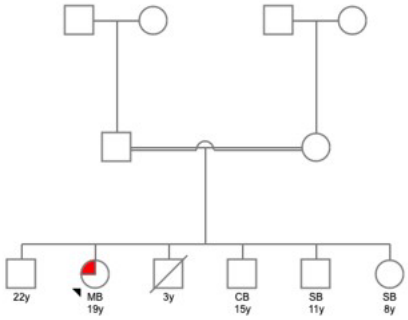

***Figure 4**: Patient 2 Family tree*

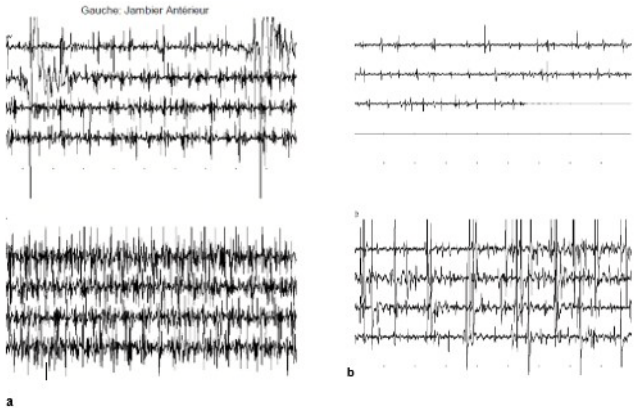

***Figure 5**: Patient 2 EMG needle 2 :a-Left tibialis anterior muscle; b-right medial gastrocnemus muscle*

Table 4: *Muscular Evaluation of Patient 2 According to the Medical Research Council (MRC) Score*

MUSCLE GROUP	RIGHT	LEFT
FACE AND NECK		
Orbicularis and facial muscles	5	5
Neck flexors	5	5
Neck extensors	5	5
UPPER LIMBS		
Shoulder abduction (deltoid)	5	5
Elbow flexion (biceps)	5	5
Elbow extension (triceps)	5	5
Wrist flexion	5	5
Wrist extension	5	5
Finger extension	4	4
Finger abduction (1st dorsal interosseous and ADM)	4	4
Thumb abduction	3	3
LOWER LIMBS		
Hip flexion (iliopsoas)	5	5
Knee extension (quadriceps)	5	5
Knee flexion (hamstrings)	5	5
Ankle dorsiflexion (tibialis anterior)	0	0
Ankle plantarflexion (triceps surae)	4	4

Table 5: *Motor Parameters of Patient 2 at Neurography*

NERVES TESTED	AMPLI-TUDES (µV)	VCM (m/s)	LD (ms)
Fibular nerve, right			
Ankle	0.7	-	-
Fibular head	0.2	-	5.5
Popliteal fossa	0.7	-	4.5
Fibular nerve, left			5.6
Ankle	0.0	-	
Fibular head	0.0	-	-
Popliteal fossa	0.0	-	-
Posterior tibial nerve, right			
Ankle	0.0	-	-
Popliteal fossa	0.0	-	-
Posterior tibial nerve, left			
Ankle	0.0	-	-
Popliteal fossa	0.0	-	-

evolution.

Physical examination founded equinovarus feet associated with an amyotrophy of the distal muscles of the lower and upper limbs. Walking without assistance was impossible, the patient moving long distances using a rolling device. Details on the assessment of segmental muscle strength are given in Table 4. The Achillean osteotendinous reflexes were abolished. No sign

Table 6: *Sensory Parameters of Patient 2 at Neurography*

NERVES TESTED	AMPLITUDES (mV)	VCS (m/s)
Musculocutaneous nerve, leg		
Right	6.1	66.7
Left	6.9	85.7
Sural		
Right	34.9	63.2
Left	10.4	63.2

of central motor neurone involvement was found. Cranial nerves examination and cerebellar functions was normal. There was no cognitive deficit, no autonomic disorders, no fasciculations and no sensitive disorders.

ENMG was realised. Sensory and motor nerve conductions were evaluated on 4 nerve trunks in the lower limbs. Needle EMG was done on 3 muscles of the lower limbs (right vastus medialis muscle, left tibialis anterior muscle and right medial gastrocnemus muscle). Nerve conduction studies revealed nearly absent excitability of the motor nerve trunks in the lower limbs (Table 5). The sensory parameters were normal (Table 6), but there was a significant difference between the sensory potential's amplitudes of the 02 sural nerves (10.4 mV on the left vs 34.9 on the right).

Needle EMG revealed spontaneous activity in the right medial gastrocnemius and tibialis anterior muscles at rest (rest was difficult to obtain in the tibialis anterior). During voluntary contraction, the recordings showed poor neurogenic patterns in these muscles (Figure 5). No biological or radiological assessments have been carried out.

The diagnosis of hereditary motor axonal and distal neuropathy of the 4 limbs was also mentioned in this patient. A whole exome (WES) sequencing from the extracted DNA of whole blood was performed (RefSeq: NM_005866.4). The same genetic variant (variant c.580C>T) was homozygotically identified in the SIGMAR1 gene (genomic position 9:34635721 based on the reference genome version GRCh37). The genetic analysis of other family members could not be carried out. Genetic advice was offered to the families.

Discussion

We presented the clinical, electrophysiological and molecular characteristics of 2 patients aged 15 years and 19 years respectively for whom the diagnosis of hereditary distal motor neuropathy associated with the same mutation in the SIGMAR1 gene was retained.

Distal hereditary motor neuropathies present a clinical polymorphism due to genetic heterogeneity. Indeed mutations in several genes have been imputed as responsible for different phenotypes of dHMN [3]. Among the rare autosomal recessive forms of dHMN, mutations in the SIGMAR1 gene (encoding the non-opioid intracellular sigma 1 sigma-1R receptor) have recently been described and are responsible for variable motor neuropathy phenotypes [8].

Our two patients presented respectively from 9 years and 10 years, a weakness of the distal extremities of installation and progressive aggravation, starting with the lower limbs and

Table 7: *Some Clinical Characteristics of dHMN Cases Associated with a SIGMAR1 Gene Mutation Found in the Literature*

Author, Year	Age/ Sex	Age of Onset	Signs and Symptoms	Motor Deficit Characteristics	Pyramidal Signs	Sensory Disturbances
Li X et al, 2015 [16]	42 yrs/M	12 yrs	-Steppage, -Varus foot, -Weakness in upper limbs	Amyotrophy and mild to moderate distal motor deficit, bilateral and symmetrical in 4 limbs, predominantly in lower limbs	Present (abolished Achilles reflex)	Absent
Li X et al, 2015 [16]	37 yrs/F	09 yrs	-Steppage, -Varus foot, -Weakness in upper limbs	Amyotrophy and mild to moderate distal motor deficit, bilateral and symmetrical in 4 limbs, predominantly in lower limbs	Present (abolished Achilles reflex, absent Babinski sign)	Absent
Li X et al, 2015 [16]	30 yrs/M	10 yrs	-Steppage, -Varus foot, -Weakness in upper limbs	Amyotrophy and moderate to severe distal motor deficit, bilateral and symmetrical in 4 limbs, predominantly in lower limbs	Present (abolished Achilles reflex)	Absent
Gregianin E et al, 2016 [15]	27 yrs/F	Childhood (age un-specified)	-Gait disturbances, -Recurrent ankle sprains, -Frequent falls, -Cavus foot and claw hands	Amyotrophy and moderate to severe distal motor deficit, bilateral and symmetrical in 4 limbs, predominantly in lower limbs	Present (abolished Achilles reflex)	Absent
Gregianin E et al, 2016 [15]	27 yrs/M	Childhood (age un-specified)	-Steppage, -Poor athletic performance at school	Amyotrophy and moderate distal motor deficit, bilateral and symmetrical in 4 limbs	Present	Absent
Horga A et al, 2016 [10]	17 yrs/M	03 yrs	Claw hands, -Bilateral dropping of fingers and feet	Amyotrophy and severe distal motor deficit, bilateral and symmetrical in 4 limbs	Present (abolished Achilles reflex)	Absent
Lee JJY et al, 2016 [12]	17 yrs/M	17 yrs/M	-Gait disturbances, -Frequent falls, -Claw hand and toe deformity	Amyotrophy and severe distal motor deficit, bilateral and symmetrical in 4 limbs	Absent	Absent
Nandhago-pal R et al, 2018 [8]	18 yrs/F	18 yrs/F	-Steppage, -Cavus foot, -Weakness in up-per limbs	Amyotrophy and mild to moderate distal motor deficit, bilateral and symmetrical in 4 limbs, predominantly in lower limbs	Present	Absent
Nandhago-pal R et al, 2018 [8]	14 yrs/F	14 yrs/F	-Gait disturbances, -Weakness in upper limbs	Amyotrophy and mild to moderate distal motor deficit, bilateral and symmetrical in 4 limbs, predominantly in lower limbs	Present	Absent
Nandhago-pal R et al, 2018 [8]	5 yrs/M	5 yrs/M	-Weakness, pain, and cramps in the left lower limb	Absence of significant motor deficit	Present	Absent
Almendra L et al, 2018 [11]	37 yrs/F	37 yrs/F	-Gait disturbances, falls, -Weakness in lower limbs (right++), -Equinovarus foot de-formity, -Claw hands	Amyotrophy and severe distal motor deficit, bilateral and symmetrical in 4 limbs	Absent	Absent

reaching the upper limbs after a few years of evolution.

In our patients, the age of onset was 9 and 10 years respectively, and they were female. Childhood onset (13 months and 2 years) was found in 11 patients with dHMN associated with a SIGMAR 1 gene mutation, and male sex was predominant, 6 boys out of 11 patients (Table 7). Consanguinity was found in some of the patients reported in the literature, as was the case for our 2nd patient. In all cases reported in the literature, the involvement was purely motor-related and length-dependent. This is consistent with the observations that were made in our 2 patients. This length-dependent damage explains the predominance of the deficit at the lower limbs found in most of the reported observations and in our two patients [9].

Sigmar-1R plays an important role in neuron survival. When

Table 8. *Electrophysiological Characteristics of dHMN Cases Associated with a SIGMAR1 Gene Mutation Found in the Literature*

Sex/Age	Time Between Onset and ENMG	Motor Conduction (VCM in m/s / Amplitude in mV)	Sensory Conduction (VCS in m/s / Amplitude in mV)	Needle EMG
Case 1 [16]	---	Not available	Not available	Not available
Case 2 [16]	---	Not available	Not available	Not available
Case 3 [16]	20 yrs	Median nerve right: 43.4 / 1.2, Peroneal nerve left: 34.9 / 0.2, Peroneal nerve right: 32.5 / 0.1	Median nerve right: 58 / 45, Peroneal nerve left: 61.2 / 34, Peroneal nerve right: 63.3 / 41, Sural nerve left: 55.5 / 39	Distal denervation signs
Case 4 [15]	Unspecified	-Inexcitability of nerves in the lower limbs, -Severe reduction in amplitudes in upper limbs with preserved VCM	Normal	Signs of chronic denervation in distal muscles of the four limbs
Case 5 [15]	Unspecified	Diffuse and severe reduction in amplitudes with slightly reduced VCM	Normal	Signs of diffuse chronic denervation in distal muscles
Case 6 [10]	14 yrs	Median nerve: 45 / 2.3, Ulnar nerve: 40 / 0.9, Peroneal nerve: 32 / 0.4, Posterior tibial nerve: -- / 0.2	Median nerve: 54 / 18, Ulnar nerve: 58 / 15, Radial nerve: 69 / 49, Superficial peroneal nerve: 46 / 18, Sural nerve: 44 / 8	Denervation signs
Case 7 [12]	03 yrs	Median nerve right: 37.5 / 0.81, Ulnar nerve right: 45.9 / 0.53, Anterior tibial nerve right: 101 / 1.73	Median nerve right: 60.4 / 13.2, Ulnar nerve right: 59.5 / 8.1, Radial nerve right: 61.7 / 30.3, Sural nerve right: 52.9 / 8.5	-
Case 8 [8]	02 yrs	Median nerve right: 46 / 1.2, Ulnar nerve right: 42 / 0.6, Peroneal nerve right: 0 / 0, Peroneal nerve left: 0 / 0.4, SPI (Short plantar interosseous) right: -- / 0.8, SPI left: -- / 0.9	Normal	-Spontaneous activity: fibrillations + positive sharp waves, -Poor effort tracing in distal muscles
Case 9 [8]	07 yrs	Median nerve right: 43 / 1.8, Median nerve left: 39 / 1.6, Ulnar nerve right: 42 / 0.3, Ulnar nerve left: 49 / 0.7, Peroneal nerve right: 39 / 0.9, Peroneal nerve left: 36 / 0.5, SPI right: 37 / 1.3, SPI left: 43 / 0.2	Normal	-Spontaneous activity: fibrillations + positive sharp waves, -Poor effort tracing
Case 10 [8]	04 yrs	Median nerve right: 50 / 8.9, Ulnar nerve right: 57.7 / 10.6, Peroneal nerve right: 40.5 / 0.6, Peroneal nerve left: 28.3 / 0.4, SPI right: 45.7 / 2.6, SPI left: 50 / 3.3	Normal	Poor tracing
Case 11 [11]	33 yrs	Inexcitability of upper and lower limbs	Normal	-Spontaneous activity: fibrillations + positive sharp waves, -Very poor tracing

it malfunctions or is absent, it disrupts communication between the endoplasmic reticulum and mitochondria, impairing mitochondrial function and axonal transport. This leads to degeneration of motor neuron axons and subsequent cell death. This degenerative process, known as « dying back » aligns with the lenght dependent damage often seen in patients with the mutations in SIGMAR1 gene [9,10].

An association with signs of pyramidal tract involvement is described in most patients with a mutation in the SIGMAR1 gene. In our two patients, no sign of first motor neuron lesion was observed, which was like 2 cases found in the literature [11,12]. This difference could be related to the genetic variant found in our patients. Indeed, pathogenic variants in the same gene can cause heterogeneous and variable phenotypes [5]. Homozygous mutations in the SIGMAR1 gene have been reported as a cause of juvenile amyotrophic lateral sclerosis (ALS) [13]. A case reported in 2022 reported a mutation in the SIGMAR1 gene associated with neuropathy with conduction block and temporal dispersion, thus highlighting the phenotypic heterogeneity of mutations in this gene [14]. The case reported by Almendra L. et al. [11] had a variant c.561_576del on exon 4 and the one reported by Lee JJY et al. in 2016 [12] had a variant c.151+1 G>T; while our two patients had the same genetic variant c.580C>T. The variant c.580C>T is a single-nucleotide substitution of a Cytosine for a Thymine (exon 4), resulting in an amino acid change at position 194 of the protein from Glutamine to a premature stop codon (p.Gln194Ter). Loss of function is a known mechanism of the disease (the gene has 55 variants «loss of functions» pathogens). We do not yet have enough cases to discuss the phenotypic characteristics of this genetic variant. Subsequent clinical follow-up will allow the observation of the appearance or not of new phenotypic characteristics in our patients.

From a neurophysiological point of view, similarities were observed between our 2 patients and the observations reported in the literature. In most cases summarized in table V the motor impairment was severe, with sometimes a near inexcitability of the nerves. In the observations made in the literature, it is noted that the amplitudes of motor responses were generally more decreased on the nerve trunks tested at the lower limbs and when neurography of the upper limbs was available, it is noted that the ulnar nerve was more severely affected than the median nerve (Table 8). In our first patient, we had inexcitability of the nerve trunks tested in the lower limbs and amplitudes of motor responses very collapsed on the nerve trunks tested in the upper limbs (without predominance of severity on a nerve trunk). For the second patient, neurography was not performed in the upper limbs and we found for the motor parameters a quasi-inexcitability of the nerve trunks tested in the lower limbs. Motor conduction velocities were normal in our patients when they were obtained. This observation is consistent with the observations reported in the literature, although for some of the patients slightly slowed MCVs were found on certain nerve trunks [8,10,15,16], which could be explained by axonal loss. The neurography of sensory nerve trunks was normal in all patients found in the literature, which was like observations made in our first patient. On the other hand, in our second patient we found a significant difference between the amplitudes of the sensory potentials of the 02 sural nerves (10.4 mV on the left vs 34.9 on the right). This difference could be related to technical hazards or indicate a phenotypic peculiarity. A subsequent neurophysiological follow-up would be interesting to control this difference and to monitor the progression of the involvement in our patients. At the needle EMG, we found in all cases signs of chronic denervation.

The neuropathy score of Charcot-Marie-Tooth (CMTNS: Charcot-Marie-Tooth Neuropathy Score (version 2) allowing to assess the severity of motor and sensory impairments length-dependent in genetic neuropathies could not be calculated in our patients because the amplitude of the sensory potential of the radial nerve was not available. This leads us to recommend including the examination of the radial nerve in the neurophysiological protocol for evaluating hereditary neuropathy.

The management remains symptomatic (surgery, functional rehabilitation, assistance with movement), combined with genetic counselling for the families concerned.

Conclusion

The dHMN constitutes a rare group of pathology; whose diagnosis sometimes seems difficult in our context where genetic analysis is not often accessible. In our two patients, the clinical description; electrophysiological and genetic is an important step to better identify the dHMN linked to mutations in the SIGMAR1 gene and to see their particularity.

Aknowledgement

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PMRC receives the support of a Junior Leader fellowship from “la Caixa” Foundation (ID100010434) and from the European Union’s Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 847648. The fellowship code is LCF/ BQ/PI21/11830012.

Conflict of interest

Author declares no conflict of interest

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