is warranted in making more generalized conclusions from our findings as there may be potential differences in needle EMG technique between institutions and examiners. Fourth, it would be beneficial and more objective in a prospective study to examine sampled sites with ultrasound for hematoma formation. This study is an initial step in evaluating the risk of hematological complications associated with needle EMG and thrombocytopenia. Further studies are needed to formulate an evidence-based guideline for severe grades of thrombocytopenia (3 and 4).

In conclusion, bleeding complications from a standard needle EMG examination were rare among thrombocytopenic oncology patients. Although thrombocytopenia is a risk for developing bruising or hematomas after needle EMG, we were not able to identify any clinically significant adverse events after our retrospective chart review.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publications and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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Distal symmetric polyneuropathy phenotype in patients with sensory neuronopathy at the time of electrodiagnosis

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Abstract

Introduction/Aims: It is unknown how often patients with sensory neuronopathy (SNN) present with a distal symmetric polyneuropathy (DSP) phenotype. In these cases, electrodiagnostic testing may discriminate SNN with a DSP phenotype from DSP.

Methods: We reviewed the records of patients who met SNN diagnostic criteria between January 2000 and February 2021 and identified patients with a DSP phenotype at the time of electrodiagnosis.

Results: Sixty-two patients fulfilled SNN diagnostic criteria. At symptom onset, 20 (32.2%) patients presented with distal symmetric sensory symptoms limited to the feet. However, most progressed rapidly over 6 months or developed asymmetric

Abbreviations: CANVAS, cerebellar ataxia, neuropathy, and vestibular areflexia syndrome; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DSP, distal symmetric polyneuropathy; EDx, electrodiagnosis; NCS, nerve conduction studies; SNAP, sensory nerve action potential; SNN, sensory neuronopathy.

symptoms. At the time of electrodiagnosis, only seven (11.3%) patients had a DSP phenotype. Of these seven patients, four had cerebellar ataxia with neuropathy and vestibular areflexia syndrome, one had vitamin B_6 deficiency, one was thought to be alcohol-induced, and one was idiopathic.

Discussion: Patients with SNN rarely present with a DSP phenotype at the time of electrodiagnosis. The finding that one third of cases resemble DSP at onset highlights the importance of clinical monitoring. In patients with a DSP phenotype, the presence of ataxia at onset or significant progression within 6 months may suggest the possibility of SNN and should prompt additional investigations, such as electrodiagnosis.

KEYWORDS
electrodiagnostic testing, distal symmetric polyneuropathy, sensory ganglionopathy, sensory neuronopathy

1 | INTRODUCTION

Sensory neuronopathies (SNN) are a subgroup of peripheral nervous system disorders caused by primary degeneration of the dorsal root ganglia and their central and peripheral sensory axons.[1] Early detection of SNN is crucial, because some cases are caused by potentially treatable immune-mediated or nutritional mechanisms.[1-3] Validated clinical and electrodiagnostic (EDx) criteria have been established to facilitate and standardize the diagnosis of SNN.[4,5]

Although SNN typically presents with ataxia and asymmetric, non–length-dependent sensory deficits,[1-5] it less commonly presents as a chronic, slowly progressive neuropathy mimicking a pure sensory distal symmetric polyneuropathy (DSP).[6,7] In these cases, EDx may be helpful to discriminate SNN with a DSP phenotype from DSP.

The aim of this study was to determine the prevalence of the clinical DSP phenotype among SNN patients who met EDx criteria for SNN, at the time of electrodiagnosis. This can better inform the discussion about when to consider EDx in patients who present with a DSP phenotype.

2 | METHODS

This study and its methods were approved by the institutional review board of the University of Michigan.

We conducted a retrospective review of University of Michigan patients diagnosed with SNN between January 2000 and February 2021. We searched for all the patients coded as SNN using both the electronic medical record and EMGPro, an institutional database of EDx study results. We included patients over 18 years of age who met the "possible" or "probable" diagnostic criteria for SNN established by Camdessanché et al.[4] All patients had to meet EDx criteria for SNN, defined as: (a) at least one sensory nerve action potential (SNAP) absent or three SNAPs with amplitudes under 30% of the lower limit of normal in the upper limbs, not explained by entrapment neuropathy; and (b) fewer than two nerves with abnormal motor nerve conduction studies (NCS) in the lower limbs.[4] Patients who fulfilled the European Federation of Neurological Societies/Peripheral Nerve Society EDx criteria for possible, probable, or definite chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) were excluded. NCS reference values established by the American Association of Neuromuscular & Electrodiagnostic Medicine were used.[8]

We reviewed the clinical data at the time of EDx diagnosis. A DSP phenotype was defined according to the Toronto criteria as a length-dependent syndrome with at least one of the following: neuropathic symptoms (decreased sensation or positive symptoms such as tingling or pain); symmetric decreased distal sensation on examination; or unequivocally decreased or absent ankle reflexes.[9] A DSP phenotype was not considered if neuropathic symptoms were not length-dependent or if they progressed rapidly over 6 months or less.

We classified patients according to the most likely etiology as paraneoplastic, immune-mediated, toxic, nutritional, infectious, genetic, or idiopathic.[10]

2.1 | Statistical analysis

Categorical variables were classified using frequencies and percentages, whereas continuous variables were described using mean ± standard deviation and median with interquartile ranges.

3 | RESULTS

From January 1, 2000 through February 28, 2021, we identified 73 patients with a diagnosis of SNN. We excluded 11 patients: 7 patients did not meet EDx criteria, and 4 patients had EDx

TABLE 1 Baseline characteristics of patients with sensory neuronopathy

Characteristic	
Age, years, mean (SD)	55 (14)
Female gender, n (%)	44 (71%)
Time between symptom onset and EDx diagnosis, months, median (IQR)	18 (6-60)
Sensory neuronopathy diagnostic criteria, n (%)	
Possible	43 (69%)
Probable	19 (31%)
Etiology, n (%)	
Immune-mediated	16 (25.8%)
Paraneoplastic	4 (6.5%)
Toxic	3 (4.8%)
Nutritional	6 (9.7%)
CANVAS	5 (8%)
Idiopathic	28 (45.2%)

Abbreviations: CANVAS, cerebellar ataxia, neuropathy, and vestibular areflexia syndrome; EDx, electrodiagnosis; IQR, interquartile range; SD, standard deviation.

performed at a different institution or the EDx data were not available, leaving a final sample of 62 patients.

Most patients were female (71%) and the median age at onset was 55 years. Baseline characteristics are shown in Table 1. Among the patients classified as immune-mediated, ten had Sjögren syndrome; one had systemic lupus erythematous; four had positive fibroblast growth factor 3 antibodies, trisulfated heparin disaccharide antibodies, or both; and one had positive anti-GD1b immunoglobulin G antibodies. Among the patients classified as paraneoplastic, two had positive anti-Hu antibodies, one had positive anti-amphiphysin antibodies, and one had colon cancer with lung metastasis with no detectable onconeural antibodies. In the nutritional group, two had vitamin B_{12} deficiency, two had copper deficiency, and two had vitamin B_6 deficiency. In the toxic group, two were chemotherapy-related and one alcohol-induced. All patients with cerebellar ataxia, neuropathy, and vestibular areflexia syndrome (CANVAS) had genetic confirmation (Table 1).

3.1 | Symptoms

At onset, 20 (32.2%) patients presented with distal symmetric sensory symptoms in the feet only, 17 (27.4%) had ataxia, 8 (12.9%) had distal symmetric sensory symptoms in the feet and hands, 7 (11.3%) had distal symmetric sensory symptoms in the hands only, 7 (11.3%) presented with asymmetric sensory symptoms, 2 (3.2%) had axial sensory symptoms (burning neck and trunk pain), and 1 (1.6%) had proximal sensory symptoms (thigh tingling). Only 1 (1.6%) patient reported facial sensory symptoms.

Of the 20 patients who presented with sensory symptoms in the feet only, 11 (55%) progressed within 6 months; 2 (10%) had slowly progressive symptoms, which became asymmetric over time; and 3 (15%) persisted with a DSP phenotype. Four (20%) patients had stable symptoms for many years, but then symptoms rapidly progressed within months. In two of these four patients, initial EDx showed only mild sensory neuropathy when the symptoms were stable; however, after the symptoms progressed, EDx was consistent with SNN. The other two patients only had EDx after the progression of symptoms.

At full development, 60 (96.8%) patients reported sensory symptoms in the upper and lower extremities, 55 (88.7%) developed ataxia, 47 (75.8%) had a rapid progression within 6 months, 46 (74.2%) had a non–length-dependent pattern, and 25 (40.3%) had asymmetric symptoms or examination findings.

3.2 | Nerve conduction studies

Sural SNAP was recorded in 61 (98%) patients (49 absent, 7 low amplitude), ulnar SNAP was recorded in 62 (100%) patients (40 absent, 20 low amplitude), median SNAP was recorded in 54 (87%) patients (40 absent, 14 low amplitude), and radial SNAP was recorded in 61 (98%) patients (36 absent, 25 low amplitude). All sensory nerves were recorded in 54 (87%) patients, among whom 25 (46%) showed absent SNAP in all nerves, 47 (87%) showed amplitude abnormalities in all nerves, and 5 (9%) showed abnormal SNAP in all upper extremities sensory nerves but normal sural SNAP. A total of 42 (68%) patients showed normal responses in all motor nerves.

TABLE 2 Neurological examination of sensory neuronopathy patients with a distal symmetric polyneuropathy phenotype at time of electrodiagnosis

Motor exam, n (%)	
Normal	6 (86%)
Proximal weakness	1 (14%)
Sensory exam, n (%)	
Small-fiber involvement	7 (100%)
Large-fiber involvement	7 (100%)
Facial involvement	0 (0%)
Reflexes, n (%)	
Diffuse hyporeflexia or areflexia	2 (29%)
Absent bilateral ankle jerk reflex only	3 (43%)
Absent bilateral ankle jerk and patellar reflexes only	1 (14%)
Normal	1 (14%)
Coordination, n (%)	
Gait ataxia	4 (57%)
Lower limb ataxia	3 (43%)
Upper limb ataxia	3 (43%)
Positive Romberg sign	4 (57%)
Abnormal pupillary light reflex, n (%)	0 (%)
Assistive device needs	
Cane	1 (14%)
None	6 (86%)

3.3 | DSP phenotype prevalence at the time of electrodiagnosis

At the time of electrodiagnosis, seven (11.3%) patients who fulfilled electrodiagnostic criteria for SNN also fulfilled clinical criteria for probable DSP based on the Toronto criteria. Four of these patients were diagnosed with CANVAS, all presenting with gait ataxia at onset. One patient was classified as idiopathic, but the presence of abnormal eye saccades and lower extremity ataxia suggested possible CANVAS. This was never confirmed by genetic testing. One patient had vitamin B_6 deficiency, and one patient was classified as having alcohol-induced neuropathy.

Neurological examination data of these seven patients are presented in Table 2. The median follow-up time from the electromyography to the last neurological evaluation was 1.25 (range, 0-11.8) years.

4 | DISCUSSION

Prevalence of the DSP phenotype among patients with SNN at the time of EDx diagnosis is low. Previous studies have reported that inherited and idiopathic SNN can present with a chronic, slowly progressive phenotype resembling a sensory polyneuropathy, which is consistent with our findings.[3,6,7,10] We did not identify any cases of potentially treatable immune-mediated SNN with a DSP phenotype.

One third of the SNN patients presented with symmetric distal lower-extremity-predominant sensory symptoms resembling a sensory polyneuropathy. However, most patients developed asymmetric symptoms or rapidly progression within 6 months, which helped differentiate these cases from DSP. This emphasizes the importance of clinical monitoring in patients with a possible DSP phenotype, particularly during the first 6 months after symptom onset. It is unknown why some patients manifested a DSP phenotype for years, and only later developed clinical and electrodiagnostic evidence of SNN. This suggests that, in patients who present with a DSP phenotype, EDx may not be able to predict whether SNN will develop.

Most patients with SNN in our cohort presented with one of the following features: rapid progression, non–length-dependent presentation, early-onset ataxia, or asymmetric examination. The presence of any of these features should prompt physicians to consider additional investigations for SNN, including EDx. Most SNN patients with a DSP phenotype were diagnosed with CANVAS, and all these patients presented with ataxia at onset, so particular attention should be paid to apparent DSP patients with early-onset ataxia.

Limitations of this study include the retrospective and single-center study design. The fact that this study was performed in a large tertiary center may limit the generalizability of our findings. It is possible that some patients classified as having "possible" SSN may have actually had a sensory axonopathy rather than a neuronopathy, because we utilized clinical criteria to define SNN rather than pathological criteria, such as a dorsal root ganglion biopsy.

In conclusion, patients with SNN rarely present with a DSP phenotype at the time of EDx. However, our finding that one third of cases resemble DSP at onset highlights the importance of clinical monitoring. In patients with a DSP phenotype, the presence of ataxia at onset or significant progression within 6 months may suggest the possibility of SNN and should prompt additional investigations, such as EDx. Further studies are needed to determine the prevalence of ataxia at onset in patients with DSP.

CONFLICT OF INTEREST

None of the authors has any conflicts of interest to disclose.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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