Clinical and electrophysiological profiles in early recognition of polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes syndrome

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Abstract

Background: The detection of polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (POEMS) syndrome at early stage is challenging for neurologists. Since polyneuropathy could be the first manifestation, it could be misdiagnosed as chronic inflammatory demyelinating polyneuropathy (CIDP). The present study aimed to determine the clinical and electrophysiological features of POEMS syndrome to distinguish from CIDP.

Methods: The data of a group of patients with POEMS ($n = 17$) and patients with CIDP ($n = 17$) in Zhongshan Hospital Fudan University from January 2015 to September 2017 were analyzed in this retrospective study. The clinical features, neurological symptoms, and electrophysiological findings were compared between the two groups.

Results: Clinically, patients with POEMS demonstrated significantly more neuropathic pain in the lower extremities than patients with CIDP (58.8% *vs.* 11.8%, $P = 0.01$). Multisystem features like edema, skin change, organomegaly, and thrombocytosis were also pointed towards the diagnosis of POEMS syndrome. Electrophysiologically, terminal latency index (TLI) was significantly higher in patients with POEMS than that in patients with CIDP (median nerve: 0.39 [0.17–0.52] *vs.* 0.30 (0.07–0.69), $Z = -2.413$, $P = 0.016$; ulnar nerve: 0.55 [0.23–0.78] *vs.* 0.42 [0.12–0.70], $Z = -2.034$, $P = 0.042$). Patients with POEMS demonstrated a higher frequency of absent compound muscle action potential of the tibial nerve (52.9% *vs.* 17.6%, $P = 0.031$), less conduction block (ulnar nerve: 0 *vs.* 35.3%, $P = 0.018$), and less temporal dispersion (median nerve: 17.6% *vs.* 58.8%, $P = 0.032$) than CIDP group. The combination of positive serum monoclonal protein and high TLI (if either one or both were present) discriminated POEMS from CIDP with a sensitivity of 94.1% and 47.1% and specificity of 76.5% and 100.0%, respectively.

Conclusions: POEMS syndrome could be distinguished from CIDP through typical clinical and electrophysiological characteristics in practice. The combination of serum monoclonal protein and high TLI might raise the sensitivity of detecting POEMS syndrome.

Keywords: Polyneuropathy; Organomegaly; Endocrinopathy; M protein and skin changes syndrome; Chronic inflammatory demyelinating polyradiculoneuropathy; Terminal latency index

Introduction

Polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes (POEMS) syndrome is a paraneoplastic syndrome due to an underlying plasma cell neoplasm.[1] Polyneuropathy is usually the dominant and sometimes the first chief complaint of patients with POEMS syndrome, prompting consultation with neurology specialists. The pattern of neuropathy of POEMS syndrome is symmetrical sensory motor polyneuropathy and radiculoneuropathy and the electrophysiological studies often showed demyelinating features, which mimics the most common acquired demyelinating neuropathy-chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The treatments of the two diseases are completely different.[2,3] If misdiagnosed as CIDP, the specific treatment for POEMS syndrome may be postponed, thereby exacerbating the condition. For acquired demyelinating polyneuropathy, serum immunofixation electrophoresis is the first study to identify the presence of a monoclonal gammopathy.[4] If IgG or IgA monoclonal gammopathy is found, vascular endothelial growth factor (VEGF) assays, skeletal surveys, and bone marrow biopsy should be conducted. However, in practice, some patients with POEMS syndrome showed a negative serum immunofixation electrophoresis result at their first visit. Nonetheless, if each patient with acquired demyelinating polyneuropathy underwent a thorough examination, it would cause a high medical cost. This led us to identify the

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000318

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Chinese Medical Journal 2019;132(14)

Received: 28-01-2019 **Edited by:** Li-Shao Guo

specific pattern of clinical features and nerve conduction study results in POEMS syndrome and to discuss its role in distinguishing the two diseases at the early stage.

Therefore, we summarized the clinical manifestations and electrophysiological characteristics of a group of patients with POEMS syndrome from January 2015 to September 2017 in Zhongshan Hospital Fudan University, Shanghai, China and compared them to a group of patients with CIDP diagnosed in the same period. We analyzed the diagnostic threshold of common clinical and electrophysiological characteristics of POEMS syndrome which can aid the neurologists in recognizing and diagnosing this syndrome.

Methods

Ethical approval

The study was approved by the Ethics Committee of Zhongshan Hospital Fudan University. Informed consents were obtained from all the patients.

Participants

This retrospective observational study was conducted in a University-Affiliated hospital. A total of 17 consecutive patients with POEMS syndrome were included between January 2015 and September 2017. All patients fulfilled the diagnostic criteria of POEMS syndrome and were diagnosed by hematologists. The major criteria for the syndrome were polyneuropathy, clonal plasma cell disorder (PCD), sclerotic bone lesions, elevated VEGF, and the presence of Castleman disease. Minor features included organomegaly, endocrinopathy, characteristic skin changes, papilledema, extra-vascular volume overload (edema or ascites), and thrombocytosis. The diagnosis was based on three of the major criteria, two of which must include polyneuropathy and clonal PCD, and at least one of the minor criteria.[5] Also, 17 patients with CIDP were enrolled in the same study period. The diagnosis of CIDP fulfilled the diagnostic criteria for definite CIDP according to 2010 European Federation of Neurological Societies/Peripheral Nerve Society guideline.[5] Briefly, the criteria include clinically progressive, stepwise or recurrent symmetric motor weakness and sensory dysfunction of all extremities, developed over at least 2 months. In addition, the cranial nerve may be affected, and tendon reflexes may be absent or reduced in all extremities; these findings were supported by electrodiagnostic criteria, cerebrospinal fluid (CSF) results, magnetic resonance imaging (MRI), nerve biopsy, or treatment response. The diagnosis of CIDP was made by two expert neurologists.

Clinical manifestations and electrophysiological findings

Demographic characteristics (age, gender, height, and weight), internal medical findings (such as skin change, edema, and organomegaly), neurological manifestations (such as muscle weakness, loss of sensory, or neuropathic pain) were compared between POEMS syndrome and CIDP groups.

Data of neurophysiological tests were gathered from all participants to identify the electrophysiological characteristics of POEMS syndrome. A Medoc electroneurogram and electromyography system (Medoc Company, Israel) was used to perform nerve conduction tests. Sural sensory, superficial peroneal sensory, tibial motor, and peroneal motor nerve conduction tests were performed in the lower extremities while ulnar sensory, median sensory, ulnar motor, and median motor nerve conduction tests were performed in the upper extremities. Also, needle electromyography was performed in the chosen muscles of the upper and lower extremities.

Terminal latency index (TLI) was used to compare the conduction slowing in the distal and intermediate segments of the median and ulnar nerves, which was calculated using the following formula: TLI = terminal distance (mm)/(distal latency [ms] × conduction velocity [m/s]). The normal range of TLI was 0.20 to 0.40 for the median nerve and 0.29 to 0.49 for the ulnar nerve.[6] Conduction block was defined as a ≥50% change in amplitude proximal: distal irrespective of the distance. Distal compound muscle action potential (CMAP) had to be ≥1 mV. Temporal dispersion was defined as the duration of the distal potential/duration of the proximal potential <0.7. In order to evaluate the extent of length-dependent axon degeneration, tibial/median CMAP amplitude ratio was calculated.

Statistical analysis

Data are presented as number (%), median (range), or mean ± standard deviation. The differences between continuous valuables were analyzed using the Mann-Whitney *U* test. The differences in the categorical variables were compared using the Fisher exact test. A *P* value of less than 0.05 was considered to be statistically significant. SPSS (version 13.0, IBM Corporation, Somers, NY, USA) was used for statistical analysis.

Results

Demographic characteristics of the patients

Demographic parameters showed that gender, age, height, and weight were similar between POEMS syndrome and CIDP groups [Table 1]. The time course from the onset of the disease to administration was also similar in both groups (6 [2–25]) *vs.* 3 [1–24] months, $Z = -1.696$, $P = 0.09$). Two patients in CIDP group received steroid treatment before enrolling to the study while other patients in both groups did not undergo specific disease-modifying treatment.

Clinical characteristics

All patients with POEMS syndrome had peripheral neuropathy and plasma cell proliferative disorder. Although all of the patients with POEMS syndrome presented clonal plasma cell proliferative disorder, only 11 (64.7%) patients showed a positive result of serum immunofixation electrophoresis (IgA or IgG gammanopathy) results for

Table 1: Demographic data and neurological features of POEMS syndrome and CIDP.

Variables	POEMS syndrome ($n = 17$)	CIDP ($n = 17$)	t value	P value
Age (years)	57.59 ± 9.10	51.88 ± 17.42	1.197	0.240
Gender (male)	7 (41.2)	10 (58.8)	NA	0.490
Height (cm)	162.59 ± 7.54	165.17 ± 9.13	–0.901	0.374
Weight (kg)	64.23 ± 8.43	65.06 ± 8.74	–0.279	0.782
BMI (kg/m^2)	24.20 ± 1.58	23.71 ± 1.22	–0.962	0.343
With diabetes	1 (5.9)	2 (11.8)	NA	1.000
With hypothyroidism	9 (52.9)	2 (11.8)	NA	0.026*
Signs and symptoms				
Skin change	13 (76.5)	1 (5.9)	NA	<0.001*
Edema	14 (82.4)	1 (5.9)	NA	<0.001*
Weakness				
Upper extremities	8 (42.1)	9 (52.9)	NA	1.000
Lower extremities	11 (64.7)	14 (82.4)	NA	0.438
Numbness				
Upper extremities	13 (76.5)	10 (58.8)	NA	0.465
Lower extremities	17 (100.0)	15 (88.2)	NA	0.485
Neuropathic pain				
Upper extremities	3 (17.6)	2 (11.8)	NA	1.000
Lower extremities	10 (58.8)	2 (11.8)	NA	0.010*
Ataxia	3 (17.6)	5 (29.4)	NA	0.688
Tremor	0	1 (5.9)	NA	0.485
Laboratory findings				
Serum monoclonal protein	11 (64.7)	0	NA	<0.001*
Thrombocytosis	7 (41.2)	0	NA	0.007*
Ultrasound findings				
Hepatosplenomegaly	14 (82.4)	0	NA	<0.001*
Ascites	9 (52.9)	0	NA	<0.001*

Data are presented as n (%) or mean ± standard deviation. *$P < 0.05$. POEMS: Polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes; CIDP: Chronic inflammatory demyelinating polyneuropathy; BMI: Body mass index; NA: Not applicable.

the first test. For six patients with negative serum immunofixation electrophoresis results for the first time, two patients changed to positive results at repeated test 1 month later. Three patients underwent bone marrow biopsy or bone lesion biopsy and exhibited clonal plasma cell proliferation in the lesion. One patient demonstrated positive light-chain immunostaining in the abdominal wall subcutaneous fat biopsy. Thirteen (76.5%) POEMS syndrome patients had sclerotic bone lesions. VEGF was detected in 15 patients; of these, 14 showed an elevated level of VEGF. One patient showed the manifestation of Castleman disease. The other multisystem clinical manifestations in the POEMS syndrome included edema in the lower extremities (14/17, 82.4%), organomegaly (14/17, 82.4%), skin changes (13/17, 76.5%), ascites (9/17, 52.9%), and thrombocytosis (7/17, 41.2%). Internal medical examination, regular blood test, and abdominal ultrasound were also performed in patients with CIDP. The frequency of edema (1/17, 5.9%), organomegaly (0/17), skin changes (1/17, 5.9%), ascites (0/17), thrombocytosis (0/17) in CIDP group was significantly lower than that in POEMS syndrome group [Table 1].

With respect to the neurological signs and symptoms, both of the groups showed progressive symmetric numbness and weakness in the lower and upper extremities. Significantly more patients with POEMS syndrome experienced neuropathic pain in the lower extremities than CIDP patients (58.8% *vs.* 11.8%, $P = 0.010$). In POEMS syndrome, neuropathic pain was mostly located in the distal lower limbs, following a length-dependent pattern. Pricking pain, burning pain, squeezing pain, or pressure pain was described by patients with POEMS syndrome. Conversely, a majority of the patients with CIDP suffered from insensate neuropathy. Only two patients described pain in both the upper and lower limbs, not with length dependent pattern. The frequency of ataxia was similar between the two groups, while tremor was reported only in two patients with CIDP [Table 1].

Electrophysiological features

The electrophysiological parameters were summarized in Tables 2 and 3. Both of the two groups demonstrated demyelinating features in the motor nerves-prolonged distal motor latency (DML), reduced motor conduction velocity, and prolonged F wave latency. The rate of apparently prolonged DML (>200% upper limit of the normal values [ULN]) was lower in POEMS syndrome group than that in CIDP group (median nerve: 5.9% *vs.* 52.9%, $P = 0.007$; ulnar nerve: 5.9% *vs.* 47.1%, $P = 0.017$). TLI was significantly higher in patients with POEMS syndrome than that in those with CIDP in both median and ulnar nerves (median nerve: 0.39 [0.17–0.52] *vs.* 0.30 (0.07–0.69), $Z = –2.413$, $P = 0.016$; ulnar nerve: 0.55 (0.23–0.78) *vs.* 0.42 (0.12–0.70), $Z = –2.034$,

Table 2: Motor nerve conduction data for patients with POEMS syndrome and CIDP.

Variables	POEMS syndrome ($n = 17$)	CIDP ($n = 17$)	*Z* value	*P* value
Median nerve				
DML				
Value (ms)	5.6 (3.6–13.2)	9.2 (2.8–21.2)	–1.119	0.263
>200% ULN	1 (5.9)	9 (52.9)	NA	0.007*
MCV (m/s)	32.9 (17.7–45.7)	33.2 (16.6–52.3)	–0.258	0.796
F lantency (s)	40.3 (32.7–55.2)	39.8 (27.4–68.1)	–0.044	0.965
TLI				
Value	0.39 (0.17–0.52)	0.30 (0.07–0.69)	–2.413	0.016*
>ULN	9 (52.9)	2 (11.8)	NA	0.026*
cMAP (mV)	5.7 (0.1–10.4)	6.7 (0.3–13.1)	–0.482	0.63
Conduction block	0	4 (23.5)	NA	0.103
Temporal dispersion	3 (17.6)	10 (58.8)	NA	0.032*
Ulnar nerve				
DML				
Value (ms)	3.7 (2.8–6.7)	4.9 (2.3–13.9)	–1.705	0.088
>200% ULN	1 (5.9)	8 (47.1)	NA	0.017*
MCV (m/s)	33.5 (16.4–49.6)	33.7 (13.1–64.8)	–0.189	0.850
F lantency (s)	39.3 (32.4–58.4)	39.3 (27.8–59.2)	–0.631	0.528
TLI				
Value	0.55 (0.23–0.78)	0.42 (0.12–0.70)	–2.034	0.042*
>ULN	12 (70.6)	4 (23.5)	NA	0.015*
cMAP (mV)	5.8 (0.3–13.6)	4.6 (0.02–12.1)	–0.293	0.770
Conduction block	0	6 (35.3)	NA	0.018*
Temporal dispersion	3 (17.6)	9 (51.9)	NA	0.071
Tibial nerve				
No potential	9 (52.9)	3 (17.6)	NA	0.031*
DML				
Value (ms)	6.2 (4.6–8.0)	7.6 (3.5–19.6)	–0.956	0.339
>150% ULN (%)	0	5 (37.5)	NA	0.115
MCV (m/s)	24.5 (19.3–36.5)	31.5 (9.8–45.6)	–1.263	0.297
cMAP (mV)	0 (0–6.7)	2.7 (0–15.6)	–2.219	0.026*
Conduction block	1 (12.5)	4 (28.6)	NA	0.613
Temporal dispersion	2 (25.0)	8 (57.1)	NA	0.204
Tibial/median cMAP ratio	0 (0–1.43)	0.20 (0–1.64)	–2.853	0.049*
Peroneal nerve				
No potential	6 (35.3)	5 (29.4)	NA	1.000
DML				
Value (ms)	5.4 (4.1–7.4)	7.1 (3.5–25.7)	–0.862	0.389
>150% ULN (%)	0	5 (41.7)	NA	0.037*
MCV (m/s)	26.4 (18.7–42.3)	35.3 (20.4–48.2)	–1.785	0.074
cMAP (mV)	0.4 (0–4.9)	1.4 (0–11.7)	–0.543	0.587
Conduction block	0	4 (33.3)	NA	0.093
Temporal dispersion	1 (9.1)	7 (58.3)	NA	0.027*

Data are presented as *n* (%), median (range). *$P < 0.05$. POEMS: Polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes; CIDP: Chronic inflammatory demyelinating polyneuropathy; DML: Distal motor latency; MCV: Motor conduction velocity; TLI: Terminal latency index; ULN: Upper limit of the normal values; cMAP: Compound muscle action potential; NA: Not applicable.

$P = 0.042$], which indicated that POEMS syndrome had more predominant demyelination in the intermediate segment than that in the distal part. Compared with the CIDP group, patients with POEMS syndrome demonstrated a higher frequency of absent CMAP of the tibial nerve. The tibial/median CMAP amplitude ratio was significantly smaller for patients with POEMS syndrome compared with the patients with CIDP (0 [0–1.43] *vs.* 0.20 [0–1.64], $Z = –2.853$, $P = 0.049$), indicating a marked axonal loss in the lower extremities in POEMS syndrome. Conduction block and temporal dispersion were less frequent in POEMS syndrome group than that in CIDP group (ulnar nerve conduction block: 0 *vs.* 35.3%, $P = 0.018$; median nerve temporal dispersion: 17.6% *vs.* 58.8%, $P = 0.032$) [Table 2]. For sensory nerve conduction, patients with POEMS syndrome showed a reduced sensory conduction velocity in the upper extremities (median nerve: 40.0 [31.0–53.8] *vs.* 47.7 [39.4–62.2], $Z = –2.772$, $P = 0.006$; ulnar nerve: 38.3 [27.8–49.6] *vs.* 43.6 [32.9–56.9], $Z = –1.985$, $P = 0.047$). More than half of the patients in both groups showed absent SNAPs in the lower extremities. The reduction of SNAPs was similar in both groups [Table 3].

Table 3: Sensory nerve conduction data for patients with POEMS syndrome and CIDP.

Variables	POEMS syndrome ($n = 17$)	CIDP ($n = 17$)	*Z* value	*P* value
Median nerve				
No potential	3 (17.6)	8 (47.1)	NA	0.141
SCV (m/s)	40.0 (31.0–53.8)	47.7 (39.4–62.2)	–2.772	0.006*
SNAP (μV)	4.1 (0–15.0)	1.5 (0–15.1)	–1.402	0.161
Ulnar nerve				
No potential	3 (17.6)	8 (47.1)	NA	0.141
SCV (m/s)	38.3 (27.8–49.6)	43.6 (32.9–56.9)	–1.985	0.047*
SNAP (μV)	2.9 (0–14.1)	0.4 (0–12.8)	–1.629	0.103
Superficial peroneal nerve				
No potential	10 (58.8)	11 (64.7)	NA	1.000
SCV (m/s)	34.0 (28.7–45.6)	43.0 (23.6–52.4)	–1.574	0.116
SNAP (μV)	0 (0–12.3)	0 (0–40.9)	–0.197	0.844
Sural nerve				
No potential	9 (52.9)	7 (41.2)	NA	0.732
SCV (m/s)	36.8 (30.4–42.7)	40.6 (23.8–52.4)	–0.674	0.501
SNAP (μV)	0 (0–7.1)	1.6 (0–54.6)	–0.902	0.367

Data presented as *n* (%) or median (range). *$P < 0.05$. POEMS: Polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes; CIDP: Chronic inflammatory demyelinating polyneuropathy; SCV: Sensory conduction velocity; SNAP: Sensory nerve action potential; NA: not applicable.

Table 4: Diagnostic features discriminating the patients with POEMS syndrome from CIDP.

Diagnostic features	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
(1) Positive serum immunofixation electrophoresis	64.7	100.0	100.0	73.9
(2) High TLI	70.6	76.5	75.0	72.2
(3) Either (1) or (2) present	94.1	76.5	80.0	92.9
(4) Both (1) and (2) present	47.1	100.0	100.0	65.4

POEMS: Polyneuropathy,organomegaly, endocrinopathy, M-protein, and skin changes; CIDP: Chronic inflammatory demyelinating polyneuropathy; PPV: Positive predictive value; NPV: Negative predictive value; TLI: terminal latency index.

Preliminary diagnostic applications

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the positive serum monoclonal protein and high TLI are shown in Table 4. TLI that exceeded the ULN of the median or ulnar nerve was defined as high TLI. The combination of positive serum monoclonal protein and high TLI (if either one or both were present) discriminated POEMS syndrome from CIDP with a sensitivity of 94.1% and 47.1%, specificity of 76.5% and 100.0%, PPV of 80.0% and 100.0%, and NPV of 92.6% and 65.4%, respectively.

Discussion

The current study demonstrated the clinical and electrophysiological characteristics of POEMS syndrome, and discussed their value to distinguish POEMS syndrome from CIDP at the first visit. The electrophysiological features of POEMS syndrome were as followings: (1) high TLI indicated more severe demyelination in the intermediated segment than that in the distal part; (2) reduced tibial/median CMAP amplitude ratio indicated length-dependent axonal loss; (3) less conduction block and temporal disperse indicated more uniform demyelination than CIDP. The combination of positive serum monoclonal protein and high TLI (if either one or both were present) discriminated POEMS syndrome from CIDP with a sensitivity of 94.1% and 47.1% and specificity of 76.5% and 100.0%, respectively. The other clinical features of POEMS syndrome included length-dependent neuropathic pain, edema, skin change, and thrombocytosis, which were all distinguishing characteristics. These features should be considered as diagnostic clues at the first visit of the patient with demyelinating neuropathy.

As demonstrated previously, the neuropathy of POEMS syndrome was a symmetrical sensorimotor polyradiculoneuropathy. A majority of the patients followed a length-dependent pattern of polyneuropathy with steady progressive numbness and weakness which began in the lower extremities.[7-9] The frequency of neuropathic pain was significantly higher in POEMS syndrome group than that in CIDP group.[7] It has been reported that neuropathic pain was frequently experienced in patients with POEMS syndrome and was closely related to a reduction in the myelinated, but not unmyelinated fiber population.[10] Conversely, patients with CIDP demonstrated more objective symptoms and signs. Some patients might report non-specific muscle soreness, but few reported neuropathic pain.[11]

The electrophysiological features of POEMS syndrome patients in our group were similar to those reported

previously.[7,12-14] Sung *et al*[14] first described the electrophysiological features of eight patients with POEMS syndrome. In 2012, two large cohort studies summarized the characteristics of POEMS syndrome as follows: (1) more uniform slowing of nerve conductions, (2) rare conduction blocks and temporal dispersion, (3) greater axonal loss in the lower extremities, (4) higher TLI.[7,13] Our study also found that POEMS syndrome had demyelination as well as axonal damage. The demyelinating feature of POEMS syndrome was uniformed and primarily localized in the intermediate segment of the nerve while the axonal damage occurred in a length-dependent manner. The demyelinating feature of POEMS syndrome might be attributed to the blood-nerve barrier disruption by M protein-mediated activation immunoreaction, and the effect of VEGF leading small vessel permeability change. Sensory nerve demyelination and axonal loss were also observed in patients with POEMS syndrome.[15] We found that patients with POEMS syndrome showed lower sensory conduction velocity in the upper extremities. As more than half of the patients in both POEMS and CIDP groups present absent SNAP amplitude in our study, the severe damage caused a "ceiling effect" and interfered with the comparison of POEMS syndrome and CIDP. Some electrophysiological markers such as blink R1 latency were considered valuable in defining demyelination and detecting improvement in severely affected patients with POEMS.[16]

In addition to summarizing the distinguishable features of POEMS syndrome, our study also discussed the implication of these profiles in clinical practice. We found that in more than 1/3 of the patients, serum protein electrophoresis failed to detect monoclonal protein for the first test. This reminds us that we could not rely on serum electrophoresis alone to suspect POEMS syndrome. Typical clinical manifestations and electrophysiological features might be critical for the diagnosis. TLI provides information on the nerve conduction tests to discriminate POEMS syndrome from CIDP with acceptably high sensitivity and specificity. The combination of high TLI and serum monoclonal protein could raise the sensitivity of diagnosing POEMS syndrome to 94.1% (if either one is presented), indicating that if either one is presented, POEMS syndrome should be suspected and follow-up examinations should be performed. Moreover, the presence of neuropathic pain, edema, organomegaly, and characteristic skin change should raise the concern for POEMS syndrome.[8,9,17] Thus, POEMS syndrome might be suspected through serum immunofixation plus preliminary clinical examination and electrophysiological tests which can be easily performed at the outpatient department. With greater certainty, more systemic examinations such as skeletal imaging, serum VEGF, and positron emission tomography and computed tomography should be ordered to confirm the diagnosis. If the result of serum electrophoresis was negative, bone marrow examination and biopsy of other tissues might be essential to find the evidence of monoclonal plasma cell proliferation. However, as the specificity of TLI was 76.5%, which means high TLI or other neurophysiological features could not rule out the possibility of CIDP. For the suspected patients, if systemic laboratory exams failed to direct to POEMS syndrome, other studies like CSF or MRI for spinal root were also needed.

Nevertheless, the limitation of the present study included the small sample size due to the rarity of POEMS syndrome. The limited sample size would influence the reliability of the parameters in the diagnostic part. A larger sample study would be warranted in the future to validate the diagnostic value of TLI and serum monoclonal protein. Furthermore, although VEGF had been proven to be a highly accurate surrogate biomarker of disease detection,[18] in our study it was tested only in POEMS patients, not in patients with CIDP; thus, we could not evaluate the discriminative power of this factor.

In conclusion, POEMS syndrome should be considered in patients with neuropathic pain, especially in the lower extremities and also in patients with polyradiculoneuropathy accompanying edema, characteristic skin lesion, thrombocytosis, or organomegaly. The electrophysiological characteristics supporting POEMS syndrome included higher TLI, less conduction block and temporal disperse, and more obvious length-dependent axonal degeneration compared to CIDP. The combination of serum monoclonal protein and high TLI might raise the sensitivity in detecting POEMS syndrome.

Conflicts of interest

None.

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How to cite this article: Wang Q, Liu P, Ji LL, Wu S, Feng GD, Wang X, Dong JH. Clinical and electrophysiological profiles in early recognition of polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes syndrome. Chin Med J 2019;132:1666–1672. doi: 10.1097/CM9.0000000000000318