



Case report

Better prognosis in POEMS patients with cerebral infarction before polyneuropathy

Xiaoxi Lan^{*}, Wanling Sun, Yixian Guo, Xiaoli Chang, Guoxiang Wang, Ronghua Hu

Xuanwu Hospital Capital Medical University, Beijing 100053, China

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ABSTRACT

POEMS syndrome is a plasma cell disease. Clinical manifestations and clinical onset are variable. In recent years, more and more cases of POEMS syndrome with cerebrovascular disease and ischemic stroke have been reported. However, it is rare for patients with POEMS syndrome to present with a cerebrovascular accident as the first clinical manifestation. We presented three cases of POEMS syndrome with cerebral infarction in different phases of the disease. We then searched the literature for studies involving POEMS syndrome complicated with cerebral infarction. There were 81 cases in total. In nine patients, cerebral infarctions occurred before polyneuropathy. Patients with cerebral infarction before polyneuropathy have better prognosis of POEMS than those with cerebral infarction after polyneuropathy.

1. Introduction

POEMS syndrome, named as the acronym for polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes, is a plasma cell disease in which monoclonal immunoglobulin is produced. Clinical manifestations are variable, and clinical onset is very different between individuals. The pathogenesis of POEMS syndrome is not yet clear. Increased vascular endothelial growth factor (VEGF) is thought to be an important biomarker to predict the treatment response and survival. VEGF can increase vascular permeability and promote vascular endothelial cell proliferation and neovascularization, which may induce thrombosis of different types. Platelet instability and the presence of a paraprotein may also result in thrombosis [1]. In recent years, an increasing number of cases of POEMS syndrome with cerebrovascular disease and ischemic stroke (IS) have been reported. A large-scale study by the Mayo Clinic [2] suggested that cerebrovascular accidents occur at a median of 23 months after the occurrence of peripheral polyneuropathy, and the risk at 5 years is 13.4%. However, another large-scale study with 510 patients reported that 8.0% of patients had a history of IS, and in 30 patients (73.1%), IS had occurred before POEMS syndrome was diagnosed [3]. Hence, it is rare for patients with POEMS syndrome to present with a cerebrovascular accident as the first clinical manifestation or before polyneuropathy. In this study, we reported three cases of POEMS syndrome with cerebral infarction. We also searched for and analyzed articles about POEMS syndrome with

stroke, especially those where stroke had been the first clinical presentation and cerebral infarction had occurred before polyneuropathy.

2. Materials and methods

2.1. Case reports

Case 1: On September 5, 2018, a 55-year-old Chinese man was admitted to our department with the complaint of weakness, numbness, and swelling of both lower limbs lasting for one month. Moreover, 4 months before, he had been admitted to a hospital because of weakness in the right lower limb and a walking disorder lasting for one day. The magnetic resonance imaging (MRI) scans showed early cerebral infarction (Figure 1c). The computed tomography angiography (CTA) showed local stenosis of the left anterior cerebral artery (Figure 1d). Diagnosed with acute cerebral infarction, the patient was treated with aspirin and atorvastatin, which led to a relief of his symptoms. His prior medical history included alcohol consumption for 20 years, about 250 mL per day, with no history of hypertension, diabetes, coronary heart disease, hyperlipidemia, smoking or vascular injury secondary to trauma. Physical examination revealed hyperpigmentation (Figure 1a and b), pale nails, and no palpable lymph nodes. Blood analysis showed $5.17 \times 10^9/L$ WBC, 138 g/L Hb, and $384 \times 10^9/L$ (normal range, $100\text{--}300 \times 10^9/L$) PLT. The level of fibrinogen was 4.5 g/L (normal range, 2–4 g/L). Immunoelectrophoresis showed a monoclonal serum immunoglobulin

* Corresponding author.

E-mail address: xiaoxi_lan@outlook.com (X. Lan).

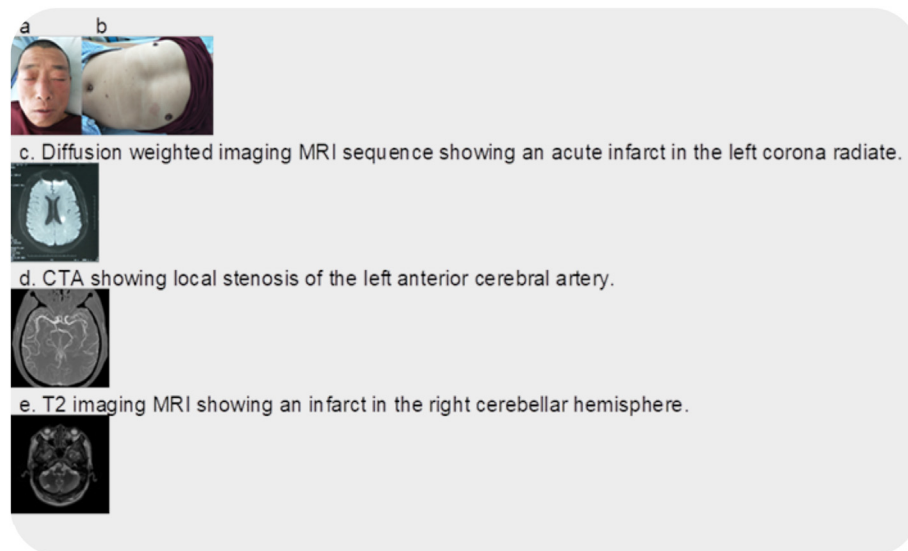


Figure 1. Patient and images of case 1.

IgA- λ . Serum VEGF level was >800 pg/mL (normal range, 0–142 pg/mL). Fundus examination revealed edema of both optic discs. Bone marrow cytology examination showed significant bone marrow hyperplasia, with plasma cells accounting for 0.5%; whole megakaryocytes were larger than 200. Flow phenotyping of bone marrow showed no evidence of monoclonal plasmacytes. Endocrine tests demonstrated a delayed C peptide-insulin release peak, cortisol and ACTH rhythm abnormality, and increased prolactin level. The MRI scans showed an infarction of the right cerebellar hemisphere, which had not been seen the previous time (Figure 1e). Thoracic and abdominal pelvic CT showed mediastinal lymphadenopathy and splenomegaly. No osteosclerosis was found by bone scanning. In summary, the diagnosis of POEMS syndrome was made, which was based on polyneuropathy, monoclonal immunoglobulin, high level of VEGF, endocrine changes, skin changes, organomegaly, optic papilledema, swelling of limbs, and thrombocytopenia. And the patient received six cycles of CTD chemotherapy (cyclophosphamide + dexamethasone + thalidomide), one course every 35 days. The date of the last cycle was March 25, 2019, after which thalidomide was continued as a maintenance treatment. After four cycles, skin hyperpigmentation and edema of both optic discs were relieved, and VEGF decreased to 140 pg/mL. After five cycles, muscle strength recovered gradually. Meanwhile, his immunoelectrophoresis showed no monoclonal immunoglobulin. At the time of the last follow-up (March 2020), the patient was still in remission and he could look after himself very well in normal daily life.

Case 2: In April 2013, a 34-year-old man was admitted to our hospital because of abdominal distension, weakness of the lower limbs, weight loss during half a year, and weakness of the upper limbs lasting for 2 months. After a detailed medical history inquiry, we found out that he had a previous bilateral breast hyperplasia 11 months before and had undergone an operation for breast reduction in the local hospital. Ten months ago, suddenly he could not speak clearly, and he was diagnosed with cerebral infarction. After the rehydration treatment, his speech recovered within one week. However, 8 months ago, blood test revealed increased PLT count ($1000 \times 10^9/L$). His prior medical history was positive for alcohol and smoking, and he had no history of hypertension, diabetes, coronary heart disease, hyperlipidemia or vascular injury secondary to trauma. Physical examination revealed hyperpigmentation of the face and body, as well as multiple palpable lymph nodes. Bilateral breast hyperplasia and abdominal distension were also found. Bone marrow cytology examination showed immature plasma cells accounting for 5.5% and mature plasma cells accounting for 4.5%. Immunoelectrophoresis showed a monoclonal serum immunoglobulin IgA- λ .

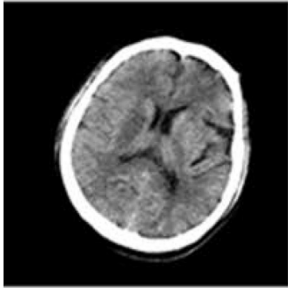
Taken together, the patient was diagnosed with POEMS syndrome, based on polyneuropathy, monoclonal immunoglobulin, high level of VEGF, endocrine changes, skin changes, organomegaly, optic papilledema, swelling of limbs, and thrombocytopenia (without VEGF analysis, bone scanning or pathologic result of palpable lymph nodes at that time). And he received one cycle of the CTD chemotherapy. However, no clinical improvement occurred. Then, he received four cycles of BD chemotherapy (bortezomib + dexamethasone), one course every 35 days. During that treatment, his abdominal distension improved after only one cycle, while his muscle strength recovered gradually, so he could walk by himself after two BD cycles. His immunoelectrophoresis showed no monoclonal immunoglobulin after four BD cycles. Then autologous hematopoietic stem cells were reinfused on October 29, 2013. The patient's last telephone follow-up was in January 2020. The patient reported being in good condition, walking almost normally, and living a normal life.

Case 3: A 41-year-old man was admitted to the neurology department of our hospital on June 17, 2020. He had numbness in both feet in February 2019, which gradually worsened along with weakness of the distal ends of both lower limbs. He was admitted to the local hospital and diagnosed with Guillain-Barré syndrome. Although he experienced slight improvement after the treatment with gamma globulin, his condition soon exacerbated, and he could not walk anymore. Moreover, he started feeling numbness and weakness in both hands, which was resistant to the treatment with gamma globulin and glucocorticoids. In February 2020, the patient felt dyspnea in supine position, relieved by side lying and sitting. His prior medical history included only smoking, with no history of hypertension, diabetes, coronary heart disease, hyperlipidemia, alcohol or vascular injury secondary to trauma. Complete blood cell count showed WBC $13.4 \times 10^9/L$, Hb 178 g/L, and PLT $324 \times 10^9/L$. Chest CT showed that the right diaphragm was raised, and the right lung was compressed (Figure 2a). Abdominal CT showed hepatosplenomegaly. No lymphadenopathy. On June 20, he suddenly became unresponsive and started drooling from the left corner of the mouth. The head CT showed an infarct of the right basal ganglia (Figure 2b). Immunoelectrophoresis showed a monoclonal serum immunoglobulin IgA- λ . VEGF level was 791.14 pg/mL. X-ray scan showed multiple dot-like dense shadows in the vertebrae, ilium, and sacrum. Fundus examination revealed edema of both optic discs. Endocrine tests demonstrated abnormal secretion of sex hormones, parathyroid hormone, and C peptide-insulin. Bone marrow cytology examination did not find plasma cells. Diagnosed with POEMS syndrome which was based on polyneuropathy, monoclonal immunoglobulin, high

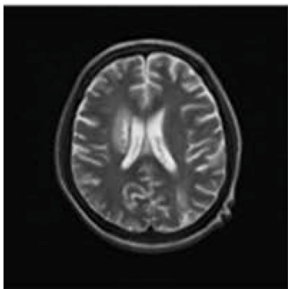
a.



b. CT showing sheet-shaped low-density shadow of the right basal ganglia.



c. T2 imaging MRI shows an increasing-area infarct.



d. Enhanced CT of the head shows bilateral distal internal carotid artery stenosis, severe stenosis, or occlusion of the distal M1 segment of the middle cerebral artery on both sides, and severe brain atrophy.

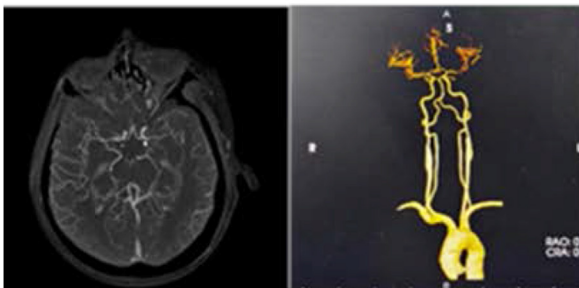


Figure 2. Images of case 3.

level of VEGF, osteosclerosis, endocrine changes, organomegaly, optic papilledema, polycythemia, and thrombocytopenia, he was transferred to our department. On July 14, 2020, BD chemotherapy was started. During the chemotherapy, the patient's dyspnea was significantly relieved, but his unresponsiveness further deteriorated. On August 13, 2020, the patient received a head-enhanced CT, after which he was returned to the ward with a sudden chill accompanied by dyspnea and urinary incontinence, and he was treated with oxygen. Later, the patient's blood pressure dropped, and hypoxemia, disturbance of consciousness, and fever developed. Contrast agent was considered an allergen, and he was treated with hydrocortisone, diphenhydramine, epinephrine, and

dopamine. He experienced two seizures, manifested as refractory response, right vision, and right upper limb tremor for 5 s. After administration of phenobarbital and diazepam, the consciousness recovered, and the vital signs gradually stabilized. The patient's MRI 9 days before showed abnormal signals in the right frontal lobe-lateral paraventricular-basal ganglia, left frontal lobe, and left parieto-occipital lobe (Figure 2c). The head-enhanced CT showed bilateral distal internal carotid artery stenosis, severe stenosis or occlusion of the distal M1 segment of the middle cerebral artery on both sides, and severe brain atrophy (Figure 2d). Afterwards, the patient was automatically discharged from the hospital due to inability to afford further treatment.

2.2. Literature review

We searched for “POEMS syndrome” and “cerebral infarction” or “stroke” on the PubMed and Wanfang databases to identify studies involving POEMS syndrome complicated with cerebral infarction. The search interval began in 1990 and was completed in July 2020. There were no language restrictions, and the selected studies included both case reports and large-scale research studies. However, articles or abstracts from scientific conferences were not included.

3. Results

Our study includes 29 articles [4, 5, 6, 7, 8, 9, 10, 3, 11, 12, 13, 14, 15, 16, 17, 18, 19, 2, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30] of which there were 10 articles in Chinese and 19 articles in English. The publication time was from 1991 to 2020. In total, there were 91 cases of POEMS syndrome with cerebral infarction; 31 of them were presented in the form of case reports. The remaining 60 cases were included in two studies: one study was conducted at the Mayo Clinic, reporting nine patients with relatively complete clinical descriptions; the other study was done at the Peking Union Medical College Hospital. Among all these cases, nine patients had ischemic stroke as the first sign of POEMS syndrome.

3.1. Characteristics of the POEMS syndrome cases with cerebral infarction in western and Asian populations

There were 28 women and 53 men. The age ranged from 24 to 79 years. The time interval between the stroke onset and POEMS syndrome onset ranged from 40 months before polyneuropathy to 64 months after polyneuropathy. Most patients (more than 70%) in Asian case reports did not have risk factors for stroke, such as hypertension, hyperlipidemia, diabetes, smoking, or family history of stroke at a young age. The Mayo Clinic data showed that among 19 POEMS patients with cerebral infarction, 47% had hypertension, 32% had hyperlipidemia, 16% had diabetes, and 53% had a history of smoking. In the Union Medical College Hospital study, 22% of the patients had hypertension, 7% had hyperlipidemia, 15% had diabetes, and 10% had a positive smoking history. At least 21 of the 81 patients were undergoing treatment for POEMS syndrome when stroke occurred. At least 15 of the 81 patients had Castleman disease at the same time.

3.2. Characteristics of the cases with ischemic stroke as the clinical onset of POEMS syndrome or with ischemic stroke before polyneuropathy

Of the nine patients [10, 17, 19, 20, 26, 27, 28], there were two women and seven men. Their median age was 40 years (range: 32–68 years). Only a 32-year-old male patient had a risk factor for stroke as he was a smoker. The median time interval from the first stroke to the diagnosis of POEMS syndrome was 6 months (range: 3–40 months). Six patients suffered from a second stroke; in one patient, the stroke occurred after the diagnosis of POEMS syndrome. However, all the patients recovered from stroke during a short time with or without antiplatelet drugs. One patient was diagnosed with biopsy-negative CNS vasculitis and was suspected of having systemic vasculitis before the diagnosis of POEMS syndrome. All nine patients had the symptoms of peripheral neuritis when they were diagnosed with POEMS syndrome. Moreover, eight of these patients had significant manifestations on the skin, including acrocyanosis, hyperpigmentation, rash, clubbing, nail changes, and hypertrichosis. One patient complained of autonomic system symptoms (increased sweating, erectile dysfunction, and orthostatic dizziness). One patient presented with edema of all four limbs. Six patients had hepatomegaly, splenomegaly, or lymphadenopathy on physical examination, and in two patients, pleural effusions or ascites were found.

The infarctions in the nine patients involved different lobes of the brain, corona radiata radial crowns, and basal ganglia. Only two patients had cerebral infarction at a single site, while others were

diagnosed with multiple-site infarctions. However, in three patients, the arteries were normal as viewed on Doppler, CTA, or MRI angiography. Six patients presented with thrombocytosis. One patient had intense hyperfibrinogenemia. In four patients, vascular endothelial growth factor (VEGF) levels were measured and demonstrated high levels. Some patients did not have monoclonal plasma cells in bone marrow. The types of M-spike included IgA-lambda (5/9), IgG-lambda (1/9), IgG-kappa (1/9), and lambda light chain (1/9). One patient was without M-spike.

Two patients received a successful autologous stem cell transplantation (ASCT), which reduced their symptoms. Two patients were successfully treated with melphalan and prednisolone. The condition of one patient improved through bortezomib and dexamethasone treatment. One patient had progression after treatment with cyclophosphamide and prednisolone. A patient who was diagnosed with POEMS syndrome 40 months after the first stroke was too ill to be treated and died.

4. Discussion

Since POEMS syndrome is a treatable but not a curable disease, with a 10-year overall survival rate of 93%, according to a report in Japan [22], treatment goals are to improve the symptoms. Thus, it is essential to make a rapid diagnosis of POEMS syndrome before irreversible neurological disabilities.

According to the most recent diagnostic criteria [31], polyneuropathy is the most important for the diagnosis of POEMS. However, there is often only hand or feet weakness or abnormal sensation in the early phase of the disease, which may be difficult to detect except by EMG. In our study, in nine reported cases that with stroke before PN, their first stroke occurred at a median of 6 months (range, from 3 to 40 months) before the diagnosis of POEMS syndrome. In cases 1 and 2 from this current study, the time interval was 4 and 10 months, respectively, and these patients complained of weakness in the lower limbs only 2 and 4 months after their stroke, respectively. Such tight intervals may suggest that polyneuropathy precedes or coincides with cerebral infarction. In addition, in most POEMS patients, organomegaly, endocrinopathy, or extravascular volume overload are not easy to detect, unlike skin changes that are easy to identify by a simple physical examination. In 11 cases in our study, all patients had skin changes, and more than half of the patients had palpable hepatomegaly, splenomegaly, or lymphadenopathy on physical examination. At present, all patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) need to be watched for POEMS syndrome. We should also pay special attention to the occurrence of stroke at a relatively young age without relevant risk factors. Strict medical history collection and physical examination are necessary to support the diagnosis of POEMS syndrome in time or remind physicians of POEMS syndrome. In a comprehensive literature analysis of cerebral infarction in POEMS syndrome [6], as well as in the Mayo Clinic study [2], it was shown that a wide spectrum of infarct topographies and abnormalities within the cervical and proximal intracranial vasculature and multiple-site cerebral infarctions were more common than simple-site infarctions. In some patients, changes in arteries did not match the area of cerebral infarction. Among the 11 cases with the onset of stroke before the onset of polyneuropathy, seven patients had speech difficulties. It is interesting that all the patients recovered from stroke within about 2 weeks only by antiplatelet drugs or even spontaneously. Further, more than half of the patients suffered a second stroke but recovered within a short time. Usually, recurrent cerebral infarction indicates a hypercoagulable state, which may result in a poor prognosis and calls patients and physicians' attention to identify the reason. Thus, clinicians should be aware that POEMS may be possible after a recurrent cerebral infarction with a good prognosis.

Fang-Wang Fu et al. [6] observed fatal outcomes in POEMS patients complicated with ischemic stroke. However, in our study, most patients who had stroke as the first clinical manifestation of POEMS syndrome

had a good prognosis. Due to the insufficient number of cases, we can't know why the patients with cerebral infarction before peripheral neuropathy have a good prognosis. We suspect that when peripheral neuropathy has no clinical manifestations, the patients are in the early stage of the disease. Although the patients are in a hypercoagulable state, they won't suffer from large-scale infarction, so they recover quickly. When peripheral neuropathy begins to appear, the patients seek medical attention actively to get more timely diagnosis and treatment of POEMS. On the contrary, the patients with cerebral infarction after peripheral neuropathy or even after POEMS treatment are in a progressive stage, and even the hypercoagulable state of the patients is not relieved and further aggravated during the treatment, so the prognosis is very poor.

Declarations

Author contribution statement

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

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References

- [1] Teruhiko Sekiguchi, Satoru Ishibashi, Sasame Jo, Recurrent stroke due to quasi-moyamoya disease associated with POEMS syndrome: an autopsy case, *J. Neurol. Sci.* 412 (2020), 116738.
- [2] Shadi Yaghi, S. V. Elkind Mitchell, Paraneoplastic progressive vasculopathy as the presenting manifestation of polyneuropathy, organomegaly, endocrinopathy or edema, M-spike, and skin manifestations: a case report, *J. Stroke Cerebrovasc. Dis.* 25 (7) (2016) e103–e107.
- [3] Jun Feng, Xue-min Gao, Hao Zhao, et al., Ischemic stroke in patients with POEMS syndrome, *Blood Adv.* 4 (14) (2020) 3427–3434.
- [4] Akihiko Mitsutake, Hideyuki Matsumoto, Keiko Hatano, Lenalidomide-induced ischemic cerebrovascular disease in polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes syndrome, *J. Stroke Cerebrovasc. Dis.* 27 (6) (2018) e102–e103.
- [5] Björn Sommer, Jens Schaumberg, Therapeutic challenges in a patient with POEMS syndrome and recurrent stroke: presentation of a case and review of the literature, *Acta Neurol. Belg.* 112 (1) (2012) 9–13.
- [6] Fang-Wang Fu, Jie Rao, Yuan-Yuan Zheng, Ischemic stroke in patients with POEMS syndrome: a case report and comprehensive analysis of literature, *Oncotarget* 8 (51) (2017) 89406–89424.
- [7] H. Fujii, H. Yashige, T. Kanoh, Progression from Crow-Fukase syndrome with double gammopathy (IgM-kappa, IgG-lambda) to primary macroglobulinemia, *Rinsho Ketsueki* 32 (8) (1991) 890–896.
- [8] Hang Yu, Fang Yao, Li Yue, Castleman disease variant of POEMS syndrome complicated with multiple cerebral infarction: a rare case report and review of literature, *Int. J. Clin. Exp. Pathol.* 8 (10) (2015) 13578–13583.
- [9] J. Huang, L. Wang, W. Zhou, Hyaline vascular castelman disease associated with POEMS and cerebral infarction, *Ann. Hematol.* 86 (1) (2007) 59–61.
- [10] Jian Jing, Zipan Zhao, Xiaomei Ren, Recurrent cerebral infarction in POEMS syndrome: a case report and literature review, *Zhong Guo Shi Yong Shen Jing Ji Bing Za Zhi* 14 (3) (2011) 46–48.
- [11] Kenichi Sakuta, Taiji Mukai, Kazuhito Suzuki, Irreversible vasculopathy proceeds rapidly in POEMS syndrome, *Intern. Med.* 58 (24) (2019) 3573–3575.
- [12] Xiaohui Li, Yuteng Ren, Shiqing Ren, A case of POEMS syndrome associated with bilateral cerebral infarction, *Yi Nan Bing Za Zhi* 9 (2015) 971–972.
- [13] Xiaoxia Liu, Quanzheng Pang, Guimei Zhang, A case of POEMS syndrome associated with cerebral infarction and literature review, *J. Apoplexy Nerv. Dis.* 33 (9) (2016) 848–849.
- [14] Mi Ra Lee, Hyo Jin Choi, Eun Bong Lee, POEMS syndrome complicated by extensive arterial thromboses, *Clin. Rheumatol.* 26 (11) (2007) 1989–1992.
- [15] Mihaela Găman, Ana-Maria Vlădăreanu, Camelia Dobrea, POEMS syndrome complicated with multiple ischemic vascular events: case report and review of literature, *OncoTargets Ther.* 11 (2018) 627 1–6276.
- [16] P. Dacci, F. Lessi, E. Dalla Bella, Ischemic stroke as clinical onset of POEMS syndrome, *J. Neurol.* 260 (12) (2013) 3178–3181.
- [17] Reza Boostani, Zahra Baghestani, Polyneuropathy, organomegaly, endocrinopathy, Monoclonal protein, skin changes (POEMS) syndrome complicated by ischemic stroke: a case report, *Iran J. Neurol.* 17 (2) (2018) 95–96.
- [18] Roopa Rajan, Vinny Wilson, Biplab Das, Stroke and POEMS syndrome: more than a chance association, *Neurol. India* 64 (6) (2016) 1318–1319.
- [19] S.A. Dupont, A. Dispenzieri, M.L. Mauermann, Cerebral infarction in POEMS syndrome: incidence, risk factors, and imaging characteristics, *Neurology* 73 (16) (2009) 1308–1312.
- [20] Keddie Stephen, M.P. Lunn, POEMS syndrome, *Peripher. Nerve Neuro-muscular Junct. Dis.* 31 (5) (2018) 551–558.
- [21] Tomoki Suichi, Sonoko Misawa, et al., Prevalence, clinical profiles, and prognosis of POEMS syndrome in Japanese nationwide survey, *Neurology* 93 (10) (2019) 975–983.
- [22] Tracey Garcia, Rima Dafer, Sara Hocker, Recurrent strokes in two patients with POEMS syndrome and Castleman's disease, *J. Stroke Cerebrovasc. Dis.* 16 (6) (2007) 278–284.
- [23] Hongyan Wang, Wei Li, Zhongyuan Zhao, A case of POEMS syndrome associated with cerebral infarction, *J. Apoplexy Nerv. Dis.* 23 (4) (2006) 421.
- [24] Jie Wang, Wei Guangru, Yan Xu, Cerebral infarction in POEMS syndrome associated with Castleman disease: a case report and literature review, *Shandong Med. J.* 59 (5) (2019) 71–74.
- [25] Zigao Wang, Guanqun Wang, Hengbing Zu, Recurrent cerebral infarction in POEMS syndrome: a case report and literature review, *J. Apoplexy Nerv. Dis.* 33 (3) (2016).
- [26] Shufang Wu, Guoqing Zhou, Zufu Zhu, A case of POEMS syndrome with recurrent acute cerebral infarction as a major manifestation, *Zhong Hua Wei Zhong Bing Ji Jiu Yi Xue* 25 (12) (2013) 753.
- [27] Wei Xu, Chen Chen, Jing Yang, Cerebral infarction in POEMS syndrome: a case report and literature review, *Pract. Clin. Med.* 19 (9) (2018).
- [28] Shuqin Zhan, Jianping Jia, Moli Wang, POEMS associated with acute cerebral infarction, *Chin. J. Med. Imaging Technol.* 18 (1) (2002) 30–31.
- [29] Huifen Zheng, A case of POEMS syndrome associated with cerebral infarction, *J. Med. Theor. Pract.* 21 (5) (2008) 533–535.
- [30] Zigao Wang, Xiong Lu, Hengbing Zu, Recurrent stroke as the clinical onset of POEMS syndrome, *J. Clin. Neurol.* 13 (2) (2017 Apr) 199–200.
- [31] A. Dispenzieri, T. Kourelis, F. Buadi, POEMS syndrome: diagnosis and investigative work-up, *Hematol. Oncol. Clin. N. Am.* 32 (2018) 119–139.