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The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes syndrome with dilated cardiomyopathy: A case report

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Abstract

BACKGROUND

Polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes (POEMS) syndrome is a rare paraneoplastic syndrome that encompasses multiple systems. The most common clinical symptoms of POEMS syndrome are progressive sensorimotor polyneuropathy, organ enlargement, endocrine disorders, darkening skin, a monoclonal plasma cell proliferative disorder, and lymph node hyperplasia. The organomegaly consists of hepatosplenomegaly and/or lymphadenopathy; cases of cardiomyopathy are rare. Diagnoses are often delayed because of the atypical nature of the syndrome, exposing patients to possibly severe disability. Therefore, identifying atypical symptoms can improve the prognosis and quality of life among POEMS syndrome patients.

CASE SUMMARY

Herein, we report the case of a 59-year-old woman with POEMS syndrome that involved dilated cardiomyopathy. The patient presented to the hospital with complaints of shortness of breath and discomfort in the chest. The patient reported previous experiences of limb numbness. During hospitalization, the brain natriuretic peptide levels were 3504.0 pg/mL. Color doppler echocardiography showed an enlarged left side of the heart, along with ventricular wall hypokinesia and compromised functioning of the same side of the heart. Abdominal color ultrasonography revealed that the patient's spleen was enlarged. Observations from cardiac magnetic resonance imaging showed that the left side of the heart was enlarged. Slight myocardial fibrosis was also observed. Electromyography was described as a symmetric sensorimotor demyelinating polyneuropathy. Further immunoelectrophoresis of the serum showed the presence of a monoclonal IGA λ M protein. The vascular endothelial growth factor levels were 622.56 pg/mL. Flow cytometric and immunohistochemical staining of the bone marrow detected no monoclonal plasma cells. Finally, the patient was diagnosed with POEMS syndrome associated with dilated cardiomyopathy. The chest-related discomfort and the shortness of breath resolved after the administration of

lenalidomide and dexamethasone.

CONCLUSION

When patients with cardiomyopathy have systemic manifestations such as numb limbs and darkening skin, the POEMS syndrome is the most possible diagnosis.

Key Words: Polyneuropathy; organomegaly; endocrinopathy; M-protein; skin changes syndrome; Dilated cardiomyopathy; Lenalidomide; Dexamethasone; Case report

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Core Tip: Polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes (POEMS) syndrome is a rare paraneoplastic syndrome that encompass multiple systems. Diagnoses are often delayed because the unusual and atypical nature of the syndrome, exposing patients to possibly severe disability. Our report presents the first case of a 59-year-old Chinese female with newly diagnosed dilated cardiomyopathy and POEMS syndrome. Although POEMS syndrome with dilated cardiomyopathy is rare, physicians should consider it when patients with cardiomyopathy have systemic manifestations.

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INTRODUCTION

Polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes (POEMS) syndrome is a rare condition that is characterized by monoclonal plasma cell disorder, peripheral neuropathy, and other systemic symptoms[1]. In 2003, a national survey that was conducted in Japan revealed a prevalence of approximately 0.3 per 100000[2]. However, more cases have been reported from China and India[3,4].

Currently, the mechanism that leads to the initiation and progression of POEMS is unclear. However, it is suggested that the vascular endothelial growth factor (VEGF), together with pro-inflammatory cytokines such as tumor necrosis factor- α , interleukin-6 (IL-6) and IL-12, might be involved in the pathogenesis of POEMS syndrome[5].

In China, the median age for the onset of POEMS syndrome is 46 years, with a male to female ratio of 2.23:1[6]. The most common symptoms of the POEMS syndrome include peripheral neuropathy, endocrine abnormalities, skin changes, organomegaly, and extravascular volume overload. Typically, the diagnosis is delayed by 12-16 mo due to a range of systemic manifestations that are often overlooked as trivial comorbidities[7]. The median survival time was only 5-7 yr in China in cases where treatment is unsuccessful[3]. The most common causes of death among patients with POEMS syndrome are cardiorespiratory failure, progressive inanition, infection, capillary leak-like syndrome, and renal failure [6]. Case reports about POEMS syndrome with dilated cardiomyopathy are relatively rare. Therefore, identifying atypical symptoms can improve the prognosis and quality of life among POEMS syndrome patients.

In this study, we report a case of POEMS syndrome with dilated cardiomyopathy in a 59-year-old woman. The clinical features and treatment methods for POEMS syndrome were summarized based on information that was obtained from literature. Some manifestations that may be overlooked during the diagnosis process were also highlighted.

CASE PRESENTATION

Chief complaints

A 59-year-old Chinese woman was admitted to the hospital with symptoms of shortness of breath and discomfort in the chest, which had been experienced for 1 mo.

History of present illness

There were no apparent triggers that were associated with the symptoms prior to presentation at our hospital. During the course of illness, the patient had abdominal distension, nausea, edema, and paroxysmal nocturnal dyspnea. However, the patient did not experience chest pain, abdominal pain, fever, cough, expectoration, and walking difficulties.

History of past illness

The patient experienced limb numbness for three years, but without systematic diagnosis and treatment. She denied the existence of underlying conditions like hypertension, diabetes, cardiomyopathy, and coronary heart disease.

Personal and family history

The patient had no significant history of smoking, drinking alcohol, and medication or food allergies. According to the information provided by the patient, there were no cases of cardiomyopathy in the family history. Moreover, the patient's children are healthy.

Physical examination

Physical examination of the patient showed the following results: body temperature was 36.8 °C; blood pressure was 159/99 mmHg; heart rate was 78 beats/min; and respiratory rate was 20 breath/min. Furthermore, the patient developed symptoms of cardiac enlargement, depressed edema of both lower limbs, and limb pigmentation.

Laboratory examinations

Upon admission, the laboratory data showed that brain natriuretic peptide levels were 3504.0 pg/mL. Blood routine tests revealed a platelet count of $492 \times 10^9/L$. The C-response protein levels were 33.78 mg/L while the urinary microalbumin concentration was 104 mg/L. There were no abnormal findings from the routine tests for the feces, urine, blood coagulation parameters, thyroid function, serum complement, rheumatoid factor, antinuclear antibody spectrum, cortisol, and adrenocorticotropic hormone rhythm. Immunoelectrophoresis of the serum showed the presence of a monoclonal IGA λ M protein. The VEGF levels were 622.56 pg/mL. Electromyography was described as a symmetric sensorimotor demyelinating polyneuropathy.

Imaging examinations

Color doppler echocardiography showed that the patient had an enlarged left atrium (inner diameter of 43.0 mm) and left ventricle (inner diameter of 62.0 mm). Ventricular wall hypokinesis and decreased functioning of the left side of the heart (ejection fraction 50%) were also observed. Cardiac magnetic resonance imaging also showed an enlarged left side of the heart, along with slight myocardial fibrosis (Figure 1). According to the results from abdominal color ultrasonography, the spleen had increased in size.

MULTIDISCIPLINARY EXPERT CONSULTATION

Bone marrow biopsy was performed when the patient was hospitalized. The findings showed megakaryocyte hyperplasia, a constant number of immature cells, and plasma cells that were scattered in a few or individual small foci (approximately 2%-20%). Flow cytometry for the bone marrow showed that normal plasma cells accounted for 0.2% of nuclear cells. Antigens such as CD38, CD138, CD27, CD19, kappa, and lamda were expressed by these plasma cells. However, antigens like CD56 and CD117 were not expressed. No monoclonal plasma cells were detected through immunohistochemical staining of the bone marrow.

FINAL DIAGNOSIS

Based on the patient's medical history, laboratory and imaging examination results, and bone marrow biopsy, the final diagnosis was POEMS syndrome with dilated cardiomyopathy.

TREATMENT

While waiting for the bone marrow biopsy report, the patient received treatment to reduce cardiac preload, diuresis, control the ventricular rate, and maintain the electrolyte balance. On the 15th of February, the bone marrow biopsy confirmed that the patient had POEMS syndrome with dilated cardiomyopathy. The prognosis of POEMS was stratified into high-risk groups. After communicating with the patient about the risks and costs of various treatments, she chose treatment with lenalidomide-dexamethasone.

OUTCOME AND FOLLOW-UP

After four months of follow-up, the shortness of breath and discomfort in the chest disappeared, while numbness significantly improved. Laboratory indicators (Table 1) such as brain natriuretic peptide also remarkably improved.

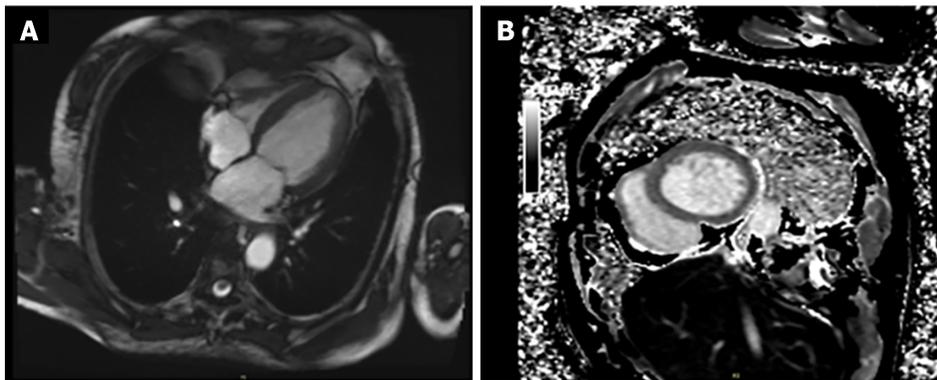
DISCUSSION

POEMS syndrome is a rare paraneoplastic syndrome caused by a plasma cell proliferative disorder. The mechanism of POEMS syndrome is complex and currently unclear. The pathogenesis of POEMS is thought to arise from a cytokine

Table 1 Changes in the laboratory examination during treatment

	Base-line	First follow-up visit	Second follow-up visit	Laboratory reference range
WBC (10 ⁹ /L)	6.55	5.75	7.45	3.69-9.16
NE (10 ⁹ /L)	4.40	3.91	3.73	2.00-7.00
PLT (10 ⁹ /L)	492	454	385	101-320
HB (g/L)	111	105	104	110-150
CRP (mg/L)	33.78	44.88	5.13	0.00-3.00
BNP (pg/mL)	3504	1469	-	0-900

WBC: White blood cell; NE: Neutrophil count; PLT: Platelet count; HB: Haemoglobin; CRP: C-reactive protein; BNP: Brain natriuretic peptide.



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Figure 1 Cardiac magnetic resonance imaging. A: The four-chamber view showed an enlarged left atrium and left ventricle; B: Linear enhancement lesions was found in the middle layer of the cardiac septal myocardium.

imbalance that is characterized by excessive production of multiple proinflammatory and angiogenic cytokines (IL-1 β , IL-6, fibroblast growth factor, and IL-12) as well as the suppression of anti-inflammatory cytokines (transforming growth factor β 1)[8]. Kourelis *et al*[9] reported an increase in programmed cell death protein 1-positive CD4⁺ T-cells and a decrease in naive CD4⁺ T-cells in patients with POEMS syndrome. This indicated a chronic antigenic stimulation of CD4⁺ T-cells and their consequent exhaustion. In addition, the serum levels of the VEGF are elevated in most patients with POEMS syndrome.

It is hypothesized that some of the manifestations of POEMS syndrome are associated with VEGF-induced endothelial dysfunction, vascular wall hypertrophy, and tissue edema[10]. Recently, treatments that target the plasma cells that produce the M-protein have shown excellent clinical responses. This suggests that the M-protein might be one of the driving factors of the disease[11]. Additionally, patients with an M-protein restricted to clonal immunoglobulin λ light variable chain -1-40 experienced severe clinical symptoms[12]. However, the mechanism underlying the pathogenesis of POEMS syndrome still needs to be explored.

The most common symptoms of POEMS syndrome are peripheral neuropathy, endocrine abnormalities, skin changes, organomegaly, and extravascular volume overload. The rate at which POEMS syndrome is misdiagnosed is extremely high due to its diverse atypical symptoms. The diagnosis of POEMS syndrome is confirmed when both of the mandatory major criteria, one of the three other major criteria, and one of the six minor criteria are positive[13]. The mandatory major criteria consists of polyneuropathy and monoclonal plasma cell-proliferative disorder (almost always λ). The other major criteria include Castleman disease, sclerotic bone lesions, and VEGF. The minor criteria is made up of organomegaly, extravascular volume overload, endocrinopathy, skin changes, papilledema, and thrombocytosis. Therefore, the diagnosis of POEMS syndrome is based on a composite of clinical and laboratory features. Moreover, POEMS syndrome should be differentiated from other plasma cell conditions like multiple myeloma and solitary plasmacytoma, and neurologic disorders such as chronic inflammatory demyelinating polyneuropathy.

Risk stratification is limited to clinical phenotypes rather than specific molecular markers. Some of the common risk factors are age, low serum albumin, pleural effusion, pulmonary hypertension, and reduced estimated glomerular filtration rate[13]. It is also important to note that the VEGF levels in the plasma and serum correlate with the activity of POEMS syndrome[13].

We report the case of a middle-aged woman with POEMS syndrome. Initially, the patient experienced shortness of breath and discomfort in the chest. The patient confirmed heart failure after the laboratory examinations. Furthermore, color doppler echocardiography showed that the left side of the heart had increased in size. Ventricular wall hypokinesia was also observed, although no previous cardiovascular risk factors and associated genetic history had been reported.

Moreover, the patient experienced limb numbness and pigmentation. Therefore, we considered the possibility that there could be other causes of myocardial enlargement in the patient. Further examinations were completed to aid diagnosis. Electromyography was described as a symmetric sensorimotor demyelinating polyneuropathy. Immunoelectrophoresis of the serum showed the presence of a monoclonal IGA λ M protein. The other results were as follows: the VEGF levels were 622.56 pg/mL; cardiac magnetic resonance imaging showed an enlarged left side of the heart as well as slight myocardial fibrosis; flow cytometric and immunohistochemical staining of bone marrow detected no monoclonal plasma cells. The clinical characteristics of this patient were as follows: Demyelinating polyneuropathy, positive M protein, VEGF elevation, splenomegaly, enlarged left heart and slight myocardial fibrosis, skin changes, and edema. After all the tests, the patient was diagnosed with POEMS syndrome associated with dilated cardiomyopathy.

Cardiac involvements in POEMS syndrome are rare and heterogenous. The most common type of cardiac involvement is pulmonary hypertension with resultant right ventricular dysfunction. However, there are few reports of cardiomyopathy, arrhythmia, and pericarditis[13-17]. Shimizu *et al*[15] reported the first case of POEMS syndrome that was accompanied by hypertrophic cardiomyopathy. Tanus and Miller[16] presented a case of POEMS syndrome that had cardiomegaly and cardiomyopathy. Abdelahad *et al*[17] presented a 28-year-old African American with a history of POEMS syndrome, in addition to an unfortunate newly diagnosed dilated, non-ischemic cardiomyopathy. Therefore, our report presents the first case of a 59-year-old Chinese female with newly diagnosed dilated cardiomyopathy and POEMS syndrome.

The evidence regarding the treatment in POEMS syndrome is largely limited to retrospective cohort studies[18,19]. However, POEMS syndrome can be treated using radiotherapy, autologous stem cell transplant, bortezomib, therapies targeting VEGF, alkylating chemotherapy, dexamethasone, thalidomide, and lenalidomide. The treatment of POEMS syndrome depends on the presence of marrow plasma cell infiltration and the number of bone lesions[8]. POEMS syndrome patients who have one to three bone lesions and no clonal plasma cells should receive radiation therapy. Once a disseminated disease is identified, systemic therapy is recommended with the caveat that large bony lesions with a significant lytic component may require adjuvant radiation therapy[13]. This indicates that autologous stem cell transplantation have significant clinical improvement in surviving patients with POEMS syndrome[13].

After treatment with melphalan-dexamethasone, hematologic response was reported in 81% of the patients with POEMS syndrome while 100% showed neurologic improvement[13]. After treatment with lenalidomide-dexamethasone, 75%-95% patients showed significant clinical and VEGF improvement[13]. Thalidomide and bortezomib are not recommended as first line treatments because they may exacerbate the risk of peripheral neuropathy[13]. On the other hand, bevacizumab does not offer consistent benefits to patients with POEMS syndrome[13].

CONCLUSION

Our report presents the first case of a 59-year-old Chinese female with newly diagnosed dilated cardiomyopathy and POEMS syndrome. Although POEMS syndrome with dilated cardiomyopathy is rare, physicians should consider it when patients with cardiomyopathy have systemic manifestations. Early diagnosis and therapy can improve the prognosis of POEMS syndrome in patients, thereby enhancing their quality of life.

FOOTNOTES

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