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ORIGINAL ARTICLE

Clinical characteristics and long-term outcome of patients with POEMS syndrome in China

Jian Li · Dao-Bin Zhou · Zhen Huang · Li Jiao · Ming-Hui Duan · Wei Zhang · Yong-Qiang Zhao · Ti Shen

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Abstract POEMS syndrome is a rare plasma cell dyscrasia characterized by polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. This study reviewed the clinical characteristics and long-term outcome of 99 consecutive Chinese patients with newly diagnosed POEMS syndrome in a single institute. The median age of 99 patients was 45 years, and the ratio of men/women was 1.4. The median time from onset of symptoms to diagnosis was 18 months. The typical five features of peripheral neuropathy, organomegaly, endocrinopathy, M protein, and skin change remained to be essential for patients with POEMS syndrome in China. The unusual features like pulmonary hypertension (36%) and renal impairment (37%) were not uncommon in China. Eighty-three percent patients were alive after follow-up time of 25 months, and 10% patients had survived more than 60 months. Melphalan-based therapy (OR, 0.076; 95% CI, 0.02–0.285) and normal renal function (OR, 0.246; 95% CI, 0.076–0.802) were independent prognostic factors for the survival of patients with POEMS syndrome. In conclusion, POEMS syndrome in Chinese patients was a multi-systemic disease with clinical features similar to non-Chinese ones. Active therapy can effectively improve the prognosis of patients with POEMS syndrome.

Keywords POEMS syndrome · Castleman's disease · Long-term outcome · Neuropathy

J. Li · D.-B. Zhou (✉) · Z. Huang · L. Jiao · M.-H. Duan · W. Zhang · Y.-Q. Zhao · T. Shen
Department of Hematology,
Peking Union Medical College Hospital,
Beijing 100730, China
e-mail: daobinzhou@yahoo.com

Introduction

POEMS syndrome, also called Crow–Fukase syndrome, is a rare plasma cell dyscrasia characterized by polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. Additional features include papilledema, extravascular volume overload, sclerotic bone lesions, and Castleman's disease [1]. The pathogenesis of POEMS syndrome is not fully understood, but there are accumulating evidences suggesting that the high level of serum vascular endothelial growth factor (VEGF) contributed to some specific features of POEMS syndrome, such as extravascular volume overload, organomegaly, and hemangioma [2]. The course of POEMS syndrome is chronic, and the neurological features typically worsen over time if treatment is unsuccessful. The median survival time of patients with POEMS syndrome is usually more than 3 years, and the main causes of death are cardiopulmonary failure, progressive inanition, infection, and renal failure [1].

Although several large series studies of POEMS syndrome have been reported in Japan and the USA [3, 4], information about relationship between POEMS syndrome and Castleman's disease, less-recognized features like pulmonary arterial hypertension and renal lesions, and long-term outcome is limited. In addition, there are few studies of POEMS syndrome in China [5–7]. Here, we present a retrospective study that reviewed the clinical features and long-term outcome of Chinese patients with POEMS syndrome and the relationship between POEMS syndrome and Castleman's disease.

Patients and methods

Ninety-nine consecutive patients with newly diagnosed POEMS syndrome were admitted to Peking Union Medical College hospital from January 2001 to December 2009.

All 99 patients met the diagnosis criteria proposed by Dispenzieri A in 2001 [4]. In brief, this diagnosis criterion consisted of two major criteria (polyneuropathy and monoclonal plasmaproliferative disorder) and seven minor criteria (bone lesion, Castleman's disease, organomegaly, edema, endocrinopathy, skin changes, and papilledema). Two major criteria and at least one minor criterion were required for diagnosis. One reviewer (L.J.) analyzed data including history, physical examination, laboratory tests, and survival. This study cited only the features present at diagnosis rather than features developed during evolution and progression of the disease unless otherwise described. All patients were followed up in the clinic or by telephone and email for survival. The last follow-up day was April 1, 2010. The present study was approved by Peking Union Medical College hospital institutional review board.

SPSS 16.0 software was used for statistical analysis. The χ^2 test was used to compare variables. Curves for overall survival were plotted according to the method of Kaplan and Meier and were compared by log-rank test. Survival and follow-up time were calculated from the time of diagnosis. Prognostic factors for overall survival were determined by the Cox proportional hazards model in the analysis of covariates. The following variables including age, sex, the time from onset to diagnosis, organomegaly, skin changes, Castleman's disease, extravascular volume overload, protein in cerebral spinal fluid, type of M protein, thrombocytosis, papilledema, renal impairment, pulmonary hypertension, and the type of therapy were analyzed.

Results

General characteristics

There were 58 men and 41 women, and the ratio of male to female was about 1.4. The median age of 99 patients was 45 years (range, 28–71 years); 27 patients (27%) were 40 years old or younger.

The most common initial symptoms that brought them to medical attention consisted of numbness and/or weakness of limbs due to peripheral neuropathy (41%), peripheral edema (27%), and skin changes (15%). Additional uncommon first symptom was ascites (4%), fever of unknown origin (3%), lymphadenopathy (3%), gynecomastia (3%), diarrhea (1%), fatigue (1%), and weight loss (1%). The misdiagnosis was common in patients (85%) with POEMS syndrome, and the time from onset of symptoms to diagnosis was from 3 to 123 months with the median time of 18 months. The top three misdiagnoses were Guillian–Barre's syndrome (12%), chronic inflammatory demyelinating polyneuritis (11%), and tuberculosis (10%). Other common misdiagnosis further included chronic nephritis, primary hypothyroidism, scleroderma, myeloma, primary pulmonary hypertension, and multiple myeloma. In addition, weight loss (60%), fatigue (44%), and fever (21%) were the most common accompanying constitutionals symptoms for patients with POEMS syndrome.

Neuropathy

One hundred percent of the patients had peripheral neuropathy, in which 95 patients had sensory-motor deficit, four patients had only motor deficit, and one patient had only sensation deficit. Twelve patients (12%) received sural nerve biopsy, a mixture of both axonal loss and segmental demyelination was disclosed in five patients, segmental demyelination alone in five patients, and axonal loss alone in two patients. Seventy-two of 99 patients received lumber puncture. Fifty patients (69%) had increased cerebrospinal fluid opening pressure with the median pressure of 72 patients as 205 mmH_2O (range, 70–330 mmH_2O; normal value, 80–180 mmH_2O). Protein level of cerebrospinal fluid was elevated in 69 patients (96%); the median protein level was 1.26 g/L (range, 0.37–3.12 g/L; normal value, 0.15–0.45 g/L). All patients had normal white cell count ($\leq 2/mm^3$).

Four patients (4%) suffered from cerebral infarction. Of these four patients, three patients had infarction before diagnosis of POEMS and one patient 1 year after diagnosis. None of these patients received any therapy for POEMS syndrome. The infarctions were located at the right basal ganglia in all four patients.

Organomegaly

Eighty-five patients (85%) had organomegaly, in which 47 patients (47%) had hepatomegaly, 70 (70%) had splenomegaly, and 74 patients (74%) had lymphadenopathy. Forty-three of these 74 patients underwent biopsy of lymph node: 18 patients (42%) had reactive changes and 25 (58%) had Castleman's disease. For detailed pathological types, 21 patients (84%) had hyaline-vascular type, and the rest were plasma cell type (8%) and unspecified type (8%). Eleven patients (11%) had both hepatosplenomegaly and lymphadenopathy.

Endocrinopathy

Thyroid gland was one of the most commonly involved endocrine glands in POEMS syndrome. Hypothyroidism was present in 67 patients (67%) of all 99 patients. Among them, 24 patients (36%) required replacement therapy with low serum thyroxine and high thyroid-stimulating hormone (TSH), and 42 (64%) was subclinical hypothyroidism with

high TSH and normal thyroxine. In addition, one patient presented with hyperthyroidism.

Impotence (89%) and gynecomastia (12%) were common findings in men. Twenty-six of those 46 men who had serum testosterone levels measured had low levels. Twenty-nine male patients had serum prolactin levels measured; eight of those had high levels. In contrast, in the 30 women tested, high serum level of testosterone and prolactin were observed in 14 and 12 women, respectively.

Of the 55 patients who underwent adrenal–pituitary tests (including serum-free cortisol, serum adrenocorticotropic hormone (ACTH), and free cortisol of 24 h urine) at diagnosis, 33 (60%) had elevated serum ACTH level, 10 (18%) had decreased free cortisol of 24 h urine, and five (9%) had decreased serum-free cortisol. Five patients received replacement therapy for adrenal insufficiency. Diabetes mellitus and glucose intolerance were noted in 12 (12%) and seven patients (7%), respectively.

Hyperphosphatemia (defined as the serum phosphate higher than 4.3 mg/dL) presented in 52% of patients in this study, and hypocalcemia (defined as the serum calcium <8 mg/dL) was documented in 36% of all 99 patients. However, only one patient (2%) had the elevated serum parathyroid hormone in 38 patients who were measured.

Monoclonal plasma cell dyscrasia

According to the diagnostic criteria proposed by Dispenzieri, all 99 patients had evidence of monoclonal plasmaproliferative disorder. Serum immunofixation electrophoresis revealed monoclonal band in 92 patients (92%) of our cases. However, serum electrophoresis only revealed M component in 24 patients (24%), which was less sensitive than immunofixation to detect M protein. Three patients without serum M protein had detectable M protein in urine by urine immunofixation. The rest four patients had abnormal bone marrow biopsy specimens with immunohistochemical stain, which was considered as one of evidences for monoclonal plasmaproliferative disorder. The types of M protein in these 99 patients consisted of IgA-λ (65%), IgG-λ (20%), λ alone (11%), IgG-κ (2%), and IgA-κ (1%).

Bone marrow aspiration and biopsy were performed in all patients. The median plasma cell counts in bone marrow smear was 2% (0–16%) and only two patients (2%) had >10% plasma cell.

Skin changes

Skin changes were found in 89 patients (89%). Local or general hyperpigmentation (83%) and skin thickening (43%) were the most common skin changes in our cases. Additional common skin changes further included hypertrichosis (35%) and skin hemangioma (35%). In 10 patients who performed biopsy of hemangioma, the pathological results were glomerular hemangioma.

The median number of classical five features of POEMS was 4 (range, 2–5) in our study.

Extravascular volume overload

Various forms of extravascular volume overload were documented in 87 (87%) of 99 patients. Among them, 84 patients (84%) had peripheral edema, 54 (54%) had ascites, 43 (43%) had pleural effusion, and 64 (64%) had pericardial effusion. Thirty-seven patients (37%) had peripheral edema, ascites, pleural effusion, and pericardial effusion simultaneously.

Papilledema

Papilledema was observed in 56 of 87 patients (64%) who received fundus examination.

Pulmonary changes

In addition to pleural effusion, the most common pulmonary manifestations in POEMS syndrome was pulmonary hypertension. Thirty-six patients (36%) had pulmonary hypertension detected by transthoracic dopplar echocardiography (defined as pulmonary systolic pressure higher than 40 mmHg). The median pulmonary systolic pressure was 52 mmHg (range, 15–101 mmHg). Two patients further underwent right heart catheterization to test vascoreactive response at diagnosis. These two patients did not respond to vasodilator.

Twenty-eight of these 99 patients received pulmonary function test at diagnosis. Seventy-nine percent (22 patients) of those pulmonary function tests was abnormal. The most common abnormal pattern was restrictive lung disease with diminished diffusing capacity of the lung for carbon monoxide (DLCO), which was documented in 15 of 28 patients (53%). Other abnormalities of pulmonary function test further consisted of restrictive lung disease alone (14%), the drop of DLCO alone (7%), and obstructive disease (1%).

Bone lesions

All patients were screened for bone lesion by X-ray of skull, vertebrae, pelvis, femur, and humerus. Some forms of bone lesions were documented in 27 patients (27%), which included sclerotic bone lesions in 19 patients (70%) and lytic bone lesions in eight patients (30%). No patients had mixed sclerotic and lytic components. Ten patients underwent biopsy of bone lesions (two lytic and eight sclerotic lesions), and plasmacytoma was diagnosed in seven patients (70%).

Renal changes

Proteinuria (defined as more than 500 mg protein in 24 h urine), and microhematuria was present in 20 (20%) and 15 patients (15%). Nine patients (9%) had proteinuria and microhematuria simultaneously. The renal impairment (defined as serum creatinine clearance rate, CrCl, <60 ml/min) was observed in 37 patients (37%), in which eight patients had CrCl of 10–30 ml/min and one patient with CrCl <10 ml/min who required hemodialysis. Renal biopsy was performed in seven patients. Membranoproliferative glomerulonephritis, endocapillary proliferative glomerulonephritis, and mesangial proliferative glomerulonephritis were observed in five, one, and one patient, respectively.

Other laboratory features

Thrombocytosis was documented in 54 of these cases (54%), and four patients (4%) had mild thrombocytopenia ($80–99\times10^9$/L). Anemia (26%) was more common than polycythemia (9%). Eighteen of these 26 patients with anemia had CCrl <60 ml/min.

The serum VEGF level was measured in 40 patients (normal range of serum VEGF level was <600 pg/mL). Twenty-eight patients (70%) had elevated serum VEGF level. The median serum VEGF level was 780 pg/mL (range, 50–1,897 pg/mL).

Treatment and survival

Data of treatment and survival were available in 75 patients of all patients (75%). The median follow-up time was 25 months. Among them, 42 patients were treated with melphalan-based chemotherapy (11 cases for melphalan and prednisone, MP, and 31 for melphalan and high dose of dexamethasone, MDex), 15 patients with high dose melphalan (200 mg/m^2) with autologous stem cell transplantation, eight patients with Chinese traditional medicine, five patient with prednisone or dexamethasone alone, one patients with thalidomide and prednisone, and the rest four patient refused treatment. None received radiation in these cases.

Clinical response was defined as stabilization or improvement of symptoms as reported by the patients or physicians. The overall neuropathy limitation scale had been used to evaluate neuropathy response since 2008. In forty-two patients receiving melphalan-based chemotherapy, the clinical response rate was 90%, and two patients died after only one cycle of treatment. Fourteen patients (93%) achieved durable response after autologous stem cell transplantation, and all responders were free of relapse or progression at median follow-up time of 26 months. One patient died from septic shock during transplantation, and transplant-related mortality was about 7%. Only one patient (12.5%) had transient response from Chinese traditional medicine. Two patients (40%) had transient response for prednisone or dexamethasone alone.

Thirteen of the 75 patients (17%) died before April 1, 2010. One patient died of septic shock during transplant, two died of bacterial pneumonia, and two of serious tuberculosis during chemotherapy. Three and two non-responders died of cardiopulmonary failure and renal failure, respectively. The cause of death was unknown in three patients. The median survival time did not reach after the median follow-up of 25 months (Fig. 1). Nine patients had survived more than 60 months, and two patients had survival over 80 months. Cox regression analysis revealed that melphalan-based therapy (including melphalan-based chemotherapy, MP and MDex and transplant; OR, 0.076; 95% CI, 0.02–0.285) and normal renal function (OR, 0.246; 95% CI, 0.076–0.802) were associated with longer survival time. The following variables are not prognostic factors for survival of POEMS syndrome: age, sex, the time from onset to diagnosis, organomegaly, skin changes, Castleman's disease, extravascular volume overload, protein in cerebral spinal fluid, type of M protein, thrombocytosis, papilledema, and pulmonary hypertension.

Comparison of patients with or without Castleman's disease

We assigned 25 patients with Castleman's disease confirmed by biopsy of lymph node into Castleman's disease group. Eighteen patients without Castleman's disease documented by biopsy, and 25 patients without lymphadenopathy were grouped together as non-Castleman's disease group. We compared the clinical characteristics and survival of these

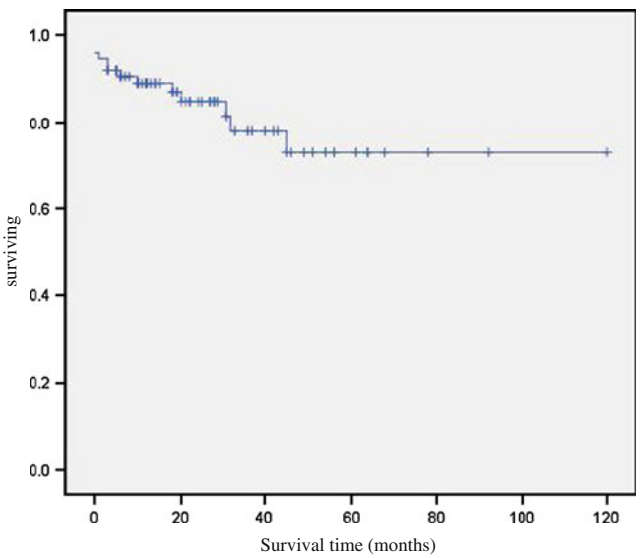

Fig. 1 Overall survival of 75 patients with follow-up data

two groups (Table 1). The results showed that there was no statistical difference in age, sex, hepatomegaly, splenomegaly, hypothyroidism, skin change, edema, bone lesions, polycythemia, pulmonary hypertension, serum VEGF level, and renal impairment between these two groups. However, patients with Castleman's disease had more thrombocytosis than those without Castleman's disease (p=0.003). At follow-up of 25 months, the median overall survival of patients with Castleman's disease and patients without Castleman's disease were not statistically different (not reached vs. not reach, p=0.072; Fig. 2).

Discussions

The misdiagnosis of POEMS syndrome is very common due to its rarity and complicated clinical manifestations. In our series, 85% patients were misdiagnosed, and the misdiagnosis is very extensive including other peripheral neuropathies, tuberculosis infection, diabetes, chronic nephritis, various skin diseases, multiple myeloma, etc., which depended on initial symptoms. The time from onset to diagnosis is very long (median, 18 months, 3–123 months). Although our study does not suggest that the time from onset to diagnosis is a prognostic factor for survival, the longer diagnosis time may be associated with worse recovery of neuropathy. Therefore, thorough knowledge of the clinical features of POEMS syndrome is essential to the frontline clinicians. POEMS syndrome should be considered when patients presented as peripheral neuropathy of unknown origins, refractory edema or ascites, chronic skin change (hyperpigmentation, thickening, or hemangioma), or organomegaly of unknown reasons. The serum or urine immunofixation electrophoresis is essential for screening POEMS syndrome. The abovementioned symptoms with positive immunofixation electrophoresis are highly suggested as POEMS syndrome.

Our study is the largest retrospective study of POEMS syndrome in China. Compared with other studies in China [5–7], our study has some advantages. First, serum immunofixation electrophoresis has been used in our hospital since 2000, and all patients diagnosed from 2001 to 2009 in our study were detected from serum and urine immunofixation electrophoresis. Therefore, the prevalence of monoclonal protein in our study was higher than those of the others. Second, besides description of typical features of POEMS syndrome, many patients further received evaluations for uncommon features of POEMS included echocardiography for pulmonary hypertension, pulmonary function test, Castleman's disease, renal function evaluations, and serum VEGF level. Third, nearly 75% patients had complete follow-up information for treatment and survival. Finally, this is the first large study on POEMS syndrome that used the diagnosis criteria proposed by Dispenzieri in 2001. Therefore, our study can be considered as the most representative sample of POEMS syndrome in China.

Compared with the two previous large studies in Japan and the USA (Table 2) [3, 4], there are similar demographic characteristics including age and sex ratio, prevalence of peripheral neuropathy, Castleman's disease, type of serum M protein, skin change, and thrombocytosis in our study. However, the prevalence of organomegaly is higher than those reported in USA. We thought that our patients were diagnosed during 2001–2009, and more advanced imaging

Table 1 Clinical features of patients with or without Castleman's disease

Clinical features	Castleman's disease (n=25)	No Castleman's disease (n=43)	p value
Age (>45 years old)	11 (44)	21 (49)	0.700
Male	15 (60)	26 (61)	0.970
Hepatomegaly	12 (48)	22 (51)	0.801
Splenomegaly	16 (64)	30 (70)	0.624
Hypothyroidism	4 (16)	13 (30)	0.191
Skin changes	22 (88)	37 (86)	0.819
Peripheral edema	21 (91)	36 (84)	0.392
Ascites	17 (74)	25 (58)	0.204
Pleural effusion	11 (48)	20 (47)	0.919
Papilledema	18 (78)	24 (67)	0.338
Bone lesions	4 (16)	13 (30)	0.191
Thrombocytosis	14 (56)	9 (21)	0.003
Polycythemia	3 (12)	5 (12)	0.963
Pulmonary hypertension	8 (32)	18 (42)	0.42
Renal impairment (CrCl <60 ml/min)	12 (48)	20 (47)	0.906
High serum VEGF level (>600 pg/ml)	5 (83)	8 (57)	0.260

Values are given as number (percent), unless otherwise indicated. The percentages for subcategories are expressed ad the percentage of patients with the abnormality among those patients who had the test performed.

CrCl creatinine clearance rate, *VEGF* vascular endothelial growth factor

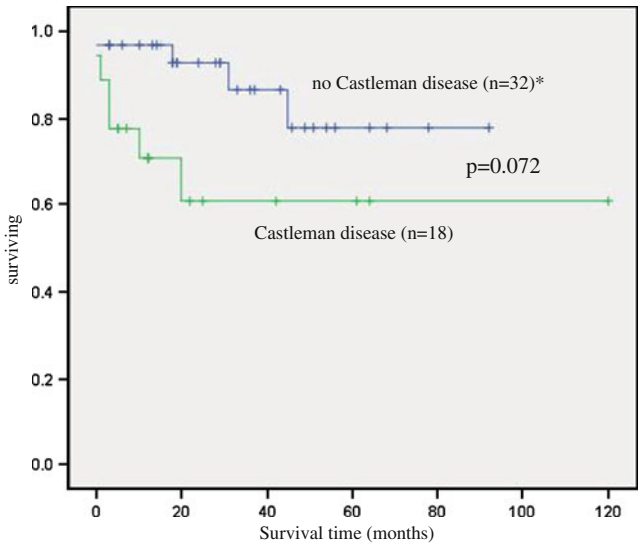

Fig. 2 Survival time of patients with or without Castleman's disease *Asterisk* 32 patients had complete survival data in 43 patients without Castleman's disease

methods like ultrasound, computed tomography and MRI are used to evaluate organomegaly in our study than those in the USA in which patients were from 1960 to 1998. In addition, the extravascular overload is very prominent in our study, and nearly 88% patients have various levels of edema and/or various effusions, which is similar to those reported in Japan. In contrast, the prevalence of extravascular overload is very low (29%) in the USA. It may be due to the racial difference between Asian and whites. Moreover, the prevalence of bone lesion in our study is much lower than those in Japan and the USA (27% vs. 55% vs. 97%), the mechanism of which is unknown yet.

Although peripheral neuropathy is the typical involvement of nervous system in POEMS syndrome, cerebral infarction is not uncommon. Dupont et al. reported that there were nine patients who suffered cerebral infarction in all 90 patients with POEMS syndrome, and thrombocytosis and bone marrow plasmacytosis are prognostic factors for cerebral infarction [8]. The prevalence of cerebral infarction is 4% in our study, and these four patients suffered cerebral infarction when the disease is active. Although the analysis of prognostic factors for cerebral infarction was not performed because of few patients at risk, the active disease may be one of risk factors for cerebral infarction in patients with POEMS syndrome.

Castleman's disease is one of the characteristics of POEMS syndrome. Although the association between Castleman's disease and POEMS syndrome is not fully understood, 11–30% of POEMS patients have documented Castleman's disease. The patients with Castleman's disease had more subtle neuropathy and higher level of VEGF and IL-6 as reported previously [3, 9, 10]. In our study, 58% patients who underwent biopsy of lymph node have Castleman's disease, and the hyaline-vascular type is the most common pathological phenotype. Our results suggested that patients with Castleman's disease have more thrombocytosis than patients without Castleman's disease, though the survival time between these two groups is comparable. More data on cytokines and other clinical information is required to explore the association of POEMS syndrome and Castleman's disease.

Many investigators have described that pulmonary hypertension develops in 25–48% of patients with POEMS syndrome, and successful treatment of POEMS syndrome can effectively reversed pulmonary hypertension [11, 12]. Pulmonary hypertension is seen in 36% of our patients, and most patients have mild to moderate pulmonary hypertension (median, 52 mmHg). The exact pathophysiological mechanism of pulmonary hypertension in patients with POEMS syndrome is unclear, but they are likely to be mediated by cytokines. Two patients receive right heart catheterization test and have no response to vasodilator in our study, which suggests that the proliferation of endothelial cell and stenosis of vessels rather than vasospasm may be the pathophysiological change in POEMS-related pulmonary hypertension.

Renal change in POEMS syndrome is reflected by proteinuria, hematuria, renal impairment, and renal failure. Nakamoto et al. documented that more than 70% patients with POEMS syndrome had mild proteinuria and hematuria, and nearly 50% patients had renal inpairment [13]. The proteinuria and hematuria was revealed in 20% and 15% patients in this study respectively. The prominent pathological change of kidney is membranoproliferative glomerulonephritis, which is similar to other reports [13, 14].

There are no standard treatments for POEMS syndrome [15]. Melphalan is the cornerstone of treatment for POEMS syndrome. Melphalan with prednisone results in approximately 40–100% of response rate in patients with POEMS syndrome [4, 16]. Moreover, recently high-dose melphalan with autologous peripheral blood stem cell transplant became a promising therapy for POEMS syndrome with high response rate and less toxicity [17]. In this study, 90% patients achieved clinical response to melphalan-based chemotherapy including MP or MDex, which is higher than about 40% response rate for MP in other studies. Several investigators have documented that MDex is superior to MP in treatment of amyloidosis. [18, 19] More than 70% patients receiving MDex may explain such high response rate in this study. Transplant resulted in response in 93% of our 15 patients, which is comparable to other studies. It may be surprising that no patients received radiation therapy in our study. It is because few patients have local bone lesion and radiation therapy has low

Table 2 Comparison of clinical features of patients in the present series and two previous series

Clinical features	Present study,% (n=99)	Nakanishi [3],% (n=102)	Dispenzieri [4],% (n=99)
Age, median, yearr	45	46	51
Male	58 (58)	69 (67)	62 (62)
Polyneuropathy	98 (99)	102 (100)	99 (100)
Organomegaly	85 (86)	NA	50 (50)
Hepatomegaly	47 (47)	80 (82)	24 (24)
Splenomegaly	70 (71)	36 (39)	22 (22)
Lymphadenopathy	74 (75)	62 (65)	26 (26)
Castleman's Disease	25 (58)	19 (63)	11 (73)
Hypothyroidism required replacement	24 (24)	5 (24)	14 (14)
increases in TSH with normal thyroxine level	42 (42)	NA	12 (12)
Monoclonal plasmaproliferative disorder	99 (100)	NA	99 (100)
Serum M protein by immunofixation	92 (92)	76 (75)	84 (85)
IgA-λ	65 (71)	29 (41)	44 (52)
IgG-λ	20 (22)	38 (54)	40 (48)
IgM-λ	0 (0)	0 (0)	1 (1)
Λ	4 (4)	0 (0)	0 (0)
IgG-κ	2 (2)	1 (1)	0 (0)
IgA-κ	1 (1)	3 (4)	0 (0)
Skin changes	89 (90)	NA	67 (68)
Extravascular volume overload	87 (88)	NA	29 (29)
Peripheral edema	84 (85)	91 (91)	24 (24)
Ascites	54 (55)	53 (62)	7 (7)
Pleural effusion	43 (43)	36 (40)	3 (3)
Hydropericardium	64 (65)	NA	1 (1)
Papilledema	56 (64)	56 (62)	29 (29)
Increased CSF protein	69 (96)	93 (97)	99 (100)
Bone lesions	27 (27)	56 (55)	97 (97)
Sclerotic only	19 (19)	31 (55)	46 (46)
Lytic only	8 (8)	8 (14)	2 (2)
Mixed	0 (0)	17 (30)	49 (49)
Thrombocytosis	54 (55)	NA	53 (54)
Polycythemia	9 (9)	19 (19)	18 (18)
Pulmonary hypertension	36 (36)	NA	5 (5)
restrictive lung disease	19 (68)	NA	5 (5)
Renal impairment	37 (37)[a]	NA	4 (4)[b]

Values are given as number (percent), unless otherwise indicated. The percentages for subcategories are expressed ad the percentage of patients with the abnormality among those patients who had the test performed.

NA not available

[a] Renal impairment was defined as creatinine clearance rate <60 ml/min

[b] No definition was given for renal failure in original article

response rate and high cost in China (about 30,000 RMB for one cycle). Therefore, physicians preferred to choose cheap and effective melphalan-based treatment or a more effective transplant.

Although the clinical course of POEMS syndrome is chronic, the survival time varies in the different studies. In Nakanishi's study, the median survival is 33 months [3]. Approximately 50% of the patients were alive for more than 5 years in a French study [9]. The median survival time is 13.3 months in Dispenzieri's study [4]. There are 83% patients who are alive after follow-up time of 25 months, and 10% patients have survived more than 60 months in this study. It is documented that only fingernail clubbing and extravascular volume overload

were significantly associated with a shorter overall survival of POEMS syndrome, and other variables like age, alkylator use, bone lesions, weight loss, Castleman's disease, organomegaly, skin, gender, thrombocytosis, or hemoglobin are not predictive factors for overall survival in Mayo series [4]. However, we revealed that active therapy (melphalan-based chemotherapy or transplant) and renal function are independent prognostic factors for survival of patients with POEMS syndrome.

In conclusion, POEMS syndrome is a multi-systemic disease involving the nerve, skin, lung, kidney, lymph node, liver, and spleen. The main clinical features are similar between Chinese and non-Chinese patients, although there is a little difference in organomegaly, extravascular volume overload, and bone lesions. Active therapy can effectively improve the prognosis of POEMS syndrome.

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