The clinical study of POEMS syndrome in China

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Abstract

OBJECTIVE: POEMS syndrome is a unique clinical entity. It was described by the presence of several typical characteristics as paraproteinemia, polyneuropathy, organomegaly, endocrinopathy, and skin changes. Few people reported characteristics of Chinese POEMS patients.

PATIENTS AND METHODS: Retrospective evaluation of Chinese patients with POEMS syndrome was carried out to reveal clinical features and compare with foreign series reported previously. In addition to typical characteristics, Chinese patients often were presented with extravascular volume overload (84%), papilledema (44%), bone lesions (41%), raynaud phenomenon (31%) and Clubbing (22%).

RESULTS: Clinical laboratory tests found most patients had increased erythrosedimentation rate, hyperlipidemia, liver disorder and renal involvement. 70% patients had hypothyroidism, including overt hypothyroidism (6 patients) and subclinical hypothyroidism (13 patients). High prevalence of positive antimitochondrial antibody (ANA) and positive antineutrophil cytoplasmic antibody (ANCA) was the more common phenomenon. Chinese patients with bone damage in the incidence are lower than in the West and Japanese reports.

CONCLUSIONS: In summary, our study demonstrate the POEMS syndrome diagnostic criteria proposed by Dispenzieri et al is also more high applicability in the Chinese population.At the time of diagnosis, we should not pay attention on the typical characteristics of the disease, but also on the changes in thyroid, liver, kidney function and lipid metabolism.

INTRODUCTION

POEMS/Crow-Fukase syndrome is a rare multisystem disorder that clinically presents with polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (Bardwick *et al.* 1980). Other typical features include edema, pleural effusions, ascites and pulmonary hypertension (Jackson *et al.* 1990).

In a retrospective review of a single institution's experience, the syndrome is more frequent in Western country and Japan where it is known

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as the Crow-Fukase syndrome (Dispenzieri *et al.* 2003; Nakanishi *et al.* 1984).

So far, very little information of the patients from the Chinese mainland has been reported. Therefore this study will retrospectively summarize clinical and laboratory features of Chinese POEMS patients presenting to our teaching hospital, and make comparison of foreign-related reports.

PATIENTS AND METHODS

We investigated 31 patients who manifested signs and symptoms characteristic of POEMS syndrome. All patients with POEMS syndrome met both major criteria and 1 minor criterion for the diagnosis of POEMS syndrome (Dispenzieri *et al.* 2003). Using a standardized data extraction form, we abstracted information from the medical records of these patients regarding their clinical features and laboratory data at the time of diagnosis of POEMS syndrome. Moreover, we compared the clinical data in our patients with Mayo, Japan and French series. Unfortunately, as the dispersion of patients, we had not complete treatment and follow-up information of these patients, as a result, the article did not involve the treatment and prognosis of them.

RESULTS

Patient characteristics are shown in Tables 1 and 2, 14 patients were 45 years or younger; 10 (33%) were men. Table 1 compares the findings in this study with those of the 3 other important patient series (Dispenzieri *et al.* 2003; Nakanishi *et al.* 1984; Soubrier *et al.* 1994).

The present series cites only the features present at diagnosis rather than features observed during disease evolution and progression like the other studies in Table 1. At the same time, we summed up the patient's common clinical test data to illustrate the characteristics of a Chinese patient.

Peripheral neuropathy

All POEMS syndrome patients have peripheral neuropathy, which generally dominates the clinical feature (Table 1). Symptoms begin at the end of limbs and consist of tingling, paresthesias, and coolness. With the involvement of motor to the emergence of feeling.

Motor involvement follows the sensory function obstacle, including decreased muscle strength and tendon reflex. Both are distal, symmetric, and progressive with a gradual proximal spread, 15 patients developed difficulty walking.

22 patients had electromyogram, the findings were 91% of peripheral, neurogenic damage with slowed nerve conduction, prolonged distal latencies and decreased F waves. 29 (92%) patients in this series had increased cerebrospinal fluid protein and cerebrospinal fluid opening pressures.

Organomegaly

26 patients (84%) had organomegaly. 13 patients (42%) had lymphadenopathy. Of these 13, 6 had Castleman disease defined by biopsy. 19 patients (61%) had hepatomegaly, and 22 (71%) had splenomegaly, 3 (10%) had renomegaly, 2 (7%) had heart enlargement. No patient had massive lymphadenopathy or organomegaly.

Endocrinopathy

Endocrine abnormality is a defining feature of POEMS. In the present study, 29 patients (87%) had at least one endocrine abnormality at presentation. Most patients did not have a thorough endocrine evaluation, lowering the reported incidence. Hypothyroidism, increased prolactin value and gonadal dysfunction are the most common endocrinopathies.

Hypogonadism was most common, though we failed to determine whether there was primary or secondary failure. 19 (90%) male patients had erectile dysfunction, 13 of these men who had serum testosterone levels measured, 8 had low levels, 5 had normal serum testosterone levels. 5 men had gynecomastia, one of the 5 men tested had high serum estradiol levels. Of the 18 patients who had serum prolactin levels measured, 9 had high levels including 1 man.

The sexual history of women was less reliably ascertained, only four women had amenorrhea within half of a year and two women had irregular menses. None of whom also had galactorrhea. Serum estradiol levels were normal in all 6 women tested. Among the 18 patients with measured serum prolactin levels, levels were high in 1 man and 8 women. (normal range, 2.5 to 17 μg/L).

6 patients (20%) had hypothyroidism requiring treatment. Another 13 patients (42%) had mild increases in thyroid stimulating hormone (normal range 0.4 to 5.0 mIU/L) and normal thyroxine levels; these patients were not treated and therefore considered to subclinical hypothyroidism in this series. 10 patients (32%) had diabetes mellitus, having high fasting glucose and glycosylated hemoglobin levels. Of the 18 patients who had adrenal-pituitary testing, 4 (22%) had abnormalities of the adrenal-pituitary axis at presentation.

Monoclonal plasmaproliferative disorder

By definition, all patients had evidence of a monoclonal plasmaproliferative disorder. 26 patients had a detectable monoclonal protein in their serum on analysis by immunofixation. The following is the characteristics: (1) M component: 8 patients had an immunoglobulin G (IgG)$^{-\lambda}$, 2 patients had an IgG$^{-\kappa}$, 10 patients had an IgA$^{-\lambda}$, 2 patients had an IgA$^{-\kappa}$, 2 patient had IgG weight chain, 1 patients had IgAλlight chain and 1patient had IgA weight chain. (2) M protein screening: full- M protein had been detected only 17 patients, 8 patients had monoclonal weight chain including 6 patients with IgA weight chain, 1 patient had monoclonalλlight chain, the other patients had no M protein in their serum,

Tab. 1. Clinical manifestations.

Characteristics	Present study % N=31	Mayo series % N=99	French series % N=25	Japan series % N=102
Media age, y (range)	51 (31–84)	51 (30–83)		
Male sex	67 (21/31)	63 (62/37)		
Polyneuropathy				
Peripheral neuropathy	100	100	100	100
Electromyogram abnormality	91 (20/22)*			
CSF protein more than 50mg/L	92	100	100	97
Organomegaly	84	50	NR	NR
Hepatomegaly	61	24	68	78
Splenomegaly	71	22	52	35
Lyphadenopathy	42	26	52	61
Castleman diseas	19	11	24	19
Endocrinopathy	87	67	NR	NR
Gonadal axis abnormality	80	55	NR	NR
Adrenal axis abnormality	22 (4/18) *	16	NR	NR
Increased prolactin value	50 (9/18) *	8	NR	NR
Gynecomastia or galactorrhea	25 (5/20) *	18	NR	NR
Diabetes mellitus	32	3	36	25
Overt Hypothyroidism	20	14	36	NR
Subclinical hypothyroidism	42	NR	NR	NR
Erectile dysfunction of men	90	NR	NR	NR
Monoclonal plasma cell dyscrasia	100	100	100	75
M component on serum protein electrophoresis	84	54	100	70
Skin changes	97	68	NR	NR
Hyperpigmentation	97	46	48	93
Acrocyanosis and plethora	16	16	NR	NR
Hemangioma/telangiectasia	16	9	32	NR
Hypertrichosis	16	26	24	74
Thickening	23	5	28	61
Papilledema	44 (8/18)*	29	40	55
Extravascular volume overload	84	29	NR	NR
Peripheral edema	74	24	80	89
Ascites	58	7	32	52
Pleural effusion	35	3	24	35
Hydropericardium	32	NR	NR	NR
Gallbladder hydrops	13	NR	NR	NR
Bone lesions	41 (7/17)*	97	68	54
Solitary lesion	6 (1/17)	45	41	45
More than 1 lesion	35 (6/17)	54	59	45
Fatigue	94	31	NR	NR
Raynaud phenomenon	31	NR	NR	NR
Clubbing	22	5	32	49

NR indicates not reported.
*Only 22, 18, 18, 20, 18, and 17 patients, respectively, were tested; percentage represents percent positive of those tested.

Tab. 2. Laboratory data.

	Present study % N=31	Mayo series % N=99	French series % N=25	Japan series % N=102
Thrombocytosis: (platelet count range 97–350 ×10³/μl)	16	54	88	NR
Polycythemia: (hemoglobin range 12–16 g/dl)	3	18	12	19
Erythrosedimentation rate more than 29mm/h	92	16	NR	NR
Lipid disorder	100	NR	NR	NR
Triglyceride disorder more than 1.70 g/L (range 0.56–1.70 g/L)	13	NR	NR	NR
Cholesterol more than 3.10 g/L (range 0.56–1.70 g/L)	89	NR	NR	NR
High density lipoprotein (HDL) less than 1.12 g/L (range 1.12–1.85 g/L)	100	NR	NR	NR
Low-density lipoprotein (LDL) high than 2.3 g/L (range 2.3–4.1 g/L)	100	NR	NR	NR
Apolipoprotein A1 less than 1.05 g/L (range 1.05–1.55 g/L)	77	NR	NR	NR
Apolipoprotein B100 more than 1.00g/L (range 0.75–1.00 g/L)	71	NR	NR	NR
Humoral immune disorder	89	NR	NR	NR
Serum IgG more than 16 g/L (range 8–16 g/L)	33	NR	NR	NR
Serum IgA more than 3.3 g/L (range 0.7–3.3 g/L)	33	NR	NR	NR
Serum IgM more than 2.2 g/L (range 0.5–2.2 g/L)	22	NR	NR	NR
Complement 3 less than 0.8 g/L (range 0.8–1.6 g/L)	11	NR	NR	NR
Complement 4 more than 0.4 g/L (range 0.1–0.4 g/L)	33	NR	NR	NR
Liver function disorder	100	NR	NR	NR
Serum glutamic-pyruvic transaminase (ALT) less than 6 (range 6–40 u/L)	13	NR	NR	NR
Serum glutamic-oxal(o)acetic transaminase (AST) more than 40 (range 6–37 u/L)	13	NR	NR	NR
AST/ ALT more than 1.15 (range 0.5–1.5)	13	NR	NR	NR
Prealbumin less than 250 mg/L (range 250–450 mg/L)	100	NR	NR	NR
Serum albumin less than 35g/L (range 35–55 g/L)	52	24	NR	NR
Serum globulin more than 35g/L (range 25–35g/L)	26	NR	NR	NR
A/G less than 1.5 (range 1.5–2.5)	65	NR	NR	NR
Renal function disorder	39	NR	NR	NR
Urea nitrogen more than 7.14 mmol/L (range 2.86–7.14 g/L)	39	NR	NR	NR
Creatinine more than 132 mmol/L (range 62–132 g/L)	10	2	NR	NR

Tab. 2 *continued on next page*

	Present study % N=31	Mayo series % N=99	French series % N=25	Japan series % N=102
Thyroid function disorder	70	NR	NR	NR
Free T3 less than 6.5 pmol/L (range 2.5–6.4 pmol/L)	33	NR	NR	NR
Free T4 less than 24 pmol/L (range 9–24 pmol/L)	33	NR	NR	NR
Thyrotropic-stimulating hormone (TSH) more than 5 mIU/L (range 0.4–5.0 mIU/L)	60	NR	NR	NR
Thyroid peroxidase antibody (TPOAB) more than 35 KIU/L (range 0–35 mIU/L)	10	NR	NR	NR
Thyroglobulin antibody (TGAB) more than 50 KIU/L (range 0–50mIU/L)	10	NR	NR	NR
Positive Antimitochondrial antibody (ANA)	63	NR	NR	NR
Positive Extractable nucler antigen (ENA)	0	NR	NR	NR
Positive Antineutrophil cytoplasmic antibody (ANCA)	60	NR	NR	NR

NR indicates not reported

urine and bone marrow. (3) The quantity of monoclonal protein: a median serum IgA M-spike was 7.84 g/L (range, 3.74 to 23.8 g/L); a median serum IgG M-spike was 20.79 g/L (range, 17.8 to 23.76 g/L). (4) Bone marrow biopsy: Of 29 patients who had a bone marrow biopsy performed, 14 patients had a normal-appearing marrow, 15 patients had a bone marrow plasmacytosis, including 13 patients with only more than 5% plasma cells and 2 patients with more than 20% plasma cells.

Skin changes

Skin changes were documented in 30 patients. The most common abnormality was hyperpigmentation (30 patients), followed by thickening (7 patients), those patients with acrocyanosis and plethora, hemangioma /telangiectasia, and hypertrichosis each accounted for 5 patients respectively. 5 patients had a skin biopsy and presented increased skin keratosis, basal cell layer hyperpigmentation, dermal collagen fibers hyperplasia, lymphocyte infiltration around small vessels, elastic fiber degeneration.

Edema and effusions

On presentation, 26 patients (84%) had some form of extravascular volume overload. Peripheral edema, ascites, and pleural effusions were present in 74%, 58%, and 35% patients, respectively (Table 1). The incidence of edema and effusions was higher in our series than in Mayo series; 10 patients had a hydropericardium. 4 patients had a gallbladder hydrops.

Sclerotic bone lesions

On presentation, 17 patients had a radiographic bone survey. 7 patients had at least one abnormality. Of the patients presenting with bone lesion, 1 had solitary bone lesions and 6 patients had more than one lesion at lease. Of the 10 patients not presenting with a bone lesion, 4 had osteoporosis and 2 had hyperosteogeny.

Papilledema

Papilledema was observed in 8 patients (44%) (Table 1). The result was similar to other series, they had been observed in 40% to 55% of patients.

Other established features

29 patients (94%) complained of significant fatigue. 7 patients (22%) had recognized clubbing at diagnosis, 10 patients had Raynaud phenomenon. 3 patients with Raynaud phenomenon had coincident clubbing. 1 patient with Raynaud phenomenon had coincident pulmonary hypertension and portal hypertension.

Laboratory features

On presentation, all patients had a laboratory examination. 5 patients (16%) had thrombocytosis, and 1 (3%) had polycythemia. 92% had the increased erythrosedimentation rate (more than 29 mm/h). Serum lipid changes were documented in all patients. 4 patients (13%) had increased triglyceride levels and 28 patients (89%) had increased cholesterol levels. All patients had the decreased High-density lipoprotein (HDL) and increased Low-density lipoprotein (LDL); decreased serum Apolipoprotein A1 and increased Apolipoprotein B100 were documented in 24 (77%) patients and 22 (71%) patients. We detected the serum immunoglobulin and complements, increased serum IgG, IgA, IgM had been found in 33% (10), 33% (10), 22% (7) patients respectively. 3 patients had the increased complement 3 levels and 10 patients had decreased complement 4 levels. Of the patients, all patients had decreased prealbumin levels. Liver function disorder had been found in 100% patients. Of these patients, 4 patients

had increased serum ALT and AST concentrations respectively, the ratio of AST/ALT had been increased in these patients. Meanwhile, 16 patients and 8 patients had the decreased serum albumin and increased serum globulin levels respectively, correspondingly the A/G ratio was less than normal range in 20 patients, only 4 patients presented both increased AST/ALT ration and decreased A/G ratio. 12 patients had the renal function disorder, including the 12 patients with increased urea nitrogen and 3 patients with increased creatinine.

The thyroid function abnormality presented in 70% (22) patients. Thyroid stimulating hormone in 19 (60%) patients significantly increased, 33 percent of them (6 patients) had decreased levels of free thyroxine, suggestive of overt hypothyroidism; 67 percent of them (13 patients) had normal free thyroxine levels, suggestive of subclinical hypothyroidism. 4 patients only had lower levels of free thyroxine, and TSH levels did not rise. 50% of those patients (3 patients) who had overt hypothyroidism were significantly increased TPO-Ab and TG-Ab titers.

On the presentation, 63 percent of 31 patients had strongly positive expression of ANA, including dot-type in 60% patients, the cytoplasm and homogeneous type in 20% patients. 60 percent of 31 patients have a positive ANCA, were all strongly positive expression PANCA.

The laboratory features were not well-captured in the other large series, but they are described elsewhere.

DISCUSSION

Clinical Manifestations

The classical definition of POEMS syndrome includes five characteristic clinical features, namely paraproteinemia, polyneuropathy, endocrinopathy, organomegaly, and skin changes. The etiology for this syndrome is obscure, and thus the necessity of all features for diagnosis. So far, a number of large-scale retrospective study in the West and Japan have been reported (Dispenzieri *et al.* 2003; Nakanishi *et al.* 1984; Soubrier *et al.* 1994), we attempted to compare our patients with the Japan and the Western in the study.

Peripheral neuropathy

Both our data and other series, the peripheral neuropathy was the most common symptom in all patients. According to the research criteria for the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) of the American Academy of Neurology, POEMS syndrome is regarded as a disease that can be concurrent with CIDP (Saperstein *et al.* 2001). Though the neuropathy resembles chronic inflammatory demyelinating polyneuropathyh, the patients with POEMS syndrome showed slowing of nerve conduction that was more predominant in the intermediate than distal nerve segments, rare conduction block, and more severe attenuation of compound muscle action potentials in the lower than upper limbs (Jia-Ying *et al.* 2003). However, we found slowed nerve conduction and prolonged latencies happened in the distal nerve segments in Chinese patients.

Some study demonstrate a combination of axonal degeneration and primary demyelination in POEMS patients and severe endoneurial edema (Sobue *et al.* 1992; Vital *et al.* 2003). Scarlato et al also suggest that VEGF are involved in the pathogenesis of polyneuropathy because high serum VEGF and peripheral nerve VEGF were all associated with more severe endoneurial vessel involvement and nerve damage (Marina *et al.* 2005). So recognition of the pattern of nerve conduction abnormalities found in our patients, as well as serum VEGF levels in other series, may be helpful for early diagnosis of this particular syndrome.

Organomegaly

In comparison of Mayo clinical series (50%), there were much more patients with organomegaly in our series (84%). The frequency of hepatomegaly, splenomegaly and lyphadenopathy were lowest in Mayo series, splenomegaly was most common in Chinese patients, lyphadenopathy and hepatomegaly was most common in Japan series. Meanwhile, we must pay attention to the other organomegaly like heart and kidney enlargement.

Between 11% and 30% of POEMS patients have documented Castleman disease (giant lymph node hyperplasia, angiofollicular lymph node hyperplasia) (Dispenzieri *et al.* 2003; Nakanishi *et al.* 1984; Soubrier *et al.* 1994; Belec *et al.* 1999).Similarly, 19% patients had Castleman disease in the study. The association between the 2 disorders is well recognized but poorly understood.

Endocrinopathy

Endocrine abnormalities are defining features of the syndrome both in our patients (80%) and Mayo series (67%), though on autopsy, endocrine glands studied appear architecturally normal and without defining characteristics (Sasano *et al.* 1998; Shichiri *et al.* 1998; Gherardi *et al.* 1988)

There were much more patients with endocrinopathy in the presentation than in Mayo series. Compared with French and Mayo series, gonadal dysfunction were also the most common endocrinopathies, but the high prevalence of thyroid dysfunction (62%) demonstrate that the thyroid damage may be the characteristic target organ in Chinese patients. we also found, unlike Mayo series other reports, no patients had parathyroid hormone abnormalities(Udge *et al.* 1993; Cabezas *et al.* 1996).

Diabetes mellitus was a common endocrine manifestation in our series, a finding that is consistent with previously reported large series in Japan and other country (Nakanishi *et al.* 1984; Soubrier *et al.* 1994). In short, it should be cautious that we regard diabetes mellitus and hypothyroidism as the endocrinopathy feature of

patients with POEMS because of the high prevalence in these patients.

The patients who had increased prolactin value (50%) was much higher than Mayo series, but only 25% of them had the gynecomastia or galactorrhea. Most of our men patients had the erectile dysfunction, so care should be taken when attributing these disorders to this syndrome such that a male patient is regarded as having POEMS syndrome.

Monoclonal plasmaproliferative disorde

On the presentation not all patients have a clue about monoclonal plasma-proliferative disorder. We should not make the exclusive diagnosis if M protein is negative, because the monoclonal protein is typically small and will be missed on serum protein electrophoresis in nearly one third of patients if immunofixation is not also done (Dispenzieri *et al.* 2003). The combination of the Japanese study, we found the M component on serum protein electrophoresis had a relatively high proportion in Asia origin than Caucasians. In the study, our experience prompts that bone marrow biopsy repeatedly is necessary because of the clonal plasma cells multifocal distribution. In the best we make biopsy where X-ray, radionuclide bone scan prompted the destruction of places and we could still determine through multisite (bone marrow and lymph nodes, kidney biopsy) organizations immunohistochemistry. The emergence of full-M rate is not high, whether because of a lack of sensitivity or the characteristics of the M protein itself is still worth further exploration.

Skin changes

Skin changes occur in 97% of patients, the ratio was much higher than other groups of case studies (50–90%), hyperpigmentation was the most common manifestations (97%) like Japanese patients (93%). Despite all Asian ethnic origin, Japanese patients had a higher incidence of hypertrichosis (74%) and skin thickening (61%).

Other features

In the study, 44% patients had papilledema, which occurs in 29% to 55% of patients, (Brazis *et al.* 1990; Bolling *et al.* 1990). The pathogenesis of papilledema in POEMS remains uncertain, but Chong *et al* proposed that increased serum levels of vascular endothelial growth factor (VEGF) as evidence that increased vascular permeability may explain the papilledema in this syndrome, the papilledema may result from capillary leakage similar to that happening elsewhere in the body (Deborah *et al.* 2007). Further investigation is needed to determine whether anti-VEGF agents, alone or in conjunction with other agents, may ameliorate the symptoms of POEMS syndrome. If anti-VEGF agents can resolve the papilledema in POEMS syndrome, that will lend further support to the hypothesis that the papilledema in this syndrome results from increased vascular permeability

By comparing we found pitting edema of the lower extremities is common. Asian ethnic ascites and pleural effusion occurred in the proportion is higher than that of Caucasians. In our patients, respectively 4 and 10 patients had gallbladder edema and pericardial effusion, which serous membrane that almost all of the chamber are leaking, attention should be on the pericardium, gallbladder and the inspection of the scrotum.

Bone lesions are a defining feature of the syndrome and occur in approximately 54%– 97% of patients (Dispenzieri *et al.* 2003; Nakanishi *et al.* 1984), but in our patients the incidence of bone damage is far lower than the above-mentioned study, whether single or multiple bone damage to the incidence of bone damage.

Clubbing may occur in up to 13% of patients (Crow *et al.* 1956; Davis *et al.* 1972). Our research proves that this result. Though it is unknown the significance of clubbed fingers for disease development and prognosis, Dispenzieri *et al* demonstrate that the presence of clubbing bodes a poor prognosis.

In particular, we found that 32 % of patients have Raynaud's phenomenon exists, which showed that Chinese patients are more often associated with significant neurovascular change and environmental changes more easily induce the phenomenon. Meanwhile, in our research the patients with Raynaud phenomenon had the more serious symptoms of POEMS, including organomegaly, endocrinopathy, skin changes, peripheral neuropathy, and plasmaproliferative disorder.

Laboratory features

We have summed up laboratory indicators of the POEMS patients that are closely related to the clinical pratice (Table 2). ESR of patient significantly speeded up, though no specific meaning, it demonstrated that the disease progression of patients in China at their acute stage is faster than patients in the Western patients.

All patients had lipid metabolism disorder in our data, in particular, cholesterol metabolism-related factors (HDL, LDL, Apo 1, Apo B100, lipoprotein (a)). Cholesterol metabolism disorder in patients with POEMS may be a result of endocrine disorder, at the same time, it may be an incentives of POEMS multiple complications. Recently, both arterial and venous thromboses (gangrene, ischemia,myocardial infarction, splenic infarcts, and strokes) have been described in the setting of POEMS (Forster *et al.* 1998; Hori *et al.* 1999; Zenone *et al.* 1996; Bova *et al.* 1998). More and more people think that high blood sugar, thrombocytosis, enhanced blood coagulation factor function will increase risk of thrombosis occurring, furthermore cholesterol metabolism disorder may enhance hypercoagulability and promote the formation of thrombus, even lipoprotein (a) has been regarded as an independent risk factor of atherosclerosis. In our series, 6 patients with strokes, 2

with myocardial infarction and 1 with lower extremity venous thrombosis had been found, so we also should pay attention to the lipid metabolism in patients with POEMS and give them positive treatment.

POEMS patients often accompanied by swelling of the liver, liver function at the same time significantly damage. In our data, all the patients have liver damage, in the performance of the enzyme changes, as well as albumin synthesis of the obstacles, the relative increase in globulin synthesis (increased prealbumin levels). Those POEMS patients with liver function disorder, as well as pleural effusion, ascites easily misdiagnosed as liver cirrhosis, two of our patients were misdiagnosed as liver cirrhosis, however, its long-term fever, swollen lymph nodes in the whole body can not be explained by the liver cirrhosis. In words, liver in the body plays an important role in the stability of the environment, so protection of liver function for the treatment of POEMS is of great significance.

In 39% of our patients, all the patients have more than 2 times higher blood urea nitrogen and 10 percent of patients have a significantly higher creatinine. Nearly half of the patients with POEMS-associated renal dysfunction have co-existent Castleman disease (Viard *et al.* 1988; Fukatsu *et al.* 1991).

The precise physiopathogenesis of POEMS syndrome and the associated nephropathy remains unknown. A specific autoantibody effect of the monoclonal protein was not identified (Miralles *et al.* 1992; Mandler *et al.* 1992).

Light-chain deposition is not observed. Membranoproliferative features and evidence of endothelial injury are characteristic (Takazoe *et al.* 1997; Mandler *et al.* 1992). Mizuiri *et al.* (1991) suggested that deposition of paraproteins in the glomeruli could play a role in the pathogenesis of renal involvement, however this could not be interpreted to the majority of patients with no deposition of light chain in the glomeruli. The occurrence of renal abnormalities in POEMS syndrome patients is rare but when present, mild proteinuria, microscopic hematuria, and renal dysfunction requiring hemodialysis can be seen on occasions (Fukatsu *et al.* 1991). As a conclusion, in this syndrome, renal involvement may lead to end stage renal failure and the course may be fatal due to severe polyneuropathy and wasting.

Thyroid axis function was found changed in many POEMS patients. Most patients had subclinical hypothyroidism, which is consistent with other reports (Miralles *et al.* 1992). Those patients with hypothyroidism, who are in need of treatment, were similar to the proportion reported by Soubrier *e*t al and higher than the Mayo series. Though the cause remains elusive, specific antibody-binding activity directed against pituitary tissue was demonstrated in a patient with POEMS syndrome and hypothyroidism (Reulecke *et al.* 1988). Some people had thought that thyroid microsomal antibodies or thyroglobulin antibodies have not been found (Bardwick *et al.* 1980). However, our work has confirmed that 50% of patients with hypothyroidism had the higher level of TPO-Ab and TG-Ab.

Final comments

We made description of the features of Chinese patients with POEMS mainly from the perspective of laboratory and clinical, and contrasted the typical foreign reports. We found Chinese POEMS patients had more obvious multi-system damage, in addition to some typical features of remarkable polyneuropathy (100%), organomegaly (84%), endocrinopathy (87%), monoclonal plasma cell dyscrasia (100%), Skin changes (97%), Chinese POEMS patients often had extravascular volume overload (84%), raynaud phenomenon (31%) and papilledema (44%). Furthermore, almost all patients have a faster sedimentation rate, liver function and blood lipid metabolism, a considerable number of patients showed renal function and thyroid function decline. It is characterized by a more than two-thirds of patients with positive ANA and ANCA testing. We also found that Chinese patients with bone damage in the incidence are lower than in the West and Japanese reports. In summary, our study demonstrate the POEMS syndrome diagnostic criteria proposed by Dispenzieri *et al.* (2003) is also more high applicability in the Chinese population, meanwhile, at the time of diagnosis, we should not only pay attention on the typical characteristics of the disease, but also on the changes in thyroid, liver, kidney function and lipid metabolism.

Unfortunately, as the dispersion of patients, we had not complete treatment and follow-up information of these patients, as a result, the article did not involve the treatment and prognosis of them. Nevertheless, we found the some typical characteristics in Chinese patients. We hope by this report to enhance awareness for Chinese patients, accurate identification of POEMS is necessary for further studies on therapy and prognosis.

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