Original Study

Clinicopathologic Analysis of POEMS Syndrome and Related Diseases☆

Xiaofeng Shi,[1,2] Shudong Hu,[2] Xianqiu Yu,[1] Qin Zhuang,[1] Min Luo,[1] Qian Jiang,[1] Lixia Wang,[1] Yilong Lu,[1] Xiaoming Fei,[1] Xiaodong Xi,[2] Yan Zhu[1]

Abstract

Polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (POEMS) syndrome is a rare and complicated disease, the diagnosis of which is difficult. We analyzed clinical characteristics of 9 patients with this disorder. Some clinical characteristics, including chronic inflammatory demyelinating polyneuropathy, low-level monoclonal plasma proliferation, and distinctive osteosclerotic lesions, can be used for differential diagnosis.

Background: POEMS syndrome, a rare paraneoplastic disease, is related to multiple organs, multiple systems, and multiple disciplines and can be mistaken for other disorders. Consequently, the diagnoses are often delayed. In this work we studied the clinicopathologic characteristics of the POEMS syndrome to improve early diagnosis to prevent irreversible damage. **Patients and Methods:** We conducted a clinicopathologic analysis of 9 cases of POEMS and made a differential diagnosis with related diseases. **Results:** The patients with POEMS syndrome were shown to have complicated clinical characteristics, including peripheral neuropathy, organomegaly, endocrinopathy, monoclonal plasma proliferative disorder, skin changes, extravascular volume overload, sclerotic bone lesions, thrombocytosis, and Castleman disease. POEMS syndrome shared many elements with other diseases and the key way to differentiate them was to determine whether there were other fundamental POEMS syndrome symptoms or signs. The level of M-protein in serum and plasma cells in bone marrow of POEMS patients was lower than that of patients with multiple myeloma (MM). Sclerotic bone lesions were a distinctive feature in patients with POEMS, compared with in those with MM. **Conclusion:** Some unique clinicopathologic characteristics of POEMS syndrome can be used for differential diagnosis. This study provides increased awareness of POEMS syndrome.

Clinical Lymphoma, Myeloma & Leukemia, Vol. ■, No. ■, ■-■
Keywords: Clinicopathologic characteristics, Differential diagnosis, Multiple myeloma, Osteosclerotic myeloma, Sclerotic bone lesions

Introduction

Polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (POEMS) syndrome, also referred to as osteosclerotic myeloma, Crow-Fukase syndrome, or Takatsuki syndrome,[1,2] is a rare paraneoplastic disorder associated with an underlying plasma cell dyscrasia. The classical definition of the acronym, POEMS syndrome, includes the following 5 characteristic features: polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes. Because symptoms of POEMS syndrome are related to multiple organs, multiple systems, and multiple disciplines, misdiagnosis is common.[3] Accurate diagnosis as early as possible is sometimes a challenge for physicians. Recognition of this disease is the first step in effectively managing the disease; therefore, in this study we analyzed the clinical features of POEMS syndrome. Because of the loss to follow-up, therapy and survival were not included in the current report.

Patients and Methods

Nine patients (8 men and 1 woman) with newly diagnosed POEMS syndrome were enrolled in the current study after informed consent was obtained between 2003 and 2011. All of the patients met both major criteria and 1 minor criterion for the

Xiaofeng Shi and Shudong Hu contributed equally to this work.

[1]Department of Hematology, Affiliated Hospital of Jiangsu University, Zhenjiang, Jiangsu, China
[2]Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai, China

Submitted: Feb 6, 2014; Revised: Mar 31, 2014; Accepted: Apr 3, 2014

Address for correspondence: Yan Zhu, MD, Department of Hematology, Affiliated Hospital of Jiangsu University, 438 Jiefang North Rd, Zhenjiang, Jiangsu, China 212001
E-mail contact: zhuyan19591959@163.com

2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2014.04.017

diagnosis of POEMS syndrome.[4] In brief, the diagnostic criteria in 2003 included 2 major criteria (polyneuropathy and monoclonal plasma proliferation) and 7 minor criteria (sclerotic bone lesions, Castleman disease [CD], organomegaly, extravascular volume overload, endocrinopathy, skin changes, and papilledema). We analyzed the available data, including histories, clinical symptoms, physical examinations, laboratory tests, imaging examinations, and diagnostic processes and made a differential diagnosis with related diseases. Nine cases of definite diagnosed multiple myeloma (MM) with λ light chain were selected to be compared with POEMS syndrome.

Results

The mean age of patients with POEMS was 49.5 ± 11.7 years, younger than that of patients with MM (65.5 ± 12.0 years; $P < .05$). The time from onset of symptoms to diagnosis was 2 to 24 months. The 9 patients were in hospitals in different departments, including departments of neurology, dermatology, cardiology, urology, hematology and osteology because of varied initial symptoms. The characteristics of all patients are shown in Table 1.

Peripheral Neuropathy

Peripheral neuropathy was the most common and earliest chief complaint. The symptoms began at the end of the extremities, including numbness, hypoalgesia, and tingling hyperalgesia. Muscle weakness was more representative than sensory loss and was a complaint of almost all of the patients; however, muscle weakness and sensory loss were easily neglected by physicians at the first visit because of the high prevalence and nonspecificity. The physical examination showed decreased muscle strength and tendon reflexes. Motor involvement followed the sensory symptoms; both were distal, symmetric, and progressive with a gradual proximal spread. Cerebrospinal fluid protein levels were increased in all of the 3 patients who underwent lumbar punctures. Six of 9 patients had electromyographic examinations, and all showed similar changes of chronic inflammatory demyelinating polyneuropathy (CIDP) with decreased nerve conduction and prolonged distal latencies. The neurogenic damage in POEMS was chronic and gradually aggravated instead of acute and self-limited, in contrast to Guillain-Barré syndrome.

Organomegaly

Eight of 9 patients had organomegaly, including splenomegaly, hepatomegaly, or lymphadenopathy. Patient 8 had massive lymphadenopathy and lymph node biopsy showed hyaline vascular type of CD (Figure 1A). Because of the difficulty in obtaining tissue, lymph node biopsies could not be obtained in the other 3 patients.

Endocrinopathy

Endocrine abnormalities are a defining feature of POEMS syndrome. All 7 patients who underwent a thorough endocrine evaluation, had at least 1 endocrine abnormality. Seven of 8 male patients had erectile dysfunction. In 4 men with significantly increased prolactin levels, all had gynecomastia. The only female patient had irregular menses. In 5 patients with hypothyroidism, only 2 required treatment and another 3 with a mild increase in the thyroid stimulating hormone displayed subclinical traits.

Monoclonal Plasma Proliferative Disorder

M-Protein. Almost all of the M-proteins were λ type, confirmed using immunofixation electrophoresis, although tests were negative using serum protein electrophoresis. The mean value of λ light chains was 6.33 ± 5.15 g/L (normal value ranges from 0.81 to 1.92 g/L), which was obviously less than that in patients with MM (33.07 ± 37.63 g/L; $P < .05$). Immunofixation electrophoresis also showed increased heavy chains, most of which were immunoglobulin (Ig)A type except 1 IgG type.

Bone Marrow Smear or Biopsy. In all 9 patients, 8 patients received bone marrow aspirate smears and 2 underwent bone marrow biopsies. Only 3 patients had 0.5% to 6% plasma cells (Figure 1B), less than that in the patients with MM (44 ± 18%; $P < .05$). The histologic patterns of plasma cell rimming around lymphoid aggregates were not be found in bone marrow biopsies from the 2 patients.

Skin Changes

Eight of the 9 patients with POEMS had skin changes. The most common abnormality was hyperpigmentation (Figure 2), followed by thickening, acrocyanosis, and plethora (Figure 3).

Extravascular Volume Overload

All of the patients with POEMS had some form of extravascular volume overload, including peripheral edema, pleural effusions (Figure 4A), hydropericardium, and ascites. Two patients underwent examinations of the ocular fundus and 1 patient had papilledema. In all patients with POEMS except for patients 2, 4, and 7, the serum albumin levels were normal, which distinguished POEMS syndrome from renal or hepatic edema. When patients 2, 4, and 7 developed hepatic cirrhosis or renal dysfunction, their albumin levels decreased.

Sclerotic Bone Lesions

All of the patients with POEMS underwent a bone survey of radiography and/or computerized tomography (CT) scan. Five patients had at least 1 abnormality. Patient 1 had a multitude of osteosclerotic lesions in the thoracic and lumbar vertebrae (Figure 4B). Patients 5 and 8 had diffuse sclerotic bone lesions; the extent of sclerotic lesions in patient 5 was seldom seen in previous clinic reports (Figure 5). Positron emission tomography (PET)/CT scans showed that the sites of osteosclerotic lesions had normal fluorine-18 fluorodeoxyglucose (FDG) uptake. Using radiographic localization, a bone tissue biopsy was taken from the sclerotic bone site of a patient and the biopsy showed slightly increased plasmacytes. Patient died from cerebral infarction half a year after diagnosis although chemotherapy was administered, and the other 8 patients were alive for at least 2 years between 2003 and 2011. All of these patients with osteosclerotic lesions had no bone pain. Patient 2 had lytic bone lesions in the ribs (Figure 4A) where he had a consistent pain. In comparison, all patients with MM had osteolysis (Figures 6 and 7) and/or osteoporosis with some degree of consistent bone pain and pathologic bone fractures.