Successful treatment of a patient with POEMS syndrome using thalidomide

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A 49-year-old woman who presented with polyneuropathy, monoclonal plasmaproliferative disorder, organomegaly, edema, endocrinopathy, papilledema, clubbing and thrombocytosis was diagnosed with POEMS syndrome. The authors treated the patient with thalidomide-based therapy, which led to a marked improvement of POEMS syndrome-related symptoms.

Key Words: *POEMS syndrome; Thalidomide*

POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) syndrome is a paraneoplastic disorder due to a clonal plasma cell neoplasm (1). Because the pathogenesis of the disease is unclear, optimal therapeutic management remains unclear. We herein describe a patient with POEMS syndrome treated with thalidomide, which led to a dramatic improvement in her clinical condition.

CASE PRESENTATION

A 49-year-old woman was admitted to the authors' affiliated hospital due to a two-month history of bilateral lower-limb numbness, weakness and night sweats in July 2009. Her height and body weight were 162 cm and 58 kg, respectively. A physical examination revealed bilateral papilledema and pitting edema in the lower limbs. Deep tendon reflexes were diminished in the lower limbs. Complete blood count, serum chemistry and tumour markers results were within normal limits except for thrombocytosis (454×10^9/L; normal range approximately 100×10^9/L to 300×10^9/L). The test for thyroid hormones suggested hypothyroidism (triiodothyronine [T_3]: 1.03 nmol/L; thyroxine [T_4]: 60.97 nmol/L; thyroid-stimulating hormone [TSH]: 6.44 mIU/L; range approximately 1.3 nmol/L to 3.1 nmol/L, 66 nmol/L to 181 nmol/L and 0.27 mIU/L to 4.2 mIU/L, respectively). The level of urine kappa light chain was slightly elevated (21.7 mg/L; range approximately 0 mg/L to 7.1 mg/L) and serum M-protein was detected using immunoeletrophoresis (immunoglobulin G [IgG]: 31.5 g/L; range approximately 8 g/L to 15 g/L). Although it was rare, the clone of IgG-kappa was detected. Unfortunately, serum levels of vascular endothelial growth factor (VEGF) concentration was not tested. X-ray and computed tomography of the patient's body revealed swelling of the supraclavicular lymph nodes, cardiomegaly, pleural effusion, pericardial effusion, splenomegaly and osteolytic lesions of right side acetabulum and pubica. The bone marrow were sampled from iliac crest and manubrium sterni. The percentages of plasma cells were normal (1.6% and 1.73%, respectively; range approximately 0% to 2.5%). A nerve conduction study confirmed polyneuropathy. Ultimately, however, the patient did not exhibit typical skin changes; she was diagnosed with POEMS syndrome.

Treatment with thalidomide (100 mg/day, increased to 200 mg/day 10 days later for eight months) was initiated plus intravenous methylprednisolone (100 mg/day for 14 consecutive days, repeated every 30 days for two months). The patient's neuropathy and abnormal laboratory test results had been markedly improved one month after the therapy, she then received radiation therapy for the bone lesions (40 Gy/20f/4w) to control the pain. The recovery of impaired nerve conduction and complete disappearance of the supraclavicular lymph nodes, pleural and pericardial effusion after thalidomide therapy was confirmed. Cardiomegaly and splenomegaly also disappeared (Figure 1). Thalidomide and methylprednisolone treatment was well tolerated except for fatigue. POEMS syndrome did not flare-up until February 2014, when the patient complained of dyspnea and progressive edema of her lower-limbs. Echocardiography detected severe tricuspid regurgitation with an estimated pulmonary arterial pressure of 50 mmHg. Serum brain natriuretic peptide (BNP) and VEGF concentrations were elevated to 1871 pg/mL (range approximately 30 pg/mL to 70 pg/mL) and 680 pg/mL (range approximately 0 pg/mL to 58 pg/mL), respectively. The patient was diagnosed with congestive heart failure.

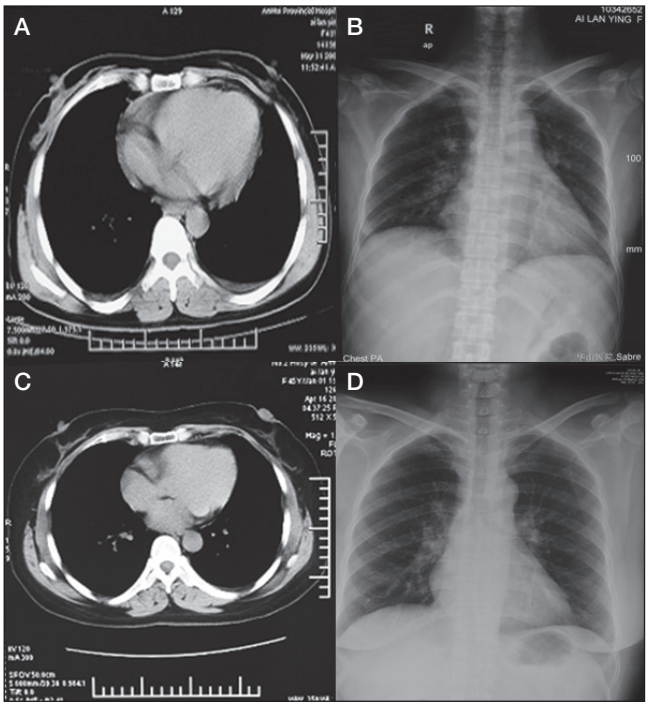

Figure 1) *Cardiomegaly, pleural effusion and pericardial effusion as shown in chest radiography before* (**A,B**) *and after* (**C,D**) *thalidomide therapy*

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She was discharged after the administration of diuretic and thalidomide therapy (100 mg/day for one month), which gradually improved the patient's dyspnea and pitting edema of the lower limbs; echocardiography confirmed improvement of the pulmonary arterial pressure, to 22 mmHg. The levels of plasma BNP and VEGF decreased to 88.4 pg/mL and 64.4 pg/mL, respectively. She currently maintains a favourable condition.

DISCUSSION

In the criteria for the diagnosis of POEMS syndrome, which was advocated by Dispenzieri et al (2), the patient met both mandatory criteria (polyneuropathy, monoclonal plasmaproliferative disorder), one major criteria (VEGF elevation) and five minor criteria (organomegaly, edema, endocrinopathy, papilledema, thrombocytosis). Furthermore, the clinical presentations including clubbing and pulmonary arterial hypertension may also be associated with POEMS syndrome.

The pathogenesis of POEMS syndrome is not completely understood, and avariety of cytokines such as VEGF, tumour necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6 and IL-12 have been reported to be associated with the disease (3). Currently, for an isolated plasmacytoma, radiation is the preferred treatment, and the systemic therapy for POEMS syndrome includes alkylators, corticosteroids, autologous stem cell transplantation, bortezomib, thalidomide and lenalidomide (4). Thalidomide has been successfully used in the treatment of multiple myeloma, and it is becoming a promising agent for POEMS syndrome. Henze et al (5) reported that steroid treatment alone exhibited limited efficacy for POEMS syndrome; therefore thalidomide, which has anti-angiogenic, anti-inflammatory and immunomodulatory actions, may have controlled abnormally secreted cytokines (6) and contributed to the improvement of POEMS syndrome-related symptoms in the present case. Furthermore, compared with autologous stem cell transplantation and bortezomib treatment, thalidomide therapy was inexpensive and may be more tolerable. The clinical course of POEMS syndrome was chronic, and Li et al (7) reviewed the long-term outcomes of 99 Chinese patients with POEMS syndrome, which revealed that 80% of patients were alive after follow-up time of 25 months and 10% patients had survived >60 months. The patient in the present case had also survived 60 months and, given the risks, benefits and costs, the result of thalidomide treatment was satisfactory. When used in the multiple myeloma patients, the thalidomide dose is 200 mg daily for four 28-day cycles; however, the optimal duration of thalidomide therapy in POEMS syndrome is unclear (8). Dispenzieri (2) suggested that the benefits of thalidomide needed to be weighed against the risks of exacerbating the peripheral neuropathy. The present patient who received eight months of continuous thalidomide therapy did not suffer from worse peripheral neuropathy, which suggested long-term thalidomide treatment is safe for POEMS syndrome patients; however, the safety of long-term usage of thalidomide for POEMS syndrome patients should be evaluated in prospective studies.

Pulmonary arterial hypertension, cardiomegaly and congestive heart failure are uncommon features of POEMS syndrome (9,10). We observed the rapid progression of these lesions with the activity of POEMS syndrome and marked improvement following thalidomide therapy. The mechanisms of pulmonary arterial hypertension and cardiomegaly in patients with POEMS syndrome are unclear. Some studies suggested that elevated plasma VEGF and TNF-α levels were important factors in the pathogenesis (11,12), while thalidomide, a drug with potential immumomodulating, antifibrotic and matrix-stabilizing properties, may attenuate the microvascular hyperpermeability and alleviate adverse myocardial remodeling.

In conclusion, we successfully treated POEMS syndrome complicated by pulmonary arterial hypertension, cardiomegaly and congestive heart failure, suggesting that thalidomide is also an effective theraputic strategy.

DISCLOSURES: The authors have no financial and personal relationships with other individuals or organizations that inappropriately influenced their work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in this article.

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