Annals of Hematology & Oncology

Open Access

Austin Publishing Group

Case Report

Poems Syndrome: A Rare and Relatively Unknown Disease

Paola Finsinger, Marta Chisini, Robin Foa and Maria Teresa Petrucci*

Department of Cellular Biotechnologies and Hematology, "Sapienza" University, Italy

***Corresponding author:** Maria Teresa Petrucci, Department of Cellular Biotechnologies and Hematology, "Sapienza" University, Via Benevento 6, 00161 Rome, Italy, Tel: 39 06 49974 430; Fax: 39 06 441639810; Email: petrucci@bce.uniroma1.it

Received: May 15, 2015; **Accepted:** June 02, 2015; **Published:** June 10, 2015

Abstract

POEMS syndrome is a rare paraneoplastic syndrome associated with plasma cell dyscrasia. We report a case of solitary plasmacytoma with osteosclerotic lesion in a 53 year-old man treated with local radiotherapy. After four years, the patient experienced peripheral polineuropathy, cutaneous hyperpigmentation, evidence of multiple bone lesions on CT scan, deep venous thrombosis of the lower extremities, and the presence of a serum M protein. The patient was diagnosed with POEMS syndrome. He received a double high-dose melphalan with autologous stem-cell support which was followed by a systemic and hematologic improvement. Plasmacytoma is very rare as an initial manifestation of POEMS syndrome. Patients presenting with plasmacytoma and an osteosclerotic lesion should be carefully observed and evaluated for the possible development of POEMS syndrome, as most bone plasmacytomas in POEMS syndrome patients are reported to be osteosclerotic

Keywords: Plasmacytoma; Neuropathy; Osteosclerotic lesion

Introduction

POEMS syndrome is a rare multiorgan disorder resulting from an underlying plasma cell dyscrasia, which is characterized by (P) Polyneuropathy, (O) Organomegaly (hepatosplenomegaly or lymphadenopathy), (E) Endocrinopathy (diabetes mellitus, hypothyroidism, or hypogonadism), (M) M-proteinemia, (S) Skin changes (most frequently hyperpigmentation) and associated manifestations, including Castleman's disease, edema (peripheral edema, as cites, pleural effusions), thrombocytosis/erythrocytosis, a predisposition towards thrombosis and abnormal pulmonary function tests [1]. In addition, 88–100% of patients with POEMS syndrome have plasmacytomas with osteosclerotic lesions [2], while the majority of plasmacytomas in patients with classical myeloma is osteolytic. The pathogenesis of POEMS syndrome is not fully understood, but the overproduction of Vascular Endothelial Growth Factor (VEGF) secreted by the plasmacytoma is thought to be responsible for the characteristic symptoms [3]. Usually the first symptom is peripheral polyneuropathy, which is more or less frequently associated with osteosclerotic bone lesions. According to the guidelines and recommendations published by the Mayo Clinic group and updated in 2014 [4,5], the POEMS syndrome diagnostic policy includes: two mandatory criteria (peripheral polyneuropathy and monoclonal paraproteinemia); one major criterion (Castleman's disease, osteosclerotic lesions, increased levels of VEGF); one minor criterion (organomegaly, extra vascular edema, endocrinopathy, skin changes, papilledema, thrombocytosis/erythrocytosis, hyperhydrosis, pulmonary hypertension, thrombotic events) (Table 1). A case of POEMS syndrome is reported below, which developed after an initial manifestation of a solitary plasmacytoma with an osteosclerotic lesion, more than 3 years before the onset of the first systemic syndrome.

Case Report

A 53-year-old man performed a X-ray of the spine in September 2008 due to the onset of pain in the dorsal region, which showed an osteosclerotic lesion around the fifth Thoracic (Th5) vertebral arch. A MRI of the spine, performed to better assess the injury, showed an osteosclerotic lesion of the fifth thoracic vertebra with erosion of the adjacent bone structure, associated to paravertebral tissue compressing the cord. The patient was immediately admitted in the neurosurgical ward, where he underwent a spinal decompression surgery with laminectomy, Th5 somatectomy and vertebral stabilization were performed. Histologic analysis of the specimen by hematoxylin and eosin staining showed a diffuse proliferation of atypical plasmacells, which were positive for CD138 and restricted for the Ig λ light chain (histologic diagnosis of plasmacytoma). The patient was then referred to our hematology institute for further evaluation, where whole-body X-ray showed no other abnormal bone lesions. Both the bone marrow aspirate and bone biopsy showed <5% plasmacell infiltration. Urine immunofixation showed an M component of light λ-chain (124 mg/24-hour urine protein), while no M component was present in the serum. The patient was diagnosed with a solitary plasmacytoma with a Th5 osteosclerotic lesion, for which he received 40Gy of local irradiation. The back and chest-wall pain disappeared after irradiation he then started a follow-up evaluation every 3-6 months and treatment with zoledronic acid every month. On February 2012, the patient had progressive walking difficulties due to weakness of his feet. He did not report any relevant family or medical history and, in particular, no history of neurotoxin exposure. The neurologic evaluation revealed muscle weakness and widespread absence of reflexes in the lower limbs, and also a loss of strength in the extension of the first finger of his right foot. To exclude a possible association of the peripheral neuropathy with monoclonal paraproteinemia and in the suspicion of a possible POEMS syndrome (due to the emergence of a concomitant cutaneous hyper pigmentation of the limbs' and chest's skin), his condition was reassessed. While waiting for the results of the tests performed, in agreement with the neurologists, the patient was treated with 6 cycles

Citation: Finsinger P, Chisini M, Foa R and Petrucci MT. Poems Syndrome: A Rare and Relatively Unknown Disease. Ann Hematol Oncol. 2015;2(5): 1042.

Table 1: POEMS: diagnostic criteria.

Mandatory criteria	1.Peripheral polyneuropathy	both present
	2.Monoclonal paraproteinemia	
Major criterion	3.Osteosclerotic lesions	at least one
	4. Castleman's disease	
	5.Increased levels of VEGF	
Minor criterion	6.Organomegaly	at least one
	7.Extravascular edema	
	8.Endocrinopathy	
	9.Skin changes	
	10.Papilledema	
	11.Thrombocytosis/erythrocytosis	

of plasmapheresis, which was associated with a partial regression of symptoms. The dermatologic evaluation confirmed the diagnosis of diffuse cutaneous hyper pigmentation on the chest and lower limbs; the endocrinologic evaluation showed no signs of endocrinopathy (normal hormonal assays). The total-body CT scan documented numerous osteosclerotic lesions (at the level of the Th8, Th9, L1, L2, L3 vertebrae, as well as the right femur, left ischio-pubic branch, right scapula), mild splenomegaly (spleen longitudinal diameter of 13.5 cm), bilateral pleural effusion and a mild pericardial effusion; the bone marrow biopsy showed a plasmacytosis of 5%; an IgA-λ M protein band was detected by serum immunofixation, and a light λ-chain was detected by urine immunofixation (24-hour urine protein of 207 mg). The patient was diagnosed with POEMS syndrome since he fulfilled required diagnostic criteria (peripheral polyneuropathy and monoclonal paraproteinemia), one major criterion (osteosclerotic lesions) and 3 minor criteria (organomegaly, edema and skin changes). Considering the patient's young age (57 years), the good performance status and the partial regression of the polyneuropathy following the plasma exchange procedures; it was decided to perform an autologous peripheral blood stem cell transplant (auto-PBSCT). In July 2012, before starting therapy, the patient reported pain and swelling of the right lower limb: a doppler ultrasound showed an extensive thrombosis from the right popliteal vein to the external iliac vein and a complete thrombosis of the great saphenous vein and some collateral branches of the thigh and leg. He was hospitalized and put on anticoagulant therapy. During hospitalization, a total-body CT scan, performed following the onset of progressive dyspnea, confirmed the deep vein thrombosis of the right leg and also documented a thrombosis in the left pulmonary artery (lobar and segmental branches to the upper and lower lobes). Following consultation with the cardiologists, a vena cava filter placement was carried out and oral anticoagulant therapy was started. Thrombophilic screening was negative; the thrombo-embolic event fell therefore within the minor diagnostic criteria of POEMS syndrome. After a complete recovery of the patient, it was decided to undergo high-dose chemotherapy followed by an auto-PBSCT. In August 2012, taking into account the partial resolution of the thrombotic event, and the pending leukapheresis procedure, the oral anticoagulant therapy was discontinued and low molecular weight heparins was initiated. The patient then underwent mobilization therapy with cyclophosphamide, followed by granulocyte colony-stimulating factor, and collected a total of $10.2x10^6$ $CD34^+$ cells/kg. In September 2012, he received high-dose melphalan (200 mg/m^2) and $2.25x10^6$ $CD34^+$ cells/kg. Both his walking difficulties and skin pigmentation remarkably improved, but the detection of serum and urine M protein continued after the first PBSCT. In November 2012, a doppler ultrasound of the lower limbs showed an almost complete resolution of the thrombosis of the right leg and, in agreement with the interventional radiologists and with the colleagues of the hemostasis/thrombosis unit, the vena cava filter was removed as planned. In March 2013, he was treated again with high dose melphalan (200 mg/m^2) and $3.2x10^6$ $CD34^+$ cells/kg were infused. The pigmentation of his skin disappeared a few months after the transplant and his walking disorder improved further. A CT scan and a spine MRI documented an improvement of the sclerotic lesions. There was no serum and urine M protein band detectable by immunofixation. In May 2013, however, an electrocardiogram performed for chest pain showed a ST segment elevation in the V3 and V4 leads, for which the patient was admitted to the Coronary Care Unit (CCU) where he underwent a coronary angiography and PCI with stenting of the middle coronary artery. He then started double antiaggregation therapy with acetylsalicylic acid and ticagrelor, and also resumed therapy with oral anticoagulant. In the event of a recurrence of the POEMS syndrome as a possible cause of the new thrombotic event, a reassessment of the disease was performed, but no evidence of relapse was found. The patient today is in complete response, in good conditions, with a good quality of life; he continues in his periodic clinical and laboratory evaluations, and remains on oral anticoagulant therapy.

Discussion

A solitary plasmacytoma is a rare manifestation of plasma cell disorders, which is reported only in 2.8-5% of all the plasma cell neoplasms [6]. The incidence of plasmacytoma in POEMS syndrome is in the range of 41-45% and in most cases it is associated with more osteosclerotic bone lesions. Plasma cell dyscrasias progress overtime from MGUS and/or smoldering myeloma to plasmacytoma or multiple myeloma but the majority of patients experienced osteolytic lesions. Therefore, patients with a solitary plasmacytoma with osteosclerotic bone lesions require careful observation because of the possible coexistence of or progression to a POEMS syndrome [7], that may develop even after many years, as reported in the present case. It has been suggested that VEGF may play an important role in the development of POEMS syndrome [3]. VEGF is a humoral factor that contributes to vascular permeability and angiogenesis, and is produced by plasma cells as well as bone marrow stromal and endothelial cells. As reported by many authors, the serum levels of VEGF are markedly elevated in patients with POEMS syndrome up to about 15–30 times those observed in multiple myeloma patients [3]. In addition, VEGF stimulates chemotactic migration of human osteoblasts and osteoblastic differentiation, and induces bone formation, resulting in the occurrence of osteosclerosis [8]. Therefore, it would be useful to measure the serum levels of VEGF in all patients with plasmacytoma and osteosclerotic lesion, as it is a simple test that correlates with POEMS syndrome, and is very useful during both the diagnostic work-up and the clinical follow-up.

Although no standard treatment for POEMS syndrome has been established, different treatments have been reported (Table

Table 2: POEMS: Therapy.

Treatment	References
Plasmapheresis ± IVIG	Dispenzieri et al. Blood 2003;101(7):2496-2506
Radiotherapy	Dispenzieri et al. Blood 2003;101:2496-2506
	Iwashita et al. Neurology 1977;27:675-681
	Humeniuk et al. Blood 2013;122:66-73
	Wong et al. Am J Opth 1998;126:452-454
Melphalan Dexamethasone	Li et al. Blood 2011;117:6445-6449
Corticosteroids	Nakanishi et al. Neurology 1984;34:712-720
	Orefice et al. Neurol Res 1994;16:477-480
	Arima et al. Acta Medica 1992;83:112-120
Autotransplantation	Sanada et al. Am J Kid Disease 2006;47:672-679
	Ganti et al. Am J Hematol 2005;79:206-210
	Soubrier et al.Bone Marr Transpl 2002;30:61-62
	Dispenzieri et al Eur J Haemat 2008;80:397-406

Table 3: POEMS: new drugs.

Treatment	References
Thalidomide Dexamethasone	Sinsalo et al. Am J Hematol 2004;76:66-68
	Kim et al. Ann Hemat 2006;85:545-546
	Kuwabara et al.J Neurol Neuros 2008;79:1255-7
Lenalidomide Dexamethasone	Dispenzieri et al. Blood 2007;110:1075-1076
	Royer et al. Am J Hematol 2013; 88:207-212
Bortezomib	Tang et al. Eur J Haematol 2009;83:609-610
	Zeng et al. Acta Haematol 2013;129:101-105
	Ohguchi et al. 2011;90:1113-1114
Bevacizumab (anti-VEGF)	Straume et al. Blood 2006;107:4972-4973
	Dietrich et al. Ann Oncol 2008;19:595
	Badros et al. Blood 2005;106:1135

2). High-dose chemotherapy supported by auto-PSCT, including a tandem transplant, is a valid therapeutic option, as demonstrated by the review of several case reports and retrospective collections of more or less numerous case studies, published in the literature [1,9]. In addition, novel therapeutic strategies for POEMS syndrome including bevacizumab (anti-VEGF), [10] thalidomide, lenalidomide [11] and bortezomib [12] have recently been reported as effective molecular-targeted therapy against plasma cells and/or VEGF (Table 3). These agents may provide new treatment options for patients with POEMS syndrome.

Clinical practice points

Plasmacytoma is very rare as an initial manifestation of POEMS syndrome.

Patients presenting with plasmacytoma and an osteosclerotic lesion should be carefully observed and evaluated for the possible development of POEMS syndrome

High-dose chemotherapy supported by auto-PSCT, including a tandem transplant, is a valid therapeutic option.

References

1. Dispenzieri A, Kyle RA, Lacy MQ, Rajkumar SV, Therneau TM, Larson DR, et al. POEMS syndrome: definitions and long-term outcome. Blood. 2003; 101: 2496-2506.
2. Michel JL, Gaucher-Hugel AS, Reynier C, Lhoste A, Philippe P, Aumaitre O, et al. [POEMS syndrome: imaging of skeletal manifestations, a study of 8 cases]. J Radiol. 2003; 84: 393-397.
3. Nobile-Orazio E, Terenghi F, Giannotta C, Gallia F, Nozza A. Serum VEGF levels in POEMS syndrome and in immune-mediated neuropathies. Neurology. 2009; 72: 1024-1026.
4. Dispenzieri A. POEMS syndrome: 2011 update on diagnosis, risk-stratification, and management. Am J Hematol. 2011; 86: 591-601.
5. Dispenzieri A. POEMS syndrome: 2014 update on diagnosis, risk-stratification, and management. Am J Hematol. 2014; 89: 214-223.
6. Bataille R, Sany J. Solitary myeloma: clinical and prognostic features of a review of 114 cases. Cancer. 1981; 48: 845-851.
7. Shindo M, Sato K, Yamamoto M, Toki Y, Hatayama M, Ichiki K, et al. Development of POEMS syndrome after an initial manifestation of solitary plasmacytoma. Int J Hematol. 2011; 93: 815-821.
8. Mayr-Wohlfart U, Waltenberger J, Hausser H, Kessler S, Günther KP, Dehio C, et al. Vascular endothelial growth factor stimulates chemotactic migration of primary human osteoblasts. Bone. 2002; 30: 472–477.
9. Jaccard A, Royer B, Bordessoule D, Brouet JC, Fermand JP. High-dose therapy and autologous blood stem cell transplantation in POEMS syndrome. Blood. 2002; 99: 3057-3059.
10. Badros A, Porter N, Zimrin A. Bevacizumab therapy for POEMS syndrome. Blood. 2005; 106: 1135.
11. Dispenzieri A, Klein CJ, Mauermann ML . Lenalidomide therapy in a patient with POEMS syndrome. Blood. 2007; 110: 1075-1076.
12. Kaygusuz I, Tezcan H, Cetiner M, Kocakaya O, Uzay A, Bayik M. Bortezomib: a new therapeutic option for POEMS syndrome. Eur J Haematol. 2010; 84: 175-177.

Ann Hematol Oncol - Volume 2 Issue 5 - 2015
ISSN : 2375-7965 | www.austinpublishinggroup.com

Citation: Finsinger P, Chisini M, Foa R and Petrucci MT. Poems Syndrome: A Rare and Relatively Unknown Disease. Ann Hematol Oncol. 2015;2(5): 1042.