



A Case with POEMS Syndrome Presenting with Loss of Vision and Skeletal Muscle Strength *Görme ve Kas Gücü Kaybı ile Gelen Bir POEMS Sendromu Olgusu*

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Summary

POEMS syndrome (osteosclerotic myeloma) is a plasma-cell proliferative disorder affecting several organs. The term POEMS is an acronym for polyneuropathy, organomegaly, endocrinopathy, monoclonal proteinemia and skin changes. Although the diagnostic criteria have been modified in time to cover those findings that are seen more frequently but are less specific to make a certain decision, the rare nature of the disease may also be associated with the fact that many patients present with symptoms or signs which are thought to be related to certain organ systems. Peripheral neuropathy is the main symptom in this disease and the most important criterion for the diagnosis of POEMS syndrome. Here, we present a case with POEMS syndrome with almost complete visual loss, dyspnea and loss of muscle strength and significant recovery after treatment. (*Turkish Journal of Neurology* 2013; 19:31-3)

Key Words: POEMS Syndrome, visual loss, loss of muscle strength, dyspnea

Özet

POEMS sendromu (osteosklerotik miyeloma) bir plazma hücresi proliferasyonu bozukluğudur ve çok sayıda organ sistemi belirtisi içerir. POEMS terimi polinöropati, organomegali, endokrinopati, monoklonal proteinemi ve cilt (skin) bulgularını tarif eden bir kısaltma olarak kullanılmaktadır. Tanı kriterleri zaman içinde daha sık görülen ama kesin tanı koymak için daha az spesifik olan bulguları içerecek şekilde değiştirilmiş olsa da, hastalığın çok ender görülüyor olması pek çok hastanın belirli organ sistemleriyle ilişkili olduğu düşünülen semptomlar ya da bulgularla gelmesiyle bağlantılı olabilir. Bu hastalıkta periferik nöropati tabloya hakim klinik bulgudur ve POEMS sendromu tanısı için en önemli kriterdir. Burada tama yakın görme ve kas gücü kaybı ve dispne ile gelen ve tedavi sonrasında semptomlarda belirgin düzelmeye görülen POEMS sendromlu bir vakayı sunmaktayız. (*Türk Nöroloji Dergisi* 2013; 19:31-3)

Anahtar Kelimeler: POEMS sendromu, görme kaybı, kas gücü kaybı, dispne

Introduction

Although a case with sensorimotor peripheral neuropathy, hyperpigmentation, elevated cerebrospinal fluid (CSF) protein level and solitary plasmocytoma was first reported in 1938, osteosclerotic myeloma, or POEMS syndrome, was fully described in 1980. The term POEMS is an acronym for polyneuropathy, organomegaly, endocrinopathy, monoclonal paraproteinemia and skin changes (1). It is defined as a distinct entity due to its characteristic signs.

However, POEMS syndrome is frequently diagnosed by exclusion of other causes of the components. Accordingly, all patients meeting the criteria may not be identified as having POEMS syndrome. Peripheral neuropathy usually dominates the clinical picture and is the most important criterion for the diagnosis. Dyspnea and loss of vision are symptoms encountered on rare occasions in case reports (2,3). Here we present a case of POEMS syndrome with almost complete visual loss, dyspnea and loss of muscle strength. The patient made significant recovery after treatment.

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Received/Geliş Tarihi: 24.11.2011 **Accepted/Kabul Tarihi:** 29.08.2012

Case Report

A 43-year-old female patient was admitted to the internal medicine outpatient clinic of Gulhane School of Medicine with complaints of visual loss for one month and nausea, diarrhea and exertional dyspnea for two days. Nausea was mild but she had diarrhea without mucous or blood 8-10 times a day. Her history revealed that an episode including loss of balance, lower extremity muscle weakness, low back pain and leg pain occurred six years ago. At that time, there were no sensory defects in the patient's neurological examination. She had a distal predominant paraparesis, a positive Gowers' sign and hypoactive patellar reflexes. The Achilles reflexes were bilaterally decreased. She was able to walk unassisted but had a duck-like gait. The upper extremities were normal. Electrophysiological studies revealed a demyelinating neuropathy associated with axonal damage. Sural nerve biopsy at that time was consistent with inflammatory polyneuropathy and she was treated with multiple doses of corticosteroids and intravenous immunoglobulin (IVIG). She had a complete clinical response to IVIG therapy and steroids and was in remission for two years. Four years ago, in conjunction with sensory symptoms, motor weakness emerged, leading to the diagnosis of a polyneuropathy. In an electromyographic (EMG) study, compound muscle action potential (CMAP) amplitude was significantly lower in the lower limbs EMG, nerve conduction velocity was slow, and F responses were prolonged; in the upper extremity, motor nerve conduction velocities were slow and the F responses were prolonged. Dorsiflexion of the toes was weak (4/5). The condition was confirmed as a relapse and there was a partial clinical response to steroid therapy. In her last admission, vital signs were as follows: blood pressure 180/120 mmHg, pulse 112/min, axillary temperature 36.4°C. She had bilateral exophthalmus, pale nail beds, hypothenar atrophy, bibasilar pulmonary rales, moderate sacral edema, hepatomegaly, closure of Traube's area, loss of sensation in both lower extremities, hyperpilosity on sacral and submandibular areas and a muscle strength of 3/5. Her neurological examination revealed weakness, distal limb muscle atrophy and hypoesthesia at bilateral distal extremities. No reflexes could be found at any of the four extremities. Other findings were normal. Initial laboratory findings including complete blood count, routine biochemistry and thyroid function tests were within the normal ranges. The serum immunoglobulin levels were IgA: 6.81 mg/dl (0.7-4.0), IgM: 1.53 mg/dl (0.4-2.3), IgG: 5.72 mg/dl (7.0-16.0). Twenty-four-hour urine catecholamine levels were within normal ranges, and 25-OH vitamin D₃ level was 10.4 µg/dl. Stool smear and culture were nondiagnostic. Eye examination revealed bilateral papilledema, hemorrhages and decreased vision to 1/10. Fundoscopic findings were suggestive of hypertensive retinopathy with optic disc edema. The patient was evaluated for increased elevated intracranial pressure but repeated lumbar puncture attempts failed, most probably due to sacral edema. Abdominal ultrasonographic examination showed hepatosplenomegaly (178 and 150 mm, respectively). Echocardiography revealed stage 1 left ventricular diastolic dysfunction, mild pericardial effusion (LV posterior 6 mm, LV lateral: 9 mm, RA lateral: 8 mm, RV free wall: 9 mm) and pulmonary hypertension (55 mmHg). Because of bilateral rales, increased blood pressure and sacral edema,

diuretic therapy with furosemide was initiated with the addition of diltiazem, lisinopril and acetazolamide. Primary amyloidosis was excluded by rectal biopsy. Lumbar and sacral X-ray revealed sclerotic bone lesions which were confirmed by bone scintigraphy and PET. Serum and urine protein electrophoresis were consistent with a light chain-weighted monoclonal gammopathy accompanying an increase in serum Ig A. Bone marrow biopsy showed focal nodular infiltration by 5-7% percent of plasma cells, and the results were consistent with a plasma cell neoplasia. These cells were immunohistochemically positive for CD138, CD56 and lambda light chain, and negative for CD20 and kappa light chain. Lymphocyte sub-group analysis revealed CD5 (41.2%), CD7 (63.7%) and CD45 (95.4%) expression. A Kongo-red stain was performed on the bone marrow biopsy and amyloidosis was excluded.

With the addition of pale nails ("white nail") that were considered to represent skin changes, and sacral hirsutism with hyperpilosity under the chin that was suggestive of endocrinopathy, the patient was finally diagnosed with POEMS syndrome. Her treatment started with melphalan and prednisolone, and autologous bone marrow transplantation was scheduled after 6 cycles of drugs. After the first cycle of medical treatment, leg pain and muscle strength improved, visual loss recovered to 7/10. Antihypertensive therapy was gradually decreased till it was discontinued and blood pressure returned to normal levels.

Discussion

The diagnosis of POEMS syndrome may be delayed unless the frequently seen diagnostic components appear. In the present case, polyneuropathy is usually essential for the correct decision-making and generally dominates the clinical picture. Our patient had a history of steroid use and intravenous immunoglobulin administration over a long period of time due to polyneuropathy, which led to loss of muscle strength, a condition that was finally resolved after treatment. Although a six-year history of neuropathy without a distinct diagnosis may suggest a delay in correct identification, for this patient it is apparently due to the late appearance of other symptoms and signs specific to POEMS syndrome. Moreover, it is unknown whether corticotherapy and immunoglobulin treatment contributed to decrease the clinical manifestations of this condition in our patient. Besides, due to the rare nature of this condition, early suspicion may not always be present; diagnosis requires a multidisciplinary approach. For example, hepatosplenomegaly is a frequent feature of the disease (4), but abdominal examination is not a part of routine neurological examination. When hirsutism cannot be recognized by the physician during a general visit, normal results of general endocrinological tests may be misleading for a diagnosis of endocrinopathy. Unaltered thyroid function tests excluded the diagnosis of hyperthyroidism for our patient; therefore, it could not be encountered as a component of the syndrome; such patients may also have proptosis due to infiltrative orbitopathy (5,6).

It has become increasingly understood that most patients with POEMS syndrome have ocular signs or symptoms. Papilledema is a minor criteria of the disease that can be seen in one third to one half of the patients (4,7). However, two thirds of the patients with optic disc edema were reported to be symptomatic in a well-

characterized follow-up series (7). Almost half of the patients were reported to have blurred vision, which was caused by optic disc edema in 72% in the same series. However, our patient was admitted with a severe degree of visual loss (1/10) which is rare in the literature. Recovery of papilledema and vision after treatment was previously defined in POEMS syndrome (7). In our case, intracranial hypertension (IH) at diagnosis with severe visual loss declined after the initial diagnosis of plasma cell dyscrasia and treatment of the primary disease. In IgA type plasma cell dyscrasias, there is a good chance of hyperviscosity syndrome, which can cause neurological symptoms. In this syndrome, severe visual disorders, headache and signs of intracranial hypertension can be seen.

Our patient was initiated with the first course of chemotherapy following the diagnosis of plasma cell dyscrasia. After that, the patient had an improvement in loss of vision, headache and symptoms of IH; in particular an increase in muscle strength was observed. According to the literature, plasma cell dyscrasias associated with hyperviscosity syndrome with a clinical improvement were observed after the first cure of chemotherapy (6,7).

Several authors reported rarer symptoms and findings associated with POEMS syndrome. Our patient had exertional dyspnea and end-inspiratory rales that were thought to be related to a hypervolemic state. Plain radiography and chest tomography did not show an abnormal finding, but increased pulmonary arterial pressure was seen in the echocardiography. Pulmonary hypertension (PH) was previously recognized as an infrequent but lethal complication of POEMS syndrome. It is reported to accompany the disease in more than 20% of the patients in the early series (8) which is not regarded to the diagnostic criteria (4). However, in a recent report PH was reported to be present in 48% of patients with POEMS syndrome (9). This suggests the condition occurs due to the increased synthesis of some vasoactive mediators (2,8,10). On the other hand, these patients may also suffer from phrenic nerve paralysis, which can cause or contribute dyspnea (11,12). Due to the increased number of patients in the literature, patients who may possibly have this condition should routinely be tested for PH.

In conclusion, POEMS syndrome may follow a slow course. Therefore, the diagnostic work-up of patients with polyneuropathy should include a multidisciplinary approach, and any vague symptom or sign should prompt a detailed examination.

Acknowledgements

The authors thank to the staff of internal medicine and medical oncology departments of Gulhane School of Medicine.

Conflict of Interest and Sources of Funding Statement

Authors declare no conflict of interests.

No source of funding was used.

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