

POEMS syndrome: A case report

POEMS sendromu: Olgu sunumu

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A 43-year-old female patient admitted with a 2.5-year history of lower extremity symmetrical sensorimotor polyneuropathy, hypertrichosis, sweating, diarrhea, weight loss, and hyperpigmentation. The clinical evaluation met the criteria for the diagnosis of POEMS syndrome. The patient was initially treated with prednisolone and responded well. We planned high-dose chemotherapy with autologous stem cell rescue and introduced a more immunosuppressive regimen containing cyclophosphamide and dexamethasone. We present a case differing from the other cases with her 2 g/day proteinuria and hypertrophic osteoarthropathy.

43 yaşındaki kadın hasta 2,5 yıldır devam eden alt ekstremitelerde simetrik sensorimotor polinöropati, hipertrikozis, terleme, ishal, kilo kaybı ve pigmentasyon artışı ile servisimize kabul edildi. Klinik değerlendirmede bulgular POEMS Sendromu'nun tanı kriterleri ile uyumluydu. Hasta başlangıçta prednisolon ile tedavi edildi ve iyi yanıt alındı. Biz otolog yüksek doz kemoterapi sonrası otolog kök hücre nakli planladık. Burada 2 gram/gün proteinürisi ve hipertrofik osteoartropatisi ile diğer olgulardan farklı bir olgu sunduk.

Anahtar kelimeler: POEMS Sendromu, proteinüri, hipertrofik osteoartropati

Key words: POEMS syndrome, proteinuria, hypertrophic osteoarthropathy

INTRODUCTION

POEMS syndrome is a rare paraneoplastic disease associated with plasma cell dyscrasia. It is also called osteosclerotic myeloma, Crow-Fukase syndrome and Takatsuki syndrome. It is characterized by polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes. These findings are the dominant characteristics of the syndrome, while on the other hand, sclerotic bone lesions, Castleman disease, thrombocytosis, papilledema, peripheral edema, ascites, pleural and pericardial effusions, increase in the levels of vascular endothelial growth factor (VEGF), fatigue and clubbing are other important findings, which are not included in the definition of the syndrome. The major clinical property of the syndrome is chronic progressive polyneuropathy, in which the motor deficit is dominant. Herein, we present our case with POEMS syndrome with an

unusually high proteinuria level and with hypertrophic osteoarthropathy.

CASE REPORT

A 43-year-old female patient admitted to the hospital with a history of lower extremity numbness and weakness that began in her toes 2.5 years before and had progressed proximally in one year, causing failure in mobility and fatigue. Anorexia, edema in the legs, increase in body hair, dyspnea, sweating, diarrhea, weight loss (45 kg), and darkening of the skin were additional symptoms. Physical examination revealed hypertrichosis (Figure 1), hyperpigmentation of the skin (Figure 2), hepatomegaly, splenomegaly, ascites, and pretibial edema, and she also had a cachectic appearance. In her neurological examination, she had tremor increasing with posture and bilateral hypoesthesi-

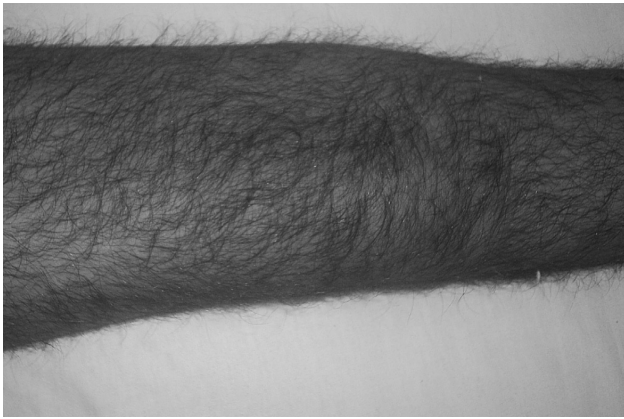


Figure 1. Photograph showing hypertrichosis.

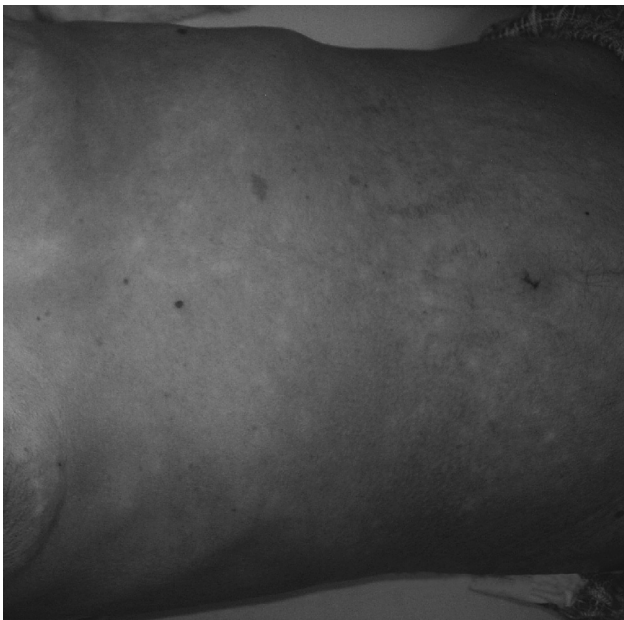


Figure 2. Photograph showing hyperpigmentation of the skin.

a under the knees. Her muscle strength was 4/5 in the proximal right lower extremity, 3-4/5 in the distal, 0/5 in right foot dorsiflexion, 1/5 in plantar flexion; and 4/5 in the proximal left lower extremity, 3-4/5 in the distal, 0/5 in the left foot dorsiflexion, and 1-2/5 in plantar flexion. There was no hypoesthesia or muscle strength deficit in the upper extremity. She was walking with her both feet taking off the floor and scissoring in every step. Laboratory values were in normal range except thrombocytosis ($591 \times 10^9/L$). Biochemical parameters were within normal ranges apart from hypoalbuminemia (2.8 mg/dl) and hyperglycemia (300 mg/dl). 2 g protein was detected in the 24-hour urine collection. A renal biopsy was performed. Minimal interstitial damage and thickening of the

vascular pole in some of the glomerules were observed and amyloid was negative, and the findings were interpreted as non-specific. For investigation of the plasma cell content, a bone marrow biopsy was performed. In the bone marrow biopsy, the bone marrow was hypercellular and was consistent with B-cell lymphoproliferative disorder, which consists of lambda monoclonal atypical plasma cells (Figure 3). M-peak was detected in the serum protein electrophoresis but not in the urine PE. Serum immunofixation was consistent with IgA lambda monoclonal gammopathy. No light chain was detected in the urine immunofixation. Hepatomegaly (20 cm), splenomegaly (15 cm), ascites and left pleural effusion were detected in thoraco-abdomino-pelvic computerized tomography. Minimal pericardial effusion was seen in the echocardiography and the pulmonary artery pressure was 30 mmHg. Respiratory function test and diffusion capacity were normal. The eye examination was irrelevant. Gastric, duodenal and colonic endoscopy and biopsies were normal. The hypothalamo-hypophyso-gonadal axis was tested as normal in the investigation for her secondary amenorrhea. Minimal sinusoidal fibrosis, minimal lobular inflammation and reactive changes were observed in the liver biopsy specimen. Neurogenic changes were observed in the musculus peroneus brevis biopsy and very severe fiber loss with perivascular inflammation was observed in the nervus peroneus superficialis biopsy (Figure 7). Very severe axonal loss in the lower extremities with a background sensorimotor demyelinating polyneuropathy and myogenic involvement in the proximal upper extremities were detected in the electromyog-

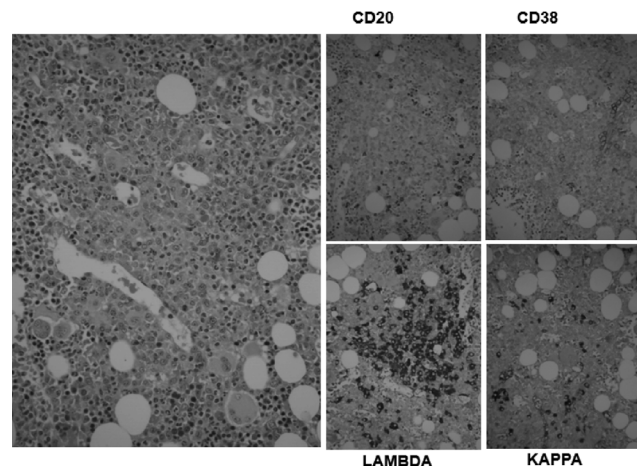


Figure 3. Bone marrow biopsy specimen of the patient showing atypical plasma cell infiltration, which has lambda predominance.

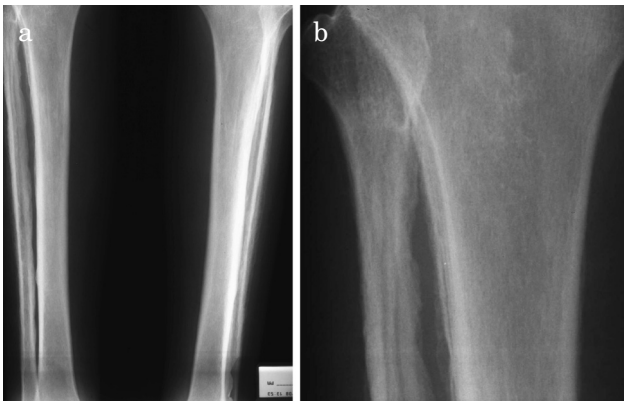


Figure 4. Hypertrophic osteoarthropathy. Undulating and rough periosteal proliferation in tibia and fibula (a). Magnified view (b).

raphy. Radiographic skeletal survey was performed to rule out possible bone involvement. On direct X-rays, solid type periosteal reaction was present bilaterally in diaphyseal regions of the tibia and the fibula (Figure 4A and B). This radiographic appearance suggested hypertrophic osteoarthropathy. Patchy ill-defined osteosclerosis in C6 vertebral body was noted on the plain films of the cervical spine (Figure 5A). Spinal magnetic resonance imaging (MRI) showed low-signal intensity in C6 and T10 vertebral bodies on both T1- and T2-weighted images, consistent with sclerosis (Figure 5B and C). MRI of the bony pelvis revealed diffuse marrow heterogeneity throughout the bones inside the field of view. Some of these lesions were seen as tiny areas of low-signal intensities on all sequences and some of them were of low-signal intensity on spin echo T1-weighted and of high-signal intensity on STIR images (Figure 6). These lesions were invisible on plain radiographs.

The patient was diagnosed as POEMS syndrome and initially treated with 1 mg/kg/day p.o. prednisolone for 6 weeks. Under this treatment, her diuresis increased and her peripheral edema, ascites, and pleural and pericardial effusions improved. Her proteinuria decreased from 2 g/day to 437 mg/day. A repeated neurologic examination revealed improvement as 4/5 in the proximal right lower extremity, 3-4/5 in the distal, 0-1/5 in the right foot dorsiflexion, 3/5 in the plantar flexion; and 4/5 in the proximal left lower extremity, 3-4/5 in the distal, 0-1/5 in the dorsiflexion, and 2-3/5 in the plantar flexion. Hypoesthesia was completely resolved. The patient was able to mobilize and walk without help. The patient was consulted with the hematology section. In the light of recent papers and better outcomes in younger patients, they offered high-dose chemotherapy with stem cell rescue (11-14). Corticosteroid therapy was ceased and cyclophosphamide 125 mg/m² p.o. and dexamethasone 40 mg/day i.v. 1-4 days therapy program was introduced.

DISCUSSION

POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes) is a rare disease that is thought to be associated with plasma cell dyscrasia (1). It is thought that proinflammatory cytokines, especially VEGF, is responsible for the pathogenesis (2). Major and minor diagnostic criteria and properties, which are certainly or probably associated with the disease, have been defined, but none of these findings can solely be used for diagnosis (3,4). In our patient, sensorimotor symmetrical polyneuropathy, monoclonal IgA gammopathy and sclerotic



Figure 5. Osteosclerosis. Oblique cervical spine radiograph shows mild increase in density of C6 vertebral body (arrow) (a). MRI reveals low-signal intensity on T1-weighted image (b) and high-signal intensity on T2-weighted image (c) in the body of C6 vertebra (arrows). Disk spaces are preserved.

bone lesions were present as the major criteria. Among the minor criteria, the patient had skin changes (hyperpigmentation, hypertrichosis), diabetes mellitus and secondary amenorrhea as endocrinopathy, hepatomegaly and splenomegaly, extracellular volume overload (ascites, peripheral edema, pleural effusion, pericardial effusion),

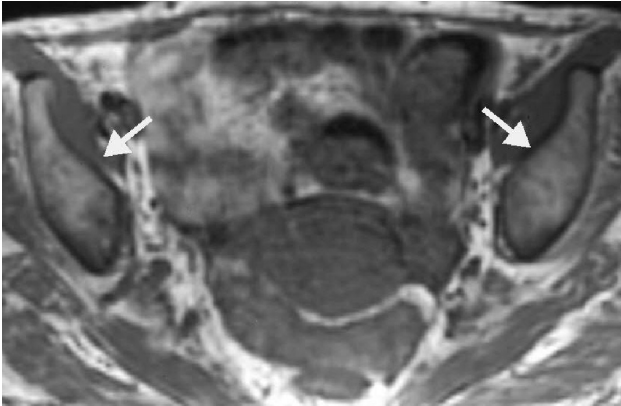


Figure 6. Diffuse bone marrow heterogeneity. Axial T1-weighted spin echo image of pelvis shows multiple areas of low-signal intensity distributed throughout iliac bone (arrows).

thrombocytosis, and polycythemia. In addition, clubbing, weight loss, severe sweating and diarrhea were also present. Our patient met the criteria for the POEMS syndrome (3,4).

Renal dysfunction is generally not the dominant characteristic of this syndrome. A slight proteinuria is generally present. About 9% of the patients have 500 mg or above levels of protein in their 24-hour urine collection tests and just 6% of cases have serum creatinine levels above 1.5 mg/dl (5). Our case had 2 g/day proteinuria, differing from the literature. Bearing in mind that she is a type 2 diabetic, it was thought that the cause of the frank proteinuria might have been the diabetic nephropathy, but her former tests, which were done two years before, revealed that she was not diabetic, and there were no findings consistent with the diabetic nephropathy in the kidney biopsy, so that concept was abandoned. In patients with Castleman disease, it was previously found that the

chance of renal disease is higher, but it was not detected in our patient. Membranoproliferative properties and endothelial damage are the most commonly detected histological properties in the renal biopsy (6), and we also found minimal interstitial damage and vascular thickening in some of the glomerules, consistent with the literature. In our case, there was an additional hypertrophic osteoarthropathy without any cardiac or pulmonary pathology, and a relation between hypertrophic osteoarthropathy and the POEMS syndrome was defined previously (7).

POEMS syndrome has no standardized therapy. Radiotherapy, alkylating agents, corticosteroids, autologous peripheral blood stem cell transplantation following high-dose chemotherapy (8,10-13), and bevacizumab, which is an antibody against VEGF (9) that has recently gained value in the pathogenesis, are among the therapy options. We treated our patient with 1 mg/kg/day corticosteroid as an induction period and observed improvement in neuropathy, edema, ascites and effusions, and platelet counts dropped to normal limits. Approximately one-fourth of the patients respond to corticosteroids. However, without the cure of the underlying plasma cell disorder, relapses are common. Therefore, we planned high-dose chemotherapy with autologous stem cell transplantation. The patient is still receiving cyclophosphamide and dexamethasone as chemotherapy.

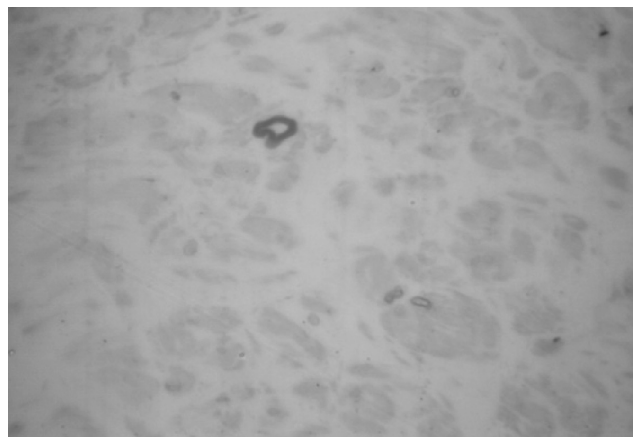


Figure 7. Severe fiber loss is seen in this section (only one thickly myelinated fiber).

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