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From hepatomegaly to POEMS syndrome: A case report

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Abstract

We present a case of POEMS syndrome from Turkiye, a rare, multisystemic condition resulting from plasma cell dyscrasia. POEMS is an acronym representing its cardinal features: Peripheral neuropathy; Organomegaly; Endocrinopathy; Monoclonal plasma-cell proliferative disorder; and Skin changes. The syndrome has an estimated prevalence of 0.3 per 100,000 individuals and typically manifests in the fifth or sixth decade of life. Progressive peripheral neuropathy is the syndrome's most prominent symptom. To ensure an accurate diagnosis, a thorough medical history, physical examination, and comprehensive diagnostic evaluations are essential. These evaluations should include serum immunoelectrophoresis, serum cytokines, and growth factors, a skeletal survey, and a bone marrow biopsy. Early recognition and treatment of POEMS syndrome are crucial to prevent debilitating progression and to optimize clinical outcomes.

Keywords: Hepatomegaly; POEMS syndrome; polyneuropathies.

Introduction

POEMS syndrome is a multisystemic disorder arising from plasma cell dyscrasia. It's named for its key features: Peripheral neuropathy, Organomegaly, Endocrinopathy, Monoclonal plasma cell proliferative disorder, and Skin changes.[1] This syndrome's clinical manifestations can be debilitating, making early diagnosis critical.[2] In Turkiye, only a few cases have been reported.[3–8] This report describes the case of a 44-year-old woman with POEMS syndrome, treated with induction chemotherapy (CyBorD).

Case Report

A 44-year-old woman presented at a general internal medicine clinic with shortness of breath and abdominal distension lasting 6–7 months. She was admitted to the gastroenterology department for ascites-related weight loss investigation. Diagnosed with Guillain-Barré syndrome five years prior, she also had a 10-year history of diabetes mellitus. In the past year, she experienced a 40 kg weight loss and had not menstruated for four months. She appeared cachectic with jugular venous fullness, lung base rales, abdominal distension, ascites, and hepatosplenomegaly. Notable skin findings included acrocyanosis, knee-level hyperpigmentation, and white nails. Laboratory tests revealed primary hypothyroidism (TSH 9.1 µIU/mL [0.27–4.2], fT4 0.62 ng/dL [0.93–1.97], fT3 1.49 pg/mL [2–4.4], anti-TG 582 U/mL [0–115], anti-TPO 84 U/mL [0–34]). Echocardiography suggested right heart failure. Abdominal ultrasonography showed hepatosplenomegaly and free abdominal fluid, with no mass lesions or signs of portal hypertension.

Amenorrhea prompted evaluation for pituitary or adrenal insufficiency. Laboratory results included FSH 0.603 mIU/mL, LH 0.1 mIU/mL, ACTH 66 pg/mL (0–46), estradiol 63 pg/mL, and basal cortisol 9.4 µg/dL (4.3–22.4). An ACTH stimulation test confirmed adrenal insufficiency, leading to the initiation of methylprednisolone (16 mg/day). Severe weight loss warranted a PET CT scan, revealing lymphadenopathy, bone marrow hyperactivity, and sclerotic bone changes.

POEMS syndrome was suspected. Immunoglobulin levels were assessed, revealing Immunoglobulin A 759 mg/dL (45–380), Kappa/Lambda 1.08 (1.35–2.65), and Lambda 294 mg/dL (90–210). Beta2 microglobulin was 0.837. A bone marrow biopsy identified plasmacytoma. An electromyogram detected sensory and motor neuropathy, and an eye examination revealed bilateral papilledema.

POEMS syndrome diagnosis was confirmed based on International Myeloma Working Group (IMWG) criteria. Hematology consultation led to a treatment regimen: subcutaneous bortezomib, intravenous cyclophosphamide, and oral dexamethasone, administered in a 28-day cycle. The ascites observed at diagnosis resolved during bortezomib-based therapy. The patient, initially wheelchair-bound due to severe neurological symptoms, was able to walk with assistance after two cycles of CyBorD.

Discussion

POEMS syndrome is a rare plasma cell disorder characterized by demyelinating peripheral neuropathy and clonal plasma cell proliferation.[2] It was first reported by Bardwick et al. in 1980.[9,10] The pathogenesis of POEMS syndrome involves proinflammatory cytokines, including interleukins, and angiogenic mediators like VEGF, although the precise mechanisms remain unclear.[11]

Our report details a case of POEMS syndrome in Turkiye, a condition with an estimated prevalence of 0.3 per 100,000 individuals.[12] Typically presenting in the fifth or sixth decade of life, progressive peripheral neuropathy is a primary feature.[9] Due to its rarity, POEMS syndrome is often underdiagnosed, sometimes mistaken for chronic inflammatory demyelinating polyneuropathy, leading to delayed treatment and worsening symptoms, particularly neuropathy.[2]

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Table 1. Diagnostic criteria for POEMS syndrome

Mandatory major criteria	1. Polyneuropathy (typically demyelinating)
	2. Monoclonal plasma cell-proliferative disorder (almost always)
Other major criteria	3. Castleman disease
One required	4. Sclerotic bone lesions
	5. VEGF elevation
Minor criteria	6. Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy)
	7. Extravascular volume overload (edema, pleural effusion, or ascites)
	8. Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, and pancreatic)
	9. Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, and white nails)
	10. Papilledema
	11. Thrombocytosis/polycythemia
Other symptoms and signs	Clubbing, weightloss, hyperhidrosis, pulmonary hypertension/restrictive lung disease, thrombotic diatheses, diarrhea, low vitamin B12 values

*: The two mandatory criteria plus ≥1 major and ≥1 minor criteria; POEMS: Polyneuropathy, monoclonal plasma cell-proliferative disorder, sclerotic bone lesions.

For a POEMS syndrome diagnosis according to IMWG, at least one major and one minor criterion from the diagnostic criteria in Table 1 are required.[11] In this case, the patient met three major criteria (polyneuropathy, monoclonal plasma cell-proliferative disorder, sclerotic bone lesions) and four minor criteria (organomegaly, ascites, endocrinopathy, skin changes), along with significant weight loss (Table 1).

Peripheral neuropathy is a dominant clinical feature in all patients, with motor symptoms typically following sensory symptoms.[13] Our patient's five-year neuropathy history, without a definitive diagnosis, suggests a delay in accurate identification, likely due to the late emergence of POEMS-specific symptoms.

Ascites, a common POEMS complication, often presents with a low serum-ascites albumin gradient (SAAG) and no portal hypertension.[14] In this case, the SAAG was 0.89, accompanied by hepatosplenomegaly (Fig. 1), but no portal hypertension was evident in Doppler ultrasonography.

Endocrine abnormalities in POEMS syndrome, present in 67% of patients, include hypogonadism, hypothyroidism, diabetes mellitus, adrenal insufficiency, and hypoparathyroidism.[15] This patient had hypogonadism, hypothyroidism, diabetes mellitus, and adrenal insufficiency.

Cutaneous disorders occur in 68% of POEMS patients, with common manifestations being diffuse cutaneous hyperpigmentation, plethora, and acrocyanosis.[15] Papilledema, a minor criterion, affects one-third to one-half of patients. Recovery of papilledema and vision post-treatment has been documented in POEMS syndrome.[14,15] This patient exhibited lower extremity acrocyanosis and hyperpigmentation, and bilateral papilledema, which resolved after treatment. Bone marrow examination typically shows monotypic plasma cells (usually lambda) in approximately two-thirds of patients, against a backdrop of increased polytypic plasma cells.[15] Serum electrophoresis is necessary to detect the classical λ-restricted M protein.[8] Over 95% of POEMS patients have a monoclonal λ plasmacytoma, confirmed by biopsy.[14,15] In this case, high serum lambda levels and bone marrow biopsy findings supported the pre-diagnosis.

Clinical trials are scarce, and treatment often borrows from myeloma therapies, including small case series. High-dose melphalan and autologous hematopoietic cell transplantation are options for eligible patients.[2] Our patient received a CyBorD treatment regimen, which was well-tolerated, significantly improving her neuropathy and other symptoms. Despite bortezomib's known neuropathic side effects, the improvement in the patient's neurological condition suggests benefits from the combined drugs in the protocol.

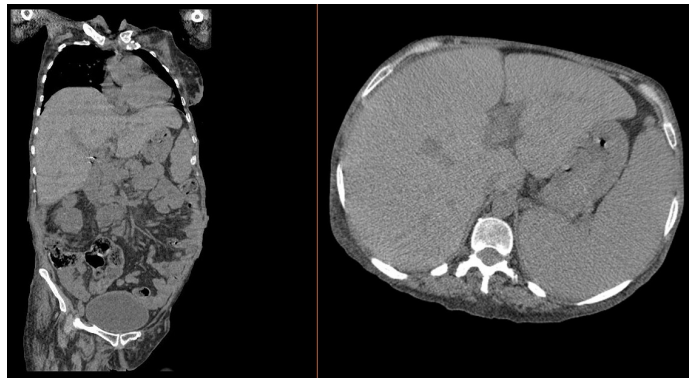

Figure 1. Abdominal computed tomography revealed hepatosplenomegaly and free fluid in the abdomen.

Conclusion

POEMS syndrome is a rare paraneoplastic syndrome with diverse clinical and pathological presentations. In patients with multisystem involvement, POEMS syndrome should be considered. Accurate diagnosis requires a thorough medical history, physical examination, and comprehensive diagnostic evaluation, including serum immunoelectrophoresis, serum cytokines and growth factors, skeletal survey, and bone marrow biopsy. Differential diagnosis is crucial to distinguish POEMS syndrome from other diseases, especially neurological ones. Early recognition and appropriate treatment are vital for optimal clinical outcomes, as the syndrome can be debilitating if not diagnosed and treated in its early stages.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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