Case Report
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POEMS syndrome presenting with colonic pseudo-obstruction and calciphylaxis

Abstract

Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes (POEMS) syndrome is a rare and poorly understood paraneoplastic syndrome driven by monoclonal plasma cell dyscrasia. Common presenting symptoms include neuropathy, endocrine dysfunction, skin changes, and volume overload. Here we describe a young female with history of neuropathy who presented to our hospital with abdominal pain and was found to have persistent colonic pseudo-obstruction .She was diagnosed with POEMS syndrome based on the International Myeloma Working Group diagnostic criteria and her intestinal dysmotility was thought to be a consequence of the underlying syndromic condition. To our knowledge, this is the first case of POEMS syndrome presenting with intestinal pseudo-obstruction.

Keywords: POEMS, monoclonal gammopathy, M protein, pseudo-obstruction, plasma cell disorder

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Vatsala Katiyar,[1] Tiago Araujo,[2] Mina Kerlos,[3] Poushali Bhattacharjee,[4] Adamsu Kumssa[4]

[1]Department of Hematology/Oncology, University of Louisville Hospital, USA
[2]Department of Hospitalist Medicine, Parkland Health Center of Farmington, USA
[3]Chicago Medical School – Rosalind Franklin University 3333 Green Bay Rd, USA
[4]Department of Internal Medicine, John H Stroger Jr Hospital of Cook County 1969 West Ogden Avenue, Chicago IL 60612

Correspondence: Vatsala Katiyar MD, Department of Hematology /Oncology, University of Louisville Hospital, 529 South Jackson Street, Louisville, KY, USA, Tel 312-522-5445, Email Vatsala.katiyar@gmail.com

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Introduction

POEMS syndrome is a multisystemic disorder that is diagnosed using International Myeloma Working Group diagnostic criteria. Although it is a rare and heterogenous disorder with diverse clinical manifestations, polyneuropathy and monoclonal plasma cell disorder are the defining features of this disease.[1] The exact pathophysiology of POEMS has not been discerned, however inflammatory cytokines and vascular endothelial growth factor (VEGF) overproduction appear to play a role in pathogenesis.[2] Herein, we describe a patient who presented with intestinal pseudo-obstruction and was diagnosed with POEMS syndrome. We also highlight the challenges associated with diagnosis of this rare and underdiagnosed condition.

Case presentation

A 39-year-old Polish woman with history of chronic inflammatory demyelinating polyneuropathy (CIDP) presented to our hospital with sudden onset of diffuse abdominal pain associated with constipation and bloating for few weeks and worsening urinary retention for 3-4 months. There was no history of weight loss, vomiting, fevers, gastrointestinal bleeding, diarrhea or substance abuse. She was taking daily prednisone for treatment of polyneuropathy. Six months earlier, patient was evaluated for unexplained persistent thrombocytosis of up to 600k which revealed presence of monoclonal protein and 28% bone marrow plasma cells (BMPCs).

On presentation, she appeared ill with significantly elevated blood pressure of 221/111 mmHg. Physical exam revealed acrocyanosis, prominent clubbing and pitting edema of lower extremities. Abdomen was distended and tender without significant rigidity. Neurological exam revealed loss of sensations, weakness and hyporeflexia. Laboratory work-up including complete blood count and complete metabolic panel were unrevealing. Whole body computed tomography (CT) scan showed pleural and pericardial effusions with moderate ascites. Paracentesis showed high serum-ascites albumin gradient of 1.8 with negative cytology. Due to autonomic and peripheral neuropathy, an abdominal fat pad biopsy was obtained to assess for Amyloid light-chain (AL) amyloidosis.

Patient was initially managed with hydromorphone for pain and antihypertensives (amlodipine and carvedilol) with brief relief of her symptoms. After two days, she developed complete bowel obstruction. Repeat CT-scan of the abdomen revealed significant colonic dilation of 9.7 cm with no transition point (Figure 1). She was managed conservatively with nasgogastric tube placement and discontinuation of oral feeds. Calcium channel blockers and opiates were discontinued. Despite clinical improvement of obstructive symptoms and gradual increase in oral intake three days later, serial abdominal X-rays continued to show significant colonic distention.

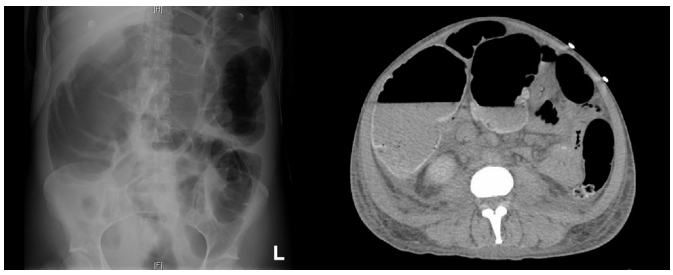

Figure 1 Coronal and axial views of CT scan evidencing severe colonic dilation over 9cm.

At this point, results from abdominal fat pad biopsy came back. It showed small vessel calcification suggestive of calciphylaxis with no evidence of amyloidosis. Due to presence of polyneuropathy, monoclonal protein, fluid overload, skin changes, and thrombocytosis, suspicion of POEMS syndrome was raised. Confirmatory VEGF levels were sent as part of diagnostic work up and came back elevated at 523 (31-86 pg/ml).She then met the diagnostic criteria for POEMS syndrome (fulfilled both mandatory and minor criteria) (Table 1).

Table 1 Diagnostic criteria for POEMS

INTERNATIONAL MYELOMA WORKING GROUP UPDATED CRITERIA FOR THE DIAGNOSIS OF POEMS SYNDROME
1. MANDATORY CRITERIA (Both required)
a) Polyneuropathy
b) Monoclonal plasma cell disorder
2. MAJOR CRITERIA (One required)
a) Sclerotic bone lesions
b) Castleman's disease
c) Elevated VEGF levels (atleast 3 times higher than the normal reference range for the laboratory)
3. MINOR CRITERIA (One required)
a) Organomegaly (hepatomgelay, splenomegaly, lymphadenopathy)
b) Extravscular volume overload (pleural effusions, ascites, edema)
c) Endocrinopathy other than diabetes and hypothyroidism
d) Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, white nails)
e) Papilledema
f) Thrombocytosis/polycythemia

Patient received her first dose of chemotherapy with cyclophosphamide, bortezomib and dexamethasone prior to discharge followed by autologous bone marrow transplant. She made full recovery with resolution of neurologic and abdominal symptoms and dramatic improvement in functional mobility.

Discussion

POEMS syndrome is a rare and poorly understood paraneoplastic disorder that is thought to be driven by a monoclonal plasma cell dyscrasia.[1] Diagnosis is made based on the International Myeloma Working Group diagnostic criteria. Due to rarity of this condition and its evolving course, prompt diagnosis is challenging. Our patient's first symptom was neuropathy and about 7 months later, she was noted to have elevated BMPCs.[2] About a year from being diagnosed with CIDP, she was found to have elevated VEGF levels, skin changes, and fluid overload which ultimately led to her diagnosis of POEMS syndrome. Gastrointestinal (GI) involvement related to this disorder seems to be limited to ascites, hepatomegaly, diarrhea, and gastrointestinal bleed secondary to hemangiomas or calciphylaxis.[1,3,4] To our knowledge, no association with adynamic ileus or colonic pseudo-obstruction has been reported so far.

The intestinal dysmotility seen with POEMS syndrome stem from many pathophysiological disturbances including the upregulation of interleukins. Deranged levels of IL-1β, IL-6 and TNF-α are a hallmark of this syndrome[5] and alterations in their levels is also associated with constipation. Overproduction of cytokines by colonic immune cells interferes with acetylcholine and noradrenaline release in the gut, in turn leading to dysregulation of various metabolic and digestive functions, potentially leading to pseudo-obstruction.[6,7] Another possible mechanism is autonomic dysregulation. Even though POEMS is characteristically thought to exclusively affect the peripheral nervous system, central nervous system demyelination has also been reported,[8] which cast doubts over the exact extent of neurologic involvement. Our patient also had persistent urinary incontinence which, along with decreased intestinal motility, could represent autonomic dysfunction as part of the disease spectrum.

Functional obstruction of intestinal transit can also be induced by numerous disorders and drugs that inhibit motility. While constipation can be attributed to medications like antihistamines, antispasmodics, antipsychotics, opiates and calcium channel blockers, drugs alone do not usually cause pseudo-obstruction in the absence of an inciting event such as trauma, surgery or severe illness.[9] In our case, amlodipine and hydromorphone given on admission were discontinued once abdominal distension was first noted but her symptoms continued to persist 30-50 hours later which outlasts the half-life of these medications. Hence, her intestinal pseudo-obstruction cannot be attributed to these drugs. Additionally, our patient was diagnosed with CIDP which is a sensorimotor-predominant neuropathy with extremely rare involvement of the autonomic system.[10]

Another key finding in our patient was presence of calciphylaxis noted on abdominal fat pad biopsy. Calciphylaxis is a life threatening vasculopathy caused by progressive deposition of calcium in small and medium vessels. Although traditionally observed in patients with end-stage renal disease and/or hyperparathyroidism, the development of calciphylaxis in patients with normal renal and parathyroid function has been reported.[11] Calciphylaxis is also seen in patients with POEMS syndrome and is thought to be a consequence of upregulation of inflammatory cytokines. It is a serious disorder which can lead to livedo reticularis, painful ischemic lesions, sepsis and death.[12] Fortunately, our patient did have livedo reticularis but no ulcerations.

Due to its rarity, randomized controlled trial have not been done to assess the best therapy for POEMS. Based on case reports, high-dose chemotherapy with autologous stem cell transplant seems effective in improving symptoms.[13] Our patient was treated with cyclophosphamide, bortezomib and dexamethasone followed by autologous stem cell transplant.

Conclusion

POEMS syndrome is a complex multisystem and relatively under-recognized disorder. Apart from ascites, hepatomegaly, diarrhea and gastrointestinal bleeding, we aim to highlight colonic pseudo-obstruction as one of the GI manifestations of POEMS. To our knowledge, this is the only reported case of POEMS syndrome presenting with colonic pseudo-obstruction.

Ackowledgments

None.

Conflicts of interest

The authors declare no conflicts of interest.

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