CLINICAL VIGNETTE

An Uncommon Cause of Neuropathy: POEMS Syndrome

Robert Nisenbaum, MD

Case Report

A 56-year-old man who presented to Urgent Care Clinic with a 1-month history of bilateral foot pain which worsened over the prior 2 weeks. He has had a history of low back pain, which was mild and intermittent without recent progression. Evaluation was notable for bilateral hallux valgus on x-ray, mild erythrocytosis on CBC, an A1C of 7.2, normal chemistries and B12/Folate levels. He was offered symptomatic treatment and follow-up.

He returned 1 month later, now with numbness in his fingers and toes. He was given a preliminary diagnosis of diabetic peripheral neuropathy and prescribed metformin and gabapentin. One month later he returned again, with new balance issues and sensory loss/hyporeflexia of his bilateral lower extremities. Repeat labs were notable for mild polycythema, with a negative HIV/RPR/JAK-2 V617F mutation, normal albumin and low-normal erythropoetin level. Of note was a positive SPEP with IFE showing a strong IgA-Lambda monoclonal protein bands in the beta-2 fraction and a weak IgA-Lambda band in the gamma region.

A bone marrow biopsy was requested, based on the progressive neuropathy, polycythemia and m-spikes, but was initially refused with a recommendation to further evaluate the polycythemia with additional peripheral blood studies and markers.

Two weeks later (now 2.5 months from initial presentation and 3.5 months from the beginning of symptoms in his feet), the patient was seen in neurology. He now was ambulating with a cane due to weakness and noted to have a bilateral foot drop. He was admitted to the hospital for expedited evaluation and treatment.

Relevant findings during hospitalization included:

Persistent polycythemia.
CSF Studies: 0 WBCs, Glucose 74, Protein 107, West Nile IGM negative, HSV/VZV DNA not detected, Cytology negative for malignant cells.
Bone survey: Negative for lytic lesions.
Abdominal ultrasound: Hepatomegaly, otherwise normal.
Spinal MRI (with contrast): No significant cord compression or foraminal stenosis. Diffuse contrast enhancement of the cauda equina. Decreased fatty marrow signal within the vertebral bodies.
EMG/NCV: Evidence of a severe axonal sensorimotor polyneuropathy.

During the hospitalization, the working diagnoses were a variant of Guillain-Barre Syndrome or acute (vs. chronic) inflammatory polyneuropathy (AIDP/CIDP). Additional potential etiologies included hematologic malignancy (paraneoplastic, the direct effect of neoplasm or related to paraproteinemia). The patient received a 5 day course of IVIG and noted some improvement in his strength, but still required a walker for ambulation. Neuropathic pain symptoms were treated with gabapentin, amitriptyline and topical lidocaine.

Subsequent to his hospitalization, additional studies were returned, including:

Sensorimotor neuropathy panel: Negative
JAK2 Exons 12 and 13: Not detected
Vascular Endothelial Growth Factor (VEGF): 533 pg/ml (H)
Cryoglobulins: Not detected
Purkinje cell (YO), Neuronal nuclear (Ri/Hu) auto antibodies: Negative
CALR mutation: Not detected
BCR/ABL mutation: Not detected
PET Scan: "No findings to suggest malignancy"

Six weeks after discharge from the hospital, the patient returned to the Hematology-Oncology for reevaluation. During those six weeks, he had gone from ambulating with a walker to being wheelchair bound, needing assistance with transfers. He had lost 21 pounds (10% of his total body weight). The studies which returned post hospitalization were reviewed and in light of his progressive decline, the possibility of a GBS variant was discounted and attention turned to a neoplastic process. In an attempt to clarify the possibility of POEMS Syndrome, radiology was asked to review the CT images associated with the PET scan and two small sclerotic lesions were noted in the vertebral spine.

At this point, the patient had met the criteria for POEMS Syndrome.

Discussion

POEMS is an uncommon paraneoplastic syndrome characterized by polyneuropathy and a monoclonal plasma cell disorder.

It is an acronym defined by Polyneuropathy, Organomegaly, Endocrinopathy, M-protein and Skin changes.

The diagnostic criteria for POEMS are as follows:

Mandatory Major Criteria (Both Required)

1. Polyneuropathy (typically demyelinating)
2. Monoclonal plasma cell-proliferative disorder (almost always λ)

Other Major Criteria (One Required)

3. Castleman disease
4. Sclerotic bone lesions
5. VEGF elevation

Minor Criteria (One Required)

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 include: Clubbing, weight loss, hyperhidrosis, pulmonary hypertension/restrictive lung disease, thrombotic diatheses, diarrhea, low vitamin B12 values.[1]

In light of this patient's progressive decline and meeting criteria for POEMS, bone marrow biopsy was performed and showed a "Slightly hypocelluar marrow for age with scattered aggregates of atypical lambda-expressing plasma cells, consistent with monoclonal gammopathy". This pattern of monoclonal plasma cells evident on bone marrow examination is typical of approximately 2/3 of patients with POEMS while the other 1/3 will have multiple solitary plamacytomas.[1]

Now, with bone marrow involvement being a target for treatment, the patient began treatment with systemic chemotherapy. Treatment for POEMS is similar to those of plasma cell disorders.[1] Because of his significant neuropathy, bortezomib was avoided, in light of its significant (35-54%) risk of inducing peripheral neuropathy.[2] The patient was treated with lenolidomide which arrested the progress of his weight loss and neurologic decline. Although he remained wheelchair bound, his ability to walk short distances and transfer improved. His polycythemia, serum electrophoretic pattern and VEGF levels all normalized. He was now referred for autologous transplant.

When this patient initially presented, he was noted to have lower extremity pain and mild weakness. He ultimately received treatment 6 months after presentation and 4 months after the initial request for bone marrow examination, which was administratively declined. During the intervening time, the patient experienced a significant decline in functional status. In addition to the administrative delay, there are phenotypic clues that retrospectively would have served to push for early bone marrow examination. Of note, 60% of patients with POEMS are initially diagnosed with Chronic Inflammatory Demyelinating Polyradiculoneuropathy. In comparison to inflammatory neuropathy, POEMS patients like this one are more likely to present with severe leg pain, muscle atrophy and distal dominant muscle weakness.[3]

Despite the delay in diagnosis, this patient's long-term survival remains good. In one study, similar patients with young age, normal albumin at outset and a complete hematologic response to initial treatment were likely to have > 62% 10 year survival.[4] Further improvement in his pain and weakness is still possible with autologous stem cell transplant,[5] for which he was referred.

REFERENCES

1. **Dispenzieri A**. POEMS syndrome: 2014 update on diagnosis, risk-stratification, and management. *Am J Hematol*. 2014 Feb;89(2):214-23. doi: 10.1002/ajh.23644. Review. PubMed PMID: 24532337.
2. Bortezomib: Drug Information. UpToDate. Watham, MA. Accessed on November 27, 2018.
3. **Nasu S, Misawa S, Sekiguchi Y, Shibuya K, Kanai K, Fujimaki Y, Ohmori S, Mitsuma S, Koga S, Kuwabara S**. Different neurological and physiological profiles in POEMS syndrome and chronic inflammatory demyelinating polyneuropathy. *J Neurol Neurosurg Psychiatry*. 2012 May;83(5):476-9. doi: 10.1136/jnnp-2011-301706. Epub 2012 Feb 15. PubMed PMID: 22338030.
4. **Kourelis TV, Buadi FK, Kumar SK, Gertz MA, Lacy MQ, Dingli D, Go RS, Kapoor P, Lust JA, Hayman SR, Hwa Y, Rajkumar SV, Zeldenrust SR, Russell SJ, Lin Y, Leung N, Kyle RA, Gonsalves WI, Dispenzieri A**. Long-term outcome of patients with POEMS syndrome: An update of the Mayo Clinic experience. *Am J Hematol*. 2016 Jun;91(6):585-9. doi: 10.1002/ajh.24356. Epub 2016 Apr 13. PubMed PMID: 26972803.
5. **Kuwabara S, Misawa S, Kanai K, Kikkawa Y, Nishimura M, Nakaseko C, Cho RK, Hattori T**. Autologous peripheral blood stem cell transplantation for POEMS syndrome. *Neurology*. 2006 Jan 10;66(1):105-7. PubMed PMID: 16401856.

Submitted November 27, 2018