

# A Case of Peripheral Neuropathy - A Presentation of Poems Syndrome with an Osteolytic Lesion

Revati Suresh<sup>1</sup>, Sureshkumar Radhakrishnan<sup>2</sup>, Sasikala L.<sup>3</sup>

## ABSTRACT

**Introduction:** POEMS syndrome is a rare paraneoplastic syndrome that can often be mistaken for other neurologic disorders.

**Case Report:** A 48-year-old gentleman presented with progressive mixed motor and sensory neuropathy involving lower limbs, with generalized hyperpigmentation and bilateral pitting pedal edema. Neurological examination showed symmetrical wasting involving both proximal and distal groups of muscles of lower limbs, decreased power (Grade 4/5) of the lower limbs with weakness being more severe distally, generalized areflexia, absence of vibration sense and proprioception over the lower limbs and graded sensory loss over the dorsum of both feet. Workup showed a demyelinating sensorimotor polyneuropathy on nerve conduction velocity study and albuminocytological dissociation in CSF. After inconclusive initial evaluation, a PET CT was done which picked up an FDG avid lytic lesion in the L1 vertebra, and lymphadenopathy, and an MRI LS spine confirmed an expansile lesion with "Mini brain sign", indicative of plasmacytoma. Serum free light chain ratio and serum protein electrophoresis were normal. Bone marrow showed no evidence of marrow involvement. Considering the constellation of findings of demyelinating sensorimotor polyneuropathy, lymphadenopathy, peripheral edema and a solitary plasmacytoma, the possibility of a rare variant of POEMS syndrome with an osteolytic lesion was thought of. The lesion was biopsied and proven to be a plasmacytoma. The patient responded well to localized radiation therapy to the lesion, along with intravenous steroids.

**Conclusion:** A subacute symmetric sensorimotor neuropathy may be a presentation of POEMS syndrome. There can be rare instances of a lytic lesion on radiography in POEMS.

**Keywords:** Peripheral Neuropathy, Poems Syndrome with an Osteolytic Lesion

weakness, indicated by difficulty clearing the ground and frequent tripping, and later progressed to involve proximal muscles as well, as indicated by difficulty getting up from a squatting position and climbing stairs. He also experienced paraesthesias over both palms and soles. He also gave a history of weight loss, quantified approximately as 5kg over 2 months. There was no history of upper limb weakness, bowel or bladder involvement, sexual dysfunction or any history of preceding febrile or diarrhoeal illness. He was a known diabetic for the past 2 years, for which he had initially taken Ayurvedic preparations, and then changed to oral hypoglycemic agents(OHA) 6 months ago. He also had a moderate level of ethanol consumption. There were no significant illnesses in the family.

On physical examination, he had stable vitals, generalized hyperpigmentation and bilateral pitting pedal edema. Neurological examination showed symmetrical wasting over lower limbs, normal tone, decreased power (Grade 4/5) of the lower limbs with weakness being more severe distally, generalized areflexia, absence of vibration sense and proprioception over the lower limbs and graded sensory loss over the dorsum of both feet. Motor functions, sensations and reflexes of both upper limbs were normal. There were no cerebellar or meningeal signs. Bilateral fundi were also normal.

Hemogram, urea and electrolytes, liver function tests, thyroid function tests and inflammatory markers were normal. Vitamin B12 levels were low normal. Details of laboratory results are given in Table 1.

The clinical presentation of a symmetric predominantly distal sensorimotor neuropathy initially alerted us to the possibility of a diabetic neuropathy – symmetrical variant. Diabetic polyneuropathy is primarily a symmetrical sensory polyneuropathy, initially affecting the distal lower extremities, and gradually ascending to cause the typical

## INTRODUCTION

POEMS syndrome is a rare paraneoplastic syndrome due to an underlying plasma cell neoplasm. The exact incidence is unknown due to the complexity of the clinical manifestations that are multisystemic, but has been estimated to constitute between 1% and 2% of plasma cell neoplasms.<sup>1</sup> Due to its rarity, diagnoses are often delayed and can also be mistaken for other neurologic disorders, most commonly chronic inflammatory demyelinating polyradiculoneuropathy.

## CASE REPORT

In November 2017, a 48 year old gentleman presented to our institution with a history of progressive weakness of both lower limbs since 2 months. Symptoms began as distal

<sup>1</sup>Resident, Department of Internal Medicine, Amrita Institute of Medical Science and Research, Kochi, <sup>2</sup>Professor, Department of Neurology, Amrita Institute of Medical Science and Research, Kochi, <sup>3</sup>Professor, Department of General Medicine, Amrita Institute of Medical Science and Research, Kochi, India

**Corresponding author:** Dr. Revati Suresh, Resident, Department of General Medicine, Amrita Institute of Medical Science and Research, Kochi, India

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WBC-Blood	4.0 - 10.0 (K/uL)	10.42
NEU-Blood	60.0 - 80.0 (%)	79.2
LYM - Blood	20.0 - 40.0 (%)	16.1
MONO -Blood	2.0 - 10.0 (%)	4.2
EOS-Blood	1.0 - 8.0 (%)	0.3
BASO-Blood	0.0 - 2.0 (%)	0.2
RBC-COUNT-Blood	4.5 - 5.5 (M/uL)	4.56
HGB-Blood	13.0 - 17.0 (g/dl)	13.9
HCT-Blood	40.0 - 50.0 (%)	40.0
MCV-Blood	88.0 - 101.0 (fL)	87.6
MCH-Blood	27.0 - 32.0 (pg)	30.4
MCHC-Blood	18.0 - 48.0 (g/dl)	34.7
RDW-Blood	11.6 - 14.8 (%)	12.4
PLT-COUNT-Blood	150.0 - 400.0 (K/uL)	359
Urea - Serum	17.0 - 43.0 (mg/dl)	10.6
Creatinine;-Serum	0.0 - 1.2 (mg/dl)	0.8
Calcium; total - Serum	8.6 - 10.0 (mg/dl)	8.9
Phosphorus inorganic (phosphate)Serum	2.5 - 4.5 (mg/dl)	4.63
Sodium; serum	136.0 - 146.0 (mmol/L)	137.8
Potassium; serum	3.5 - 5.1 (mmol/L)	5.0
Uric acid - Serum	3.5 - 7.2 (mg/dl)	6.2
Bilirubin Total -Serum	0.0 - 1.1 (mg/dl)	0.68
Bilirubin Direct - Serum	0.0 - 0.2 (mg/dl)	0.2
Protein, total-serum	6.6 - 8.3 (g/dl)	6.8
Albumin; serum	3.5 - 5.2 (g/dl)	4.0
Globulin	2.5 - 4.0 (g/dl)	2.79
AST (SGOT) - serum	0.0 - 40.0 (IU/L)	11.0
ALT [SGPT]-serum	0.0 - 41.0 (IU/L)	8.7
ALP[Alkaline Phosphatase]-serum	42.0 - 128.0 (IU/L)	75.00
Glucose [F]-Serum/Plasma	74.0 - 106.0 (mg/dl)	112.6
HB A1C[Glycated Hemoglobin]	0.0 - 5.9 (%)	6.1
PSA - Total [Prostate Specific Antigen]serum	0.0 - 2.0 (ng/ml)	0.5
TSH [Thyroid Stimulating Hormo-Serum	0.27 - 4.2 (uIU/ml)	3.48
T4 [Thyroxine] free-Serum	1.0 - 1.7 (ng/dl)	1.27
CRP (C-reactive protein) (Ultrasensitive)	0.0 - 1.0 (mg/L)	4.5
Cyanocobalamin (Vitamin B-12);	187.0 - 883.0 (pg/ml)	154.90
Cell count, misc. body fluids,		No Cells/mm <sup>3</sup>
CSF Glucose	40.0 - 70.0 (mg/dl)	119.0
CSF Protein	15.0 - 45.0 (mg/dl)	113.1
Anti CCP	0.0 - 17.0 (U/ml)	<7.00
C3 [Complement Fraction]	90.0 - 180.0 (mg/dl)	89.8
C4 [ Complement Fraction]	10.0 - 40.0 (mg/dl)	18.3
C-ANCA, P-ANCA	- (U/ml)	Negative
Kappa freelite	3.3 - 19.4 (mg/L)	51.91
Lambda freelite	5.7 - 26.3 (mg/L)	55.75

Table-1: Laboratory Investigations

"stocking-glove" sensory loss. Motor involvement with frank weakness occurs in the same pattern, but only later and in more severe cases. In our patient, considering the rapid progression of the illness, along with severe motor component in the setting of a well-controlled diabetic status (HbA1c 6.1), made the diagnosis unlikely.

Taking into consideration the presence of other systemic symptoms like weight loss and generalized hyperpigmentation, other possibilities such as paraneoplastic and paraproteinemic neuropathy were considered. Workup for myeloma (serum free light chains, serum protein electrophoresis, serum immunofixation) was not suggestive

of a plasma cell proliferative disorder. Autoimmune workup (ANA IFA, complement levels, c-anca and p-anca) was also negative.

An NCV showed demyelinating sensorimotor polyneuropathy. A lumbar puncture done subsequently showed albuminocytological dissociation in CSF (Cells 0, Protein 119). Considering paraneoplastic neuropathy as a differential for subacute progressive sensorimotor neuropathy with elevated protein in CSF, a PET CT scan was done which showed FDG avid lytic lesion in the L1 vertebra, along with multiple FDG non-avid supra and infradiaphragmatic lymph nodes. To characterize the lesion,

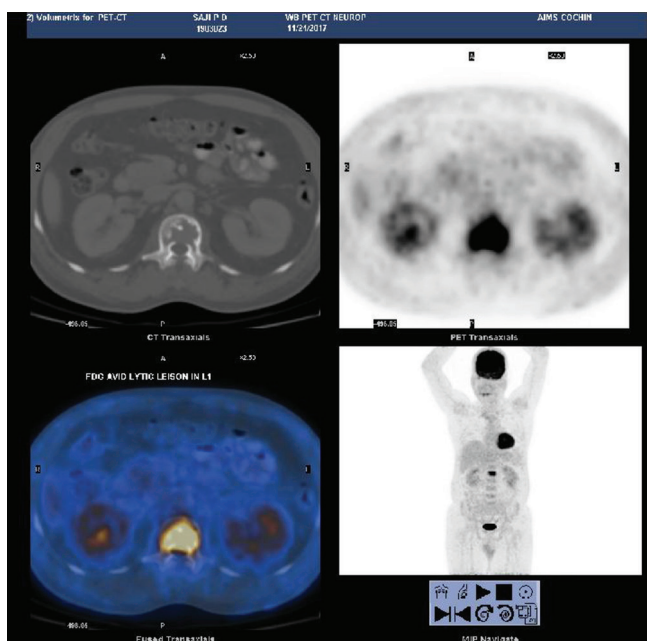


Figure-1: PET-CT - FDG avid lytic lesion L1

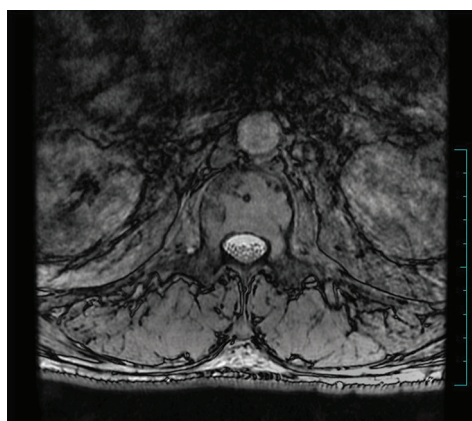


Figure-2: MRI – Axial 3D cosmic sequence



Figure-3: MRI Axial T1 post contrast sequence

an MRI lumbar spine was done. It showed an expansile lesion with intermediate signal intensity noted in the L1 vertebral body and pedicles with well-defined hypodense margins and condensed thick trabeculae within - giving rise to "Mini brain sign" - and showing uniform enhancement on post contrast scan, which was indicative of plasmacytoma. Considering the constellation of findings of demyelinating

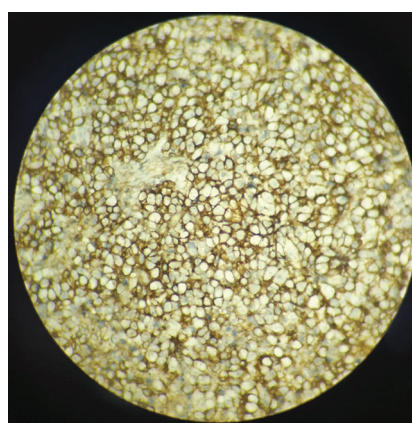


Figure-4: Photomicrograph showing CD138 expression

sensorimotor polyneuropathy with no autonomic or cranial nerve involvement, lymphadenopathy, peripheral edema and a probable plasmacytoma, the diagnosis of POEMS syndrome was considered.

An intra-tumoral decompression of the L1 body tumour with D12 to L2 posterior fusion under GA was done. Operative findings were a tan grey tumour, friable, moderately vascular, involving posterior part of body and left pedicle of L1 vertebra. Histopathology of the lesion confirmed a solitary plasmacytoma, with CD138 positivity. Bone marrow studies showed no evidence of marrow involvement. The patient was started on treatment with radiation therapy localized to the L1 lesion, along with intravenous steroids, and had significant improvement in symptoms.

**DISCUSSION**

The International Myeloma Working Group (IMWG) criteria for the diagnosis of POEMS syndrome require both of the mandatory major criteria, one of the three other major criteria, and one of the six minor criteria to be present.

International Myeloma Working Group (IMWG) criteria for the diagnosis of POEMS syndrome
Mandatory criteria -
<ul style="list-style-type: none"> <li>• Polyneuropathy</li> <li>• Monoclonal plasma cell proliferative disorder</li> </ul>
Major criterion -
<ul style="list-style-type: none"> <li>• Osteosclerotic or mixed sclerotic/lytic lesion visualized on plain films or computed tomography</li> <li>• Castleman's disease</li> <li>• Elevated serum or plasma VEGF levels (at least three to four times the upper limit of normal)</li> </ul>
Minor criterion -
<ul style="list-style-type: none"> <li>• Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy)</li> <li>• Extravascular volume overload (peripheral edema, ascites, or pleural effusion)</li> <li>• Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, or pancreatic disorder excluding diabetes mellitus or hypothyroidism)</li> <li>• Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomas, plethora, acrocyanosis, flushing, white nails)</li> <li>• Papilledema</li> <li>• Thrombocytosis or polycythemia<sup>2</sup></li> </ul>

The pathogenesis of POEMS syndrome has not been well defined however, an imbalance of proinflammatory cytokines has been implicated as a factor. Significantly raised VEGF levels appear to be important in the pathogenesis.<sup>3</sup>

In POEMS syndrome, purely lytic lesions, like the one that was seen in our case, are infrequent. Osseous lesions in POEMS syndrome are commonly sclerotic on radiographs and computed tomography (CT), demonstrate low T1 and T2 signal intensity on magnetic resonance imaging (MRI), and have variable degrees of avidity on positron emission tomography (PET) imaging using 18-fluorodeoxyglucose (18F-FDG).<sup>4</sup> However, there have been few reported cases of POEMS syndrome that manifested with osteolytic lesions as well. In a study of 99 patients with POEMS syndrome at Mayo Clinic, forty-seven percent had only sclerotic lesions, 51 percent had mixed sclerotic and lytic lesions, while lytic lesions without evidence of sclerosis were seen in only 2 percent of patients with bone lesions.<sup>1</sup> Clark et al. studied a case series of 3 such patients with osteolytic lesions concluding that POEMS syndrome should not be discounted as a diagnostic consideration in the setting of osteolytic lesions with non-aggressive imaging characteristics on radiographs or CT, especially in the presence of other supportive clinical features.<sup>5</sup>

Another diagnostic challenge in this case was the undetectable monoclonal gammopathy. An abnormal serum free light chain ratio (sFLC-R) is almost always found in plasma cell disorders, ranging from one third in monoclonal gammopathy with undetermined significance (MGUS) to most in multiple myeloma or primary amyloidosis (AL). However, review of recent studies showed that only 18% of patients with POEMS syndrome had abnormal sFLC-Rs.<sup>5</sup> On flow cytometry on an aspirated bone marrow specimen or immunohistochemistry on a biopsy section, a monoclonal population of plasma cells is detected in a majority of cases.<sup>6</sup> Immunohistochemical stains on focal lesions reveal either IgA or IgG cytoplasmic immunoglobulin in the neoplastic plasma cells. In more than 90% of cases, they are lambda light chain restricted.<sup>1</sup>

The treatment for single or multiple osteosclerotic lesions in a limited area is radiation, and all patients have improvement of their neuropathy over time<sup>7</sup>

In conclusion, the presentation of a subacute symmetric sensorimotor neuropathy should prompt clinicians to keep the possibility of POEMS syndrome as a differential diagnosis, in the setting of inconclusive initial evaluation. In cases with a strong clinical suspicion of POEMS syndrome, the finding of a lytic lesion on radiography should not be a reason to exclude the diagnosis.

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