October 2017

# An Adult with Polyneuropathy and Hypogonadism due to Poems Syndrome

Saba Zaidi
*Aga Khan University*

Sidra Sattar
*Aga Khan University*

Bhojo A Khealani
*Aga Khan University*, bhojo.khealani@aku.edu

CASE REPORT

# An Adult with Polyneuropathy and Hypogonadism due to Poems Syndrome

Saba Zaidi[1], Sidra Sattar[2] and Khealani Bhojo Asumal[3]

## Abstract

POEMS (acronym for polyneuropathy, organomegaly, endocrinopathy, M protein myeloma and skin changes), is a rare disease which occurs in the setting of plasma cell dyscrasias. We describe a case of an adult lady who presented with gradual onset weakness of all four limbs and multisystem involvement characterized by pedal edema, ascites, hyperpigmentation and hypogonadism. Nerve conduction study showed severe sensorimotor polyneuropathy. Serum immunofixation showed lambda light chain restricted monoclonal gammopathy. Bone marrow biopsy consistent with plasma cell dyscrasia. Hormonal assay showed decreased FSH, LH and estradiol levels which led us to diagnosis of hypogonadotrophic hypogonadism. The patient responded well to combination therapy of thalidomide, melphalan and dexamethasone. Eight months after the therapy, she noted decreased paresthesias and increased strength. She had reduced edema and ascites.

**Key Words:** *Polyneuropathy. POEMS syndrome. Edema. Ascites. Hyperpigmentation. Hypogonadism.*

## INTRODUCTION

POEMS syndrome, also known as Takatsuki syndrome or Crow-Fukase syndrome, is defined as a combination of peripheral polyneuropathy, monoclonal plasma cell disorder, and other systemic features like organomegaly, endocrinopathy, skin changes, edema, effusions, ascites and thrombocytosis. POEMS syndrome is 2.5 times more common in men than women. The median age of patients diagnosed with POEMS is 51 years. Neuropathy is the presenting symptom in over 90% of patients with POEMS syndrome.

Here we report POEMS syndrome in an adult lady presented with sensorimotor polyneuropathy along with other characteristics of the disease.

## CASE REPORT

A 38-year lady presented with three years history of numbness and tingling in her soles with weakness of lower extremities. Her symptoms started from lower extremities and later involved the upper extremities. She denied any associated pain. Her condition worsened gradually to an extent that she became bed-bound and dependent for all her routine daily activities. There was no diurnal variation in her symptoms. She felt nauseating for most of the time. She noticed that her skin had darkened, especially her face and hands. She also gave the history of amenorrhea for the past one year. She was married and a product of consanguineous marriage.

On examination, she was an adult cachectic lady, having hyper pigmented wrinkled skin, with bilateral pitting pedal edema. Abdominal examination showed positive fluid thrill. Her neurological examination revealed normal orientation with coherent speech, but unable to hold her head while talking. Extraocular movements were full. There was no facial or palatal weakness. Motor examination showed gross muscle wasting, clawing deformities of both hands with any fasciculation (Figure 1), and bilateral foot drop. Tone was decreased in all the limbs. Power in upper extremities was grade 3/5 proximally and 1/5 distally; in lower extremities, it was 3/5 proximally and 0/5 distally. Reflexes were absent all over and not elicited on reinforcement. Plantar reflex was flexor response bilaterally. Sensory examination

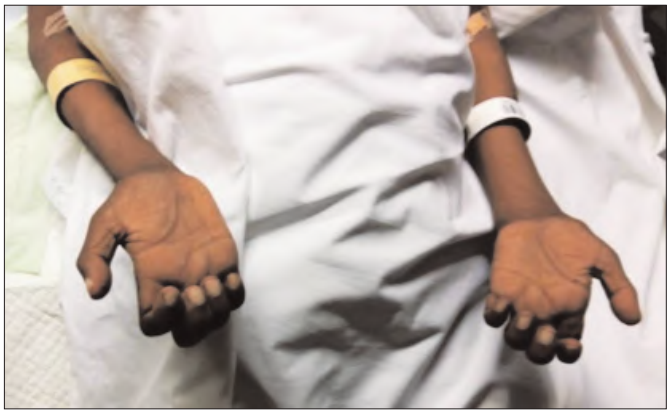

**Figure 1:** Bilateral clawed hands.

[1] *Department of Neurology, The Aga Khan University Hospital, Karachi.*
[2] *Department of Community Health Sciences, Ziauddin University Hospital, Karachi.*
[3] *Department of Neurology, National Medical Centre, Karachi.*

*Correspondence: Dr. Saba Zaidi, Research Officer, Department of Neurology, The Aga Khan University Hospital, Stadium Road, Karachi.*
*E-mail: drsabazaidi@gmail.com*

*Received: June 28, 2016; Accepted: August 07, 2017.*

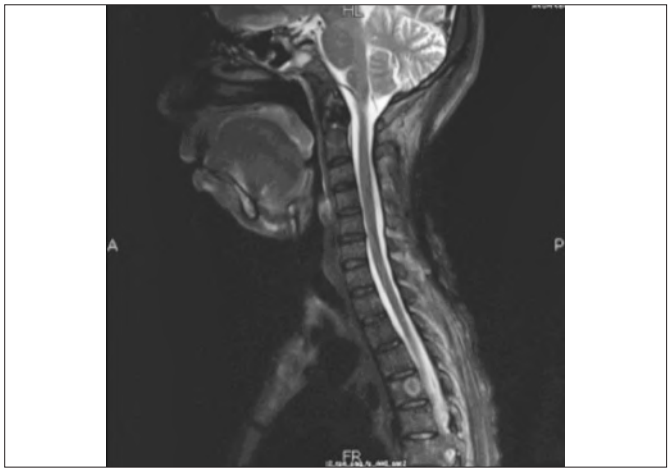


**Figure 2:** Discrete lesion in D4-vertebral body.

showed decreased pain and temperature sensation in a glove and stocking distribution, loss of joint position and vibration in all the four extremities.

Her complete blood picture showed platelet count of 786,000/mm3, ESR 53 mm after first hour and serum albumin at 2.5 gm/dl. CT scan of abdomen showed moderate ascites. Ascitic fluid detailed report suggested non-portal hypertension ascites, (SAAG <1.1). Gene expert for *mycobacterium* tuberculosis and cytology were negative. Nerve conduction study showed severe sensorimotor axonal polyneuropathy, affecting both upper and lower extremities. Her MRI cervical spine showed patchy marrow infiltration in all visualized bones with a discrete lesion at D4 vertebral body showing post contrast enhancement (Figure 2). Serum protein electrophoresis was suggestive of monoclonal gammopathy. Serum IgA level was raised (9.32 gm/l) with lamba light chain restriction. Bone marrow biopsy findings were consistent with plasma cell dyscrasia. Hormonal assays showed FSH=4.2 mUI/ml 4.7, LH=0.10 mUI/ml 2.4 and Estradiol=16 pg/ml, consistent with hypogonadotrophic hypogonadism. Serum TSH, cortisol and random sugar values were in normal range.

Based on clinical picture and laboratory data suggestive of multisystemic illness with predominant polyneuropathy, diagnosis of POEMS syndrome was made. Patient received thalidomide, melphalan and dexamethasone. Eight months after the therapy, she noted decreased paresthesias and increased strength. On follow-up, edema and ascites had also reduced.

## DISCUSSION

Schneiker, in 1938, described first case of POEMS syndrome in a 39-year man with sensorimotor polyneuropathy, solitary plasmacytoma and tanned skin on the anterior chest wall. Crow in 1956 described two cases of peripheral neuritis with myelomatosis. The term Crow-Fukase syndrome was first used in 1984 in a study that involved 102 Japanese patients. The acronym POEMS was given in 1986, by Bardwick *et al*., that represents the important clinical features of this syndrome.[1]

The diagnosis of POEMS syndrome is made by the presence of two major criteria (polyneuropathy and monoclonal plasma cell proliferative disorder) in conjunction with at least one minor criteria (sclerotic bone lesions, organomegaly, edema, ascites, endocrinopathy, skin changes, thrombocytosis and Castleman's disease). A review of 14 cases of POEMS syndrome from 2005 to 2010 showed that initial clinical presentation was motor weakness in 57.1%, numbness in 35.7%, skin hyperpigmentation in 78.6%, edema in 50%, and abdominal distension in 37.3%.[2]

Pathogenesis of this multiorgan disorder is not clearly understood. Elevated levels of cytokines such as TNF alpha, interleukins and VEGF have been involved in the manifestations of POEMS syndrome.[3] VEGF is present in platelets and is primarily responsible for increasing vascular permeability; thereby inducing edema, ascites and pleural effusions. Demyelination can occur due to complement mediated destruction of myelin.

Neuropathy is the presenting symptom in more than 90% of patients with POEMS syndrome. It is sensorimotor, demyelinating and bears striking resemblance to chronic inflammatory demyelinating polyneuropathy (CIDP).[4,5] Neurophysiological features of POEMS neuropathy show nerve conduction abnormalities consistent with demyelination. In contrast to chronic inflammatory demyelinating polyneuropathy (CIDP), conduction block was noted to be rare in POEMS syndrome and conduction slowing was more marked in intermediate nerve segments. Furthermore, there was evidence of greater reduction in compound motor action potential amplitudes in POEMS syndrome, suggesting severe axonal loss.[5] In this case, nerve conduction study findings were consistent with severe sensorimotor axonal polyneuropathy. Most patients have multiple endocrine abnormalities.[3] Various endocrinopathies are associated with POEMS like hypogonadism, hypothyroidism, diabetes mellitus, adrenal insufficiency, hyperprolactinemia and hypoparathyroidism. Hypogonadism has a high prevalence and is primary gonadal failure in 70% of cases.[6] This patient had history of amenorrhea and she was diagnosed on the basis of hormonal workup as hypogonadotrophic hypogonadism. Other possibilities like hypothyroidism, hypocortisolism and diabetes were excluded.

Skin changes in POEMS syndrome include diffuse hyperpigmentation, hypertrichosis, skin thickening, angiomas, whitening of nails, clubbing, alopecia, flushing and ichthyosis. This patient also had diffuse hyperpigmentation and white nails.

Pitting edema of lower limbs, ascites and pleural effusion are other signs appreciated in these patients. A

review of 106 patients in Chinese PLA General Hospital, concluded that ascites is a common complication of POEMS syndrome and has characteristics of non-portal hypertension, based on low SAAG.[8] Increased immune activation and inflammatory status could contribute to the pathogenesis of ascites in POEMS syndrome.[8]

The monoclonal gammopathy is the characteristic feature of POEMS syndrome, which was present in 95% of patients; and it is always restricted to lamba light chain protein associated with IgG and IgA.[9] In view of multiple organ involvement including polyneuropathy, extravascular volume overload, i.e. pedal edema and ascites, hypogonadism, skin changes and lambda-chain monoclonal gammopathy, this patient was diagnosed with POEMS syndrome.

Importance of recognizing this rare syndrome lies in its potential for treatment and relatively better response compared to neuropathies associated with other plasma cell dyscrasias like monoclonal gammopathy of unknown significance or Waldenstorm macroglobulinemia.[10]

Neuropathy with POEMS syndrome is often mis-diagnosed as CIDP. Patients commonly receive immunomodulatory therapies including intravenous gamma globulin, plasmapheresis, azathioprine and cyclosporine which have no role in the management of POEMS syndrome. So correct diagnosis is essential, as therapies that may be effective in patients with CIDP are not effective in patients with POEMS. Instead, the mainstays of therapy for these patients include irradiation, corticosteroids, alkylator-based therapy, and chemotherapy.

## REFERENCES


1. Humeniuk MS, Gert MA, Dispenzieri A. Outcomes of patients with POEMS syndrome treated initially with radiation. *Blood* 2013; **122**:68-73.
2. Ji ZF, Zhang DY, Weng SQ, Shen XZ, Liu HY, Dong L. POEMS syndrome: a report of 14 cases and review of the literature. *ISRN Gastroenterol* 2012; **1**:2012.
3. Daroff RB, Fenichel GM, Jankovic J, Mazziotta JC. Bradley's Neurology in Clinical Practice. 7th edition.
4. Krishnan AV. Polyneuropathy in POEMS syndrome: Alterations in nerve function and morphology. *Clin Neurophysiol* 2015; **126**:1845-6.
5. Nasu S, Misawa S, Noto Y, Fujimaki Y, Shibuya K, Isose S, *et al.* Patterns of nerve conduction abnormalities are different in POEMS syndrome and CIDP. *Clin Neurophysiol* 2010; **121**: e25.
6. Zou ZZ, Cui LL, Sun QQ. Electrophysiological features in POEMS syndrome in patients of China. *In Muscle And Nerve* 2011; **44**:649-9.
7. Dispenzeri A. POEMS syndrome (osteosclerotic myeloma) *Blood Rev* 2007; **21**:285-99.
8. Cui RT, Yu SY, Huang XS, Zhang JT, Li F, Pu CQ. The characteristics of ascites in patients with POEMS syndrome. *Ann Hematol* 2013; **92**:1661-4.
9. Dao LN, Hanson CA, Dispenzieri A, Morice WG, Kurtin PJ, Hoyer JD. Bone marrow histopathology in POEMS syndrome: a distinctive combination of plasma cell, lymphoid, and myeloid findings in 87 patients. *Blood* 2011; **117**:6438-44.
10. Latov N. Diagnosis and treatment of chronic acquired demyelinating polyneuropathies. *Nat Rev Neurol* 2014; **10**: 435-46.