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(CASE REPORT)

POEMS syndrome masquearading as Tuberculosis

Sonika Mayanglambam [1,*], LH Ghotekar [2], Madhur Yadav [2], Shivraj Meena [3], Shubham Goswami [4] and Bangkim Kshetrimayum [5]

[1] *Senior Resident, Department of Medicine, Lady Hardinge Medical College, New Delhi, India- 110001.*
[2] *Director Professor, Department of Medicine, Lady Hardinge Medical College, New Delhi, India -110001.*
[3] *Associate Professor, Department of Medicine, Lady Hardinge Medical College, New Delhi, India -110001.*
[4] *Senior Resident, Department of Clinical hematology and Oncology, Rajiv Gandhi Cancer Institute and Research, Rohini, New Delhi, India-110085.*
[5] *Assistant Professor, Department of Architecture, School of Planning and Architecture, New Delhi, India-110002.*

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Abstract

POEMS syndrome, also called Osteosclerotic myeloma or Takatsuki syndrome or Crow-Fukase syndrome, is a rare multisystemic disease paraneoplastic syndrome under the plasma cell dyscrasias. POEMS is an acronym for Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein elevation, and skin changes. It is usually 1.5 times more common in male than female. Patients often present in the fifth to sixth decades of life and have a median survival rate of 8 to 14 years without successful treatment.

Here we described a case of POEMS syndrome in a young 30 years old adult who presented with anasarca, polyneuropathy as initial manifestation and masquerading as tuberculosis. He was successfully treated with Melphalan-Dexamethasone therapy with clinical improvement.

Therefore, patients with unexplained polyneuropathy especially when it is associated with endocrinopathy, skin changes or oedema, should be evaluated for POEMS syndrome.

Keywords: POEMS syndrome; Anasarca; Polyneuropathy; Tuberculosis

1. Introduction

POEMS syndrome is a rare multisystemic disease paraneoplastic syndrome under the plasma cell dyscrasias. POEMS is an acronym for Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein elevation, and skin changes. The syndrome was first described in 1956 by Crow and then by Fukase et al in 1968 in Japan [1]. Therefore, it was also termed as Crow-Fukase syndrome in 1984 in a study performed in 102 Japanese patients by Nakanishi et al. [2]. The term "POEMS" was coined by Bardwick et al. in 1980 [3]. Other synonyms include Osteosclerotic myeloma, Takatsuki syndrome and PEP syndrome (polyneuropathy endocrinopathy plasma cell dyscrasia). Because of its rarity, it is usually underdiagnosed. It usually is 1.5 times more common in male than female [1]. Patients often present in the fifth to sixth decades of life and have a median survival rate of 8 to 14 years without successful treatment [4]. Neither a single clinical feature nor a single test can confirm the diagnosis of POEMS syndrome. Diagnosis of POEMS syndrome needs two mandatory criteria, one major and one minor criteria [5]. Diagnosis criteria based on International Myeloma Working Group (IMWG) [5] are shown in table1. The pathogenesis is unclear, but high circulating levels of the proinflammatory cytokines IL-1, IL-6, VEGF and TNF have been documented.

* Corresponding author: Sonika Mayanglambam

2. Case

A 30 years gentleman resident of Delhi, Swiggy delivery boy by occupation, diagnosed case of previously treated pulmonary tuberculosis (treated for 6 months) 4 years back, presented with chief complaints of abdominal distension for 3 months followed by bilateral lower limbs swelling since1 month; burning paresthesia in bilateral upper and lower limbs for 2 months; difficulty in walking and slippage of chappals since 1 month and shortness of breath since 1month. He was also giving history of weight loss, sexual (erectile) dysfunction & skin hyperpigmentation since last 2 months. On examination, he was found to be cachexic, had mild pallor, bilateral pedal oedema, generalized hyperpigmentation and skin thickening (sclerodermoid). Respiratory system revealed reduced bilateral chest wall expansion (right >left), stony dullness at right infra-axillary, axillary and infra-scapular areas. On per abdomen; shifting dullness was present. Central nervous system examination revealed bilateral symmetrical LMN (lower motor neuron) quadriparesis with small plus large fiber sensory neuropathy. On laboratory investigation, complete blood count, biochemistry panel, seropositive status & viral hepatitis panel were unremarkable. ANA was negative. Ascitic fluid analysis showed low SAAG ascites with lymphocytic predominance [TLC=650 cells, Lymphocytes 85%] with borderline ADA.

As the patient was a case of previously treated pulmonary tuberculosis, suspecting the tubercular ascites, patient was started on anti-tubercular drugs. But as he wasn't responding to the anti-tubercular drugs, we further ordered relevant investigations suspecting POEMS syndrome. The suspicion of POEMS was in view of polyneuropathy, skin changes and possible endocrine abnormality. His serum protein electrophoresis (SPEP) showed M spike in gamma fraction. Nerve conduction velocity study showed sensorimotor demyelinating polyneuropathy and he was found to have primary hypothyroidism. Radiological investigations including chest x-ray, x-ray bilateral pelvis & abdomen, CECT abdomen and MRI spine were performed suspecting plasma cells dyscrasias with paraneoplastic manifestations. Chest x-ray film (Figure 1) shows few osteosclerotic lesions in bilateral humerus and ribs and right sided pleural effusion. Figure (2) shows multiple variable sized scattered osteosclerotic lesions noted involving axial skeleton- pelvis and spine. Most of the lesions have well-defined margins while few showed fluffy sclerosis likely due to confluent nature of few lesions. Few of these similar lesions were also noted in ribs and scapula.

Table 1 Diagnostic Criteria for POEMS SYNDROME

Mandatory major criteria [both required]	1. Polyneuropathy (Typically Demyelinating) 2. Monoclonal Plasma Cell Proliferative disorder (always almost lambda)
Other major criteria [once required]	3. Castleman disease 4. Sclerotic bone lesions 5. Vascular endothelial growth factor (VEGF) elevation
Minor criteria [one required]	6. Organomegaly (Splenomegaly, Hepatomegaly or Lymphadenopathy) 7. Extravascular volume overload (ascites, oedema or pleural effusion) 8. Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic) 9. Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, white nails) 10. Papilledema 11. Thrombocytosis/ Polycythaemia
Other symptoms/signs	12. Digital clubbing, weight loss, hyperhidrosis, pulmonary hypertension/ restrictive lung disease, thrombotic diathesis, diarrhea, low vitamin B12 values

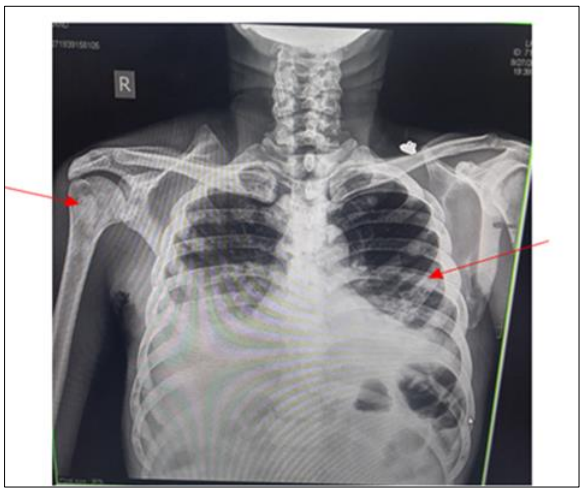

Figure 1 Chest-X ray image showing few osteosclerotic lesions in bilateral humerus and ribs (red arrows) and Right sided pleural effusion

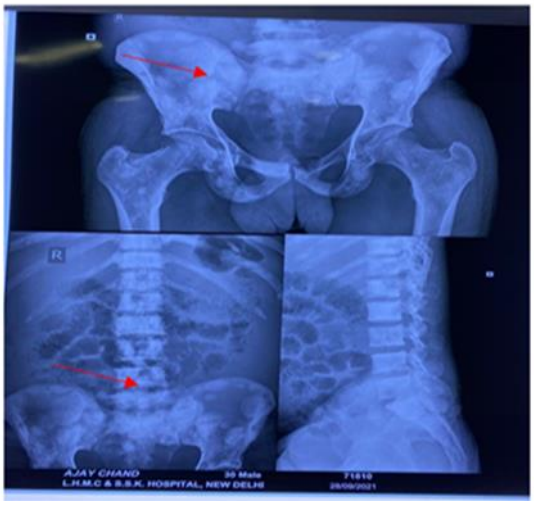

Figure 2 X-Ray film revealed multiple variable size scattered osteosclerotic lesions involving axial skeleton -pelvis and spine (red arrow)

CECT chest and abdomen (Figure 3) showed bilateral pleural effusion, moderate ascites, and splenomegaly. CT bone (Figure 4) window revealed multiple sclerotic lesions of varying sizes involving the axial skeleton- vertebral bodies, posterior elements, ribs, sternum, pelvis, proximal humerus, femur and scapula.

MRI Spine revealed numerous low signal intensity lesions of varying sizes appearing hypointense on T1WI, T2WI and STIR Images noted involving vertebral bodies of cervical, dorsal, lumbar and sacral spine – extending to involve the posterior elements, suggestive of sclerotic foci. Few of these lesions appeared hyperintense on T2 and STIR sequences extending into posterior elements and shows contrast enhancement- Marrow Infiltration. Evidence of focal destruction with associated soft tissue mass appearing heterogeneously hyperintense on T2WI in S1 vertebral body, left sacral ala and sacral crest, extending to involve S1-S2 IVD, S2 body and prevertebral space- similar lesion with enhancing soft tissue of L1-L2IVD were found. Diffuse disc bulge, with ventral thecal compression with spinal canal narrowing was there suggesting of polyneuropathy. Multifocal sclerotic lesions were present at multilevel of spine with focal vertebral body destructive lesions, associated soft tissue masses showing homogenous contrast enhancement, feature suggestive of spectrum of multiple myeloma.

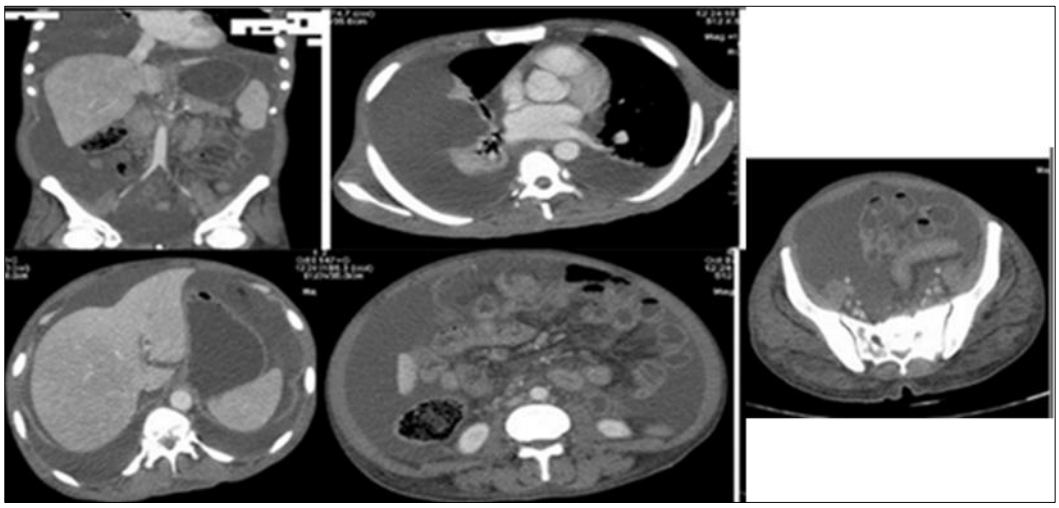

Figure 3 CECT Chest and abdomen showing bilateral pleural effusion, moderate ascites

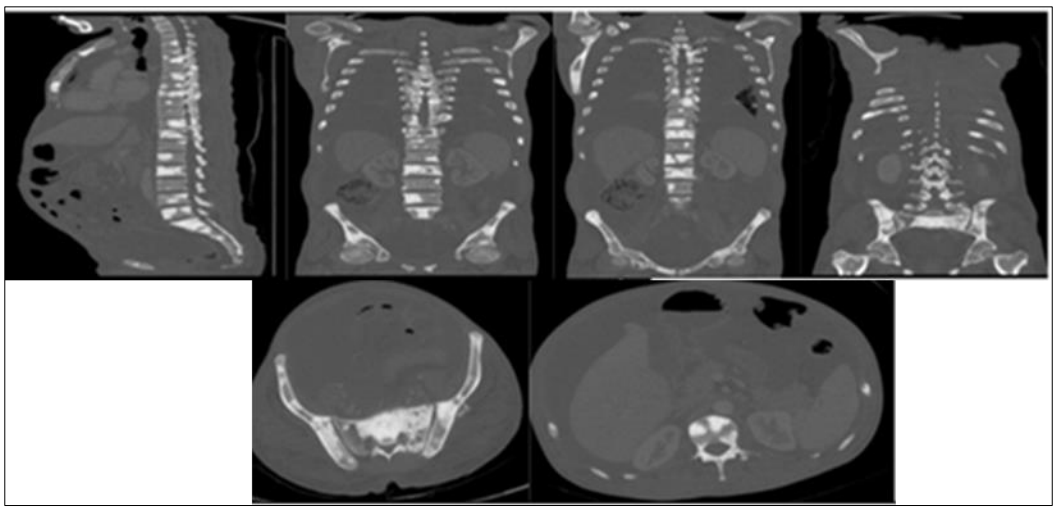

Figure 4 CT Bone Window revealing multiple sclerotic lesions

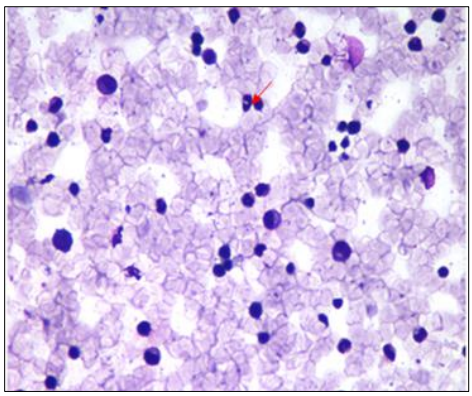

Figure 5 Marrow showing clusters of plasma cells (red arrow)

Bone marrow analysis revealed evidence of sheets of plasma cells and CD138 positive cells [Fig.5]. Clinical features of anasarca with sub-acute progressive bilateral symmetrical LMN quadriparesis with small plus large fiber sensory

neuropathy with impotence with generalized skin hyperpigmentation along with laboratory findings of hypothyroidism; M-spike gammopathy & evidence of sheets of plasma cells on bone marrow analysis; with radiological findings suggestive of splenomegaly and multiple sclerotic bony lesions; the diagnosis of POEMS syndrome was confirmed. He was started on Melphalan-Dexamethasone therapy and he responded well to the therapy with clinical improvement.

3. Discussion

POEMS Syndrome is extremely rare paraneoplastic syndrome owing to an underlying plasma cell dyscrasia, pretty much rarer in young adults. Patients usually present with a progressive sensorimotor polyneuropathy, primary gonadal failure (70%), diabetes (50%), and a plasma cell dyscrasia with sclerotic bony lesions. The pathogenesis of POEMS syndrome is not well understood. It is associated with a rise in pro-inflammatory cytokines. The severity of the disease activity correlates best with the levels of vascular endothelial growth factor (VEGF) [6] and then IL-12[9]. VEGF is expressed by osteoblasts, megakaryocytes, macrophages and plasma cells [7,8]. It targets endothelial cells inducing a rapid reversible increase in vascular permeability, and thus playing an important role in angiogenesis. Both IL-1β and IL-6 have been found to stimulate VEGF production [7]. In more than 95% of the time, the plasma cells in POEMS syndrome are lambda light chain restricted with restricted immunoglobulin light chain variable gene usage [10]. It is very important to differentiate POEMS syndrome from other certain diseases like chronic inflammatory demyelinating polyneuropathy (CIDP), multiple myeloma, monoclonal (MGUS) gammopathy of undetermined significance neuropathy, and light chain amyloidopathy as they mimic POEMS syndrome [11] and the treatment modalities are totally different for each of the mentioned conditions. Our patient was fitted into both the mandatory criteria of demyelinating sensorimotor polyneuropathy and M- spike protein; one major criteria of multiple sclerotic bone lesions and multiple minor criteria of Organomegaly (Splenomegaly), Extravascular volume overload (anasarca), hypothyroidism, impotence and skin changes (hyperpigmentation) of the POEMS syndrome. Treatment options include Melphalan-Dexamethasone (MelDEX), Lenalidomide-Dexamethasone (LENDEX), Cyclophosphamide-Dexamethasone, Bortezomib, Bevacizumab, Thalidomide-dexamethasone (not first line because of risk of neuropathy), Radiation therapy and ASCT (Autologous stem cell transplantation). The Eligibility criteria for ASCT includes (1) <65 years (2) Without concomitant systemic disease/MODS/ active infection/severe pulmonary hypertension/severe capillary leak syndrome (refractory ascites / hypotension (3) Successful collection of adequate peripheral blood stem cells. Treatment Response Evaluation includes A) Complete hematologic response, CRH B) Vascular Endothelial Growth Factor (VEGF) Complete Remission, CRV and C) Neurological Response (RN). The course of POEMS syndrome is chronic but with advancements in treatment modalities like the advent of stem cell transplantation and immunomodulatory therapies, overall survival rate has improved over the years. Favorable prognostic factors include albumin >3.2g/dL, attainment of complete hematologic response, and younger age at diagnosis [12]. Four baseline Clinical variables associated with poorer Overall survival (OS) rate are Age > 50 years, Pulmonary hypertension, Pleural effusion and eGFR < 30 ml/min/1.73m^2 [13].

4. Conclusion

POEMS syndrome has myriad presentation with multisystem involvement and heterogenous laboratory features. Diagnosis and management posed a major challenge. But a good history and physical examination followed by appropriate testing—including radiographic assessment of bones, measurement of VEGF, and a bone marrow biopsy—can differentiate this syndrome from other plasma cell disorders. Prompt multidisciplinary action is needed for better care and to reduce complications. We are reporting here a case of POEMS syndrome in a young adult presented with anasarca as initial manifestation and timely treated with Melphalan-Dexamethasone therapy with clinical improvement.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There are no conflicts of interest.

Statement of informed consent

Informed consent was obtained from the patient to publish this case report.

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