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Case Reports

POEMS Syndrome - Rare Paraneoplastic Syndrome in a Young Female

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Abstract:

POEMS syndrome is defined by the presence of peripheral neuropathy (P), organomegaly (O), endocrinopathy (E), a monoclonal plasma cell disorder (M) and skin changes (S). We report a case of POEMS syndrome in a 34-year-old female who presented with three month history of back pain, pain in lower limbs, weakness, numbness and edema in both lower limbs. Patient was unable to walk and bed ridden with worsening general condition, shortness of breath and fever for three days. Further clinical examinations (hyperpigmentation), systemic examination (hepato-splenomegaly), laboratory investigation (hypothyroidism), CT showed sclerosis in sacral bone and left acetabular lytic lesion, which on biopsy and immunohistochemistry showed plasma cell dyscrasia and confirmed by increased plasma cells in bone marrow biopsy and presence of M band in immunofixation study. Here we describe, in detail, an unusual clinical presentation of this rare paraneoplastic syndrome with multisystemic involvement which need multidisciplinary approach with strong clinico-pathological & radiological correlation to diagnose this rare entity.

Key Words: *POEMS syndrome; Osteolytic lesions; Guided cyto-histology; plasma cell dyscrasia.*

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Introduction:

POEMS syndrome is a rare disease, estimated to account for <1% of plasma cell neoplasm, first coined by Bardwick et al. in 1980,[1] to characterize polyneuropathy, organomegaly, endocrinopathy, M-protein and skin changes.It is more prevalent in men with male to female ratio of 1.4 :1 and usually manifest in 5th- 6 th decade of life . POEMS syndrome is characterized by fibrosis and osteosclerotic changes in bone trabeculae and often lymph node changes resembling the plasma cell variant of Castlemans disease. The diagnostic criteria revised in last decade after vascular endothelial growth factor (VEGF) correlates best with disease activity.[2]

We describe this because of its nonspecific presentation with complex radiological and pathological findings suggesting need of strong collaboration among physician, neurologist, pathologist and radiologist to reach final diagnosis and preventing complications as seen in previously reported cases.

Case Summary:

A 34-year-old female patient presented to emergency room with complaints of tingling, numbness of both upper and lower limbs, weakness of both upper and lower limbs, shortness of breath, low back ache and pedal edema for 3 months. There was history of breathlessness with high grade fever for three days. The illness was of insidious onset, continuous course and deteriorating progression along with no significant past and family history.

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General examination revealed puffiness of face, hyperpigmentation of skin (Figure 1a & 1b), pallor, clubbing with white nails/leuconychia (Figure 1c), ascites and edema. Cardio vascular examination was normal.

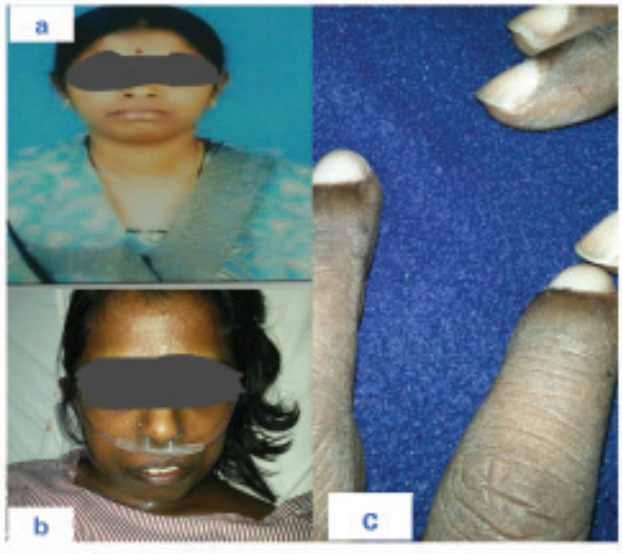

Figure 1: *Four months before illness (1a); skin hyperpigmentation during illness (1b); leuconychia & clubbing (1c)*

There was decreased breath sound in bilateral infra-axillary and infrascapular regions. Abdomen was distended, shifting dullness was positive and hepato-splenomegaly noted. CNS examination performed revealed decreased power and deep tendon reflexes and on sensory examination light touch, vibration, joint sense, pain & temperature sense were also decreased in both upper & lower limbs, but more in lower reflexes and on sensory examination light touch, vibration, joint sense, pain & temperature sense were also decreased in both upper & lower limbs, but more in lower limbs. Nerve conduction studies showed sensory motor neuropathy. Fundoscopic examination was normal.

Chest radiograph showed cardiomegaly (likely pericardial effusion), bilateral pleural effusions which were confirmed on CT chest. USG of abdomen revealed hepatosplenomegaly, ascites, bilateral moderate pleural effusions. Radiograph of pelvis showed well defined lytic lesions in left ischium and pubis (Figure 2a) which on CT scan revealed well defined lytic lesions in left ischial bone, acetabulam and pubis (Figure 2b) and osteosclerosis lesion in sacral bone. CT guided biopsy from lytic lesion in left ischial tuberosity section shows plasmacytoid cells in sheets. The cells had round nuclei with perinuclear pale cytoplasm. Few binucleate forms were seen (Figure 2c & 2d).

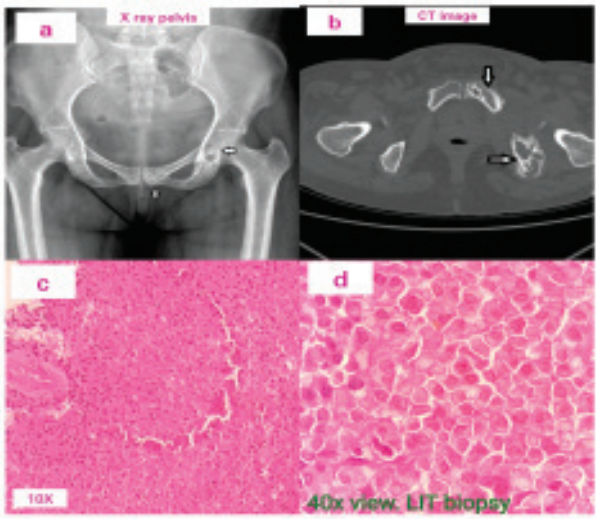

Figure 2: *X-ray pelvis (2a); CT image show expansile lytic lesions in left ischial bone and acetabulum (2b); Left ischial tuberosity biopsy section with plasmacytoid cells (2c & 2d).*

On immunohistochemistry, the tumor cells diffusely expressed CD138 (Figure 3a). Expression of lambda light chains (Figure 3b) was more diffuse and stronger than kappa light chains (Figure 3c). LCA, CD20 and CD3 highlight scattered lymphoid cells. Syanptophysin, CK were negative and stain for CD56 was non-contributory.

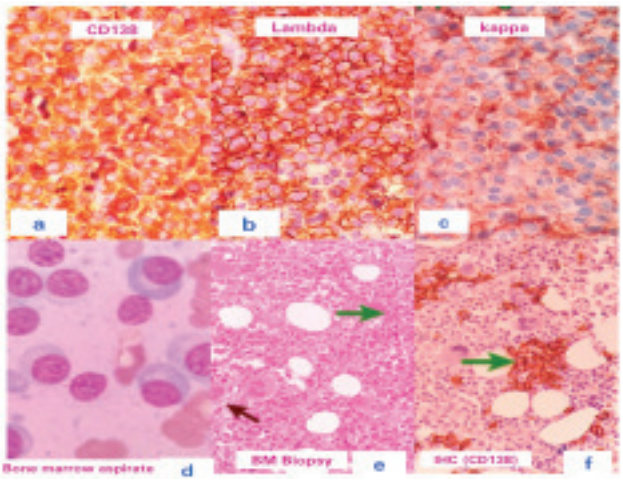

Figure 3: *Immunohistochemistry on left ischial tuberosity (LIT Biopsy) CD 138 Positive (3a); Lamda positive (3b); Kappa negative (3c); bone aspirate plasma cells (3d); bone marrow biopsy plasma cells confirmed by IHC CD138 positive (3e & 3f).*

Serum immunofixation was positive for M band with increased IgG and lambda light chain (Table 1). Bone marrow aspiration (Figure 3d) and biopsy showed cellular reactive marrow with prominence of plasma cells (Figure 3e) comprising 30% of marrow nucleated cells and with CD138 (Figure 3f) positivity on IHC suggesting plasm cell dyscrasia.

Table 1: *Immunofixation by chemiluminescence method*

Test report status	Results	Biological reference interval
Myeloma band	Detected	Not detected
IgG band	Positive	Not detected
IgM band	Not detected	Not detected
IgA band	Not detected	Not detected
Kappa band	Not detected	Not detected
Lambda band	Detected	Not detected
Total IgA	3.76 g/l	0.52 - 4.68 g/l
Total IgG	29.5 g/l	6.5 - 16.4 g/l
Total IgM	1.12 g/l	0.39 - 3.38 g/l
Serum light chains (kappa & lambda)		
Kappa light chain	14.8 mg/l	.30 - 19.40 mg/l
Lambda light chain	85.20 mg/l	5.71 - 26.30 mg/l
Kappa lambda ratio	0.17	0.26 - 1.65
B2-microglobulin	4175 ng /ml	609.0 - 2366.0 ng/ml

Considering peripheral neuropathy (P), hepatosplenomegaly (O), hypothyroidism (E), monoclonal plasma cell proliferation (M), hyperpigmentation (S) diagnosis of POEMS syndrome is made. As per criteria (Table 2), this case show two mandatory criteria, one major and four minor criteria.

Table 2: *Criteria for POEMS syndrome*

Mandatory criteria	Polyneuropathy
	Monoclonal plasma proliferative disorder
MajorCriteria (one or more)	Castleman's disease
	Sclerotic bone lesions
	Elevated serum or plasma vascular endothelial growth factor (VEGF) levels
Minor criteria (one or more)	**Organomegaly** (**splenomegaly, hepatomegaly**, or lymphadenopathy)
	Extravascular volume overload (peripheral edema, ascites or pleural effusion)
	Endocrinopathy (adrenal, **thyroid,** pituitary, gonadal, parathyroid, pancreatic)
	Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails)
	PapilledemaThrombocytosis or polycythemia.

The existence of both mandatory criteria, one major and at least one of the minor criteria are necessary for the diagnosis.

Discussion:

POEMS syndrome is also known as Crow–Fukase syndrome or osteosclerotic myeloma. The pathogenesis of POEMS syndrome is not well understood, particularly mechanism of peripheral neuropathy**,** however markedly elevated levels of vascular epithelial growth factor (VEGF), presumably secreted by plasmacytoma, important pathologic factor responsible for the characteristic symptoms such as angiomata, edema, effusion and organomegaly.[3]

Clinical features associated with POEMS include the polyneuropathy typically spreads proximally and motor symptoms predominate. Skin changes include haemangiomata, skin thickening, hyperpigmentation (90% cases), hypertrichosis, white nails (lukonychia) and clubbing. Organomegaly is seen in 50% cases and lymphadenopathy is also seen in POEMS**.** The typical endocrinological symptoms are present in four major endocrine axes (gonadal, thyroid, glucose and adrenal). Osteosclerotic bone lesions seen in 95% of patients and characterised by infiltration of plasma cells.[4] In our case

patient had hypothyroidism and osteolytic lesion showing plasma cell infiltration.

The mandatory criteria for diagnosis of POEMS syndrome are a chronic progressive polyneuropathy and monoclonal plasma cell proliferative disorder.There is usually an associated M protein of either IgG or IgA type, with lambda light chainrestriction in almost all cases, like in our IgG and lambda. The quantity of M protein is typically below myeloma levels.[2] The recommended standard investigations for identifying bone lesions are a CT-Scan or bone scintigraphy. CT is superior to X-ray in detecting bone lesions. However CT is unable to differentiate active from non-active form of lesions. Whole body FDG-PET/CT is useful to detect hypermetabolic bone lesions and monitor treatment response for patients with FDG avid bone lesions.[5] In addition CT guided biopsy play crucial role in final diagnosis.

Diagnosis of POEMS syndrome can be difficult. Most authors agree that the presence of two major and at least one minor criterion are confirmatory (Table 2).[2] This present case had polyneuropathy, plasma cell dyscrasia as major criteria while diffuse hyperpigmentation, organomegaly, extravascular volume overload (edema over feet) & hypothyroidism as four minor criteria enough to label this case under POEM syndrome.

Treatment of choice depends on extent of disease and patients characteristics. The main treatment is to target underlying plasma cell clone. Radiotherapy is treatment of choice for localised sclerotic bone lesions. High dose melphalan and autologus stem cell transplantation is an effective treatment in patient with disseminated disease.[6, 7]

If appropriately treated, prognosis of POEMS is good, independent of number of disease symptoms, median overall survival as long as 165 months and five year survival rate of 60-94%.[2] Shorter survival more seen with patient with fluid overload, effusion, nail clubbing and pulmonary hypertension. There are no known genetic findings that are predictor of prognosis.[8]

Conclusion:

To conclude, POEMS syndrome is rare plasma cell neoplasm with associated paraneoplastic syndrome. As patients present with multisystemic disease manifestation, diagnosis is often difficult. Thorough clinical, neurological, radiological and pathological correlations are needed to diagnose this complex and rare disease to avoid misdiagnosis but also to prevent complications.

Conflict of interest: None.

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