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POEMS Syndrome: A Rare Cerebrovascular Presentation of A Unique Paraneoplastic Syndrome

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ABSTRACT

POEMS Syndrome1 (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy, Skin changes) is a rare paraneoplastic disorder due to underlying plasma cell dyscrasia. This condition is usually misdiagnosed as Multiple Myeloma or MUGS but a detailed and extensive history and clinical examination leads to a proper diagnosis of POEMS syndrome, which is a multisystem disorder and even although few cases are reported till date, varied presentation makes its diagnosis a clinical challenge.

Here we present an interesting and rare cerebrovascular presentation of this unique paraneoplastic disorder.

KEYWORDS POEMS, Paraneoplastic, Plasma cell, Polyneuropathy, Cerebrovascular

Introduction:

POEMS Syndrome is a rare paraneoplastic disorder of plasma cells also known as Crow – Fukase Syndrome or Takatsuki's disease or Shimpo Syndrome.

The acronym POEMS was coined by Bardwick in 1980 on the basis of five characteristics features (Peripheral Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy, Skin changes). It is more prevalent in men (M: F - 2.5: 1), usually in the 5^{th} – 6^{th} decade of life. It is of uncertain pathophysiology and inheritance.

Case Report – A 45 year old male, a field worker developed sudden onset weakness of right upper limb with deviation of the angle of mouth to the left and 2-3 days later developed weakness of right lower limb around 3 year back from the date of admission in our hospital. He was unable to walk and lift his right hand or hold or grasp. He was then evaluated and diagnosed as left MCA territory infarct[2]. His symptoms gradually improved on physiotherapy and was able to walk with support over next 2-3 months.

Three months later, he began to develop tingling and pain over his left lower limb followed by the weakness in the same, which gradually progressed over 2 -3 months to make him bed bound. There was also history of hard bony swelling not increasing in size, associated with pain over his right shoulder causing restriction of movements of his right upper limb. He also had complain of blurring of vision along with the complain of double vision for the past 6 months. He also had low back ache for past 6 month which was radiating downwards to both the lower limb. There was significant history of loss of appetite and weight gain over past one year. There was no history of altered sensorium, cerebellar involvement and other cranial nerve involvement. No history of fever, vomiting, seizure and headache. No history of alopecia, photosensitivity, oral ulcer, rash, joint pain, loose stool, pain abdomen, malena and jaundice.

He is a diagnosed case of type 2 diabetes mellitus and hypertension for the past one year and during his evaluation and treatment for the above symptoms, he had two episode of acute myocardial infarction, of which one was during in hospital stay.

Examination

Patient was fully conscious and oriented.

BP - 134/80 mm of Hg, PR - 80 /min, regular

JVP – not raised

No Pallor, Icterus, Cyanosis was present.

Bilateral pedal oedema and diffuse skin hyperpigmentation was present.

Clubbing was present

Lymph node – multiple enlarged mobile lymph node were present in the right axillary and supraclavicular region.

Bilateral parotid swelling was present.

Completely white nail was present.

Hard bony swelling over the right shoulder area was present and had restricted range of movement of the right shoulder.

Nervous system examination:
Higher mental function was normal.

Cranial nerve examination was normal.

Fundus examination – bilateral disc pallor present.

Motor system –

Bulk – decreased in bilateral lower limb and upper limb.

Tone – decreased in all limb except left upper limb and fixed deformity was present in right upper limb.

Power – 3/5 right upper limb, 4/5 left upper limb, 3/5 both lower limb.

No involuntary movement was present.

Sensory examination –

Pain and touch sensation - decreased

Vibration sense and Joint position – absent

Bladder and Bowel examination – normal

Reflex Examination –

Superficial abdominal reflex were present in all four quadrant.

Deep tendon reflex –

	Biceps	triceps	supinator	knee	ankle
Right	-	-	-	-	-
Left	+	+	+	-	-

Plantar reflex – Bilaterally extensor

Signs of Cerebellar dysfunction – absent

Gait – bed bound

Neck – soft

Kernig – negative

Respiratory system examination – normal

Cardiovascular system examination – normal

Abdominal examination – Distended and fluid thrill was present

Investigation:

ESR – 58 mm /hr

Hb – 17 gm /dl

WBC – 14400/cumm, N (54) L (37) M (8) E (1) B (0)

Platelet – 595000/cumm

PT- INR -

Patient – 11.4 sec

Normal – 10 -12.5sec

INR – 1.06

APTT – 38.4 sec

Urinary examination – within normal limit

Liver function test – within normal limit

LDH -400 U/L

Urea - 21 mg% Creatinine - 0.8 mg%

Uric acid – 5 mg%

Glucose – Fasting - 132mg/dl and Post Prandial - 230mg/dl

Fibrinogen – 270 mg/dl

TSH – 12 microIU/ml

Urine BENCE JONES PROTEIN - Negative

SERUM PROTEIN ELECTROPHORESIS - M Band Present

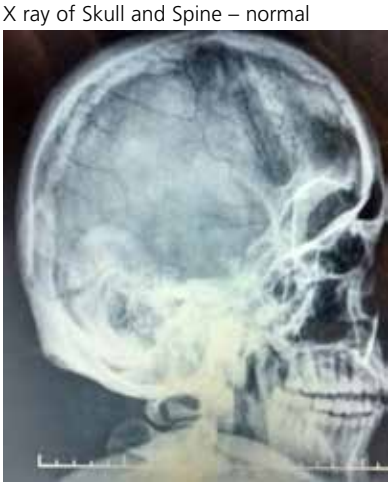
Serum Calcium and Phosphorus – normal

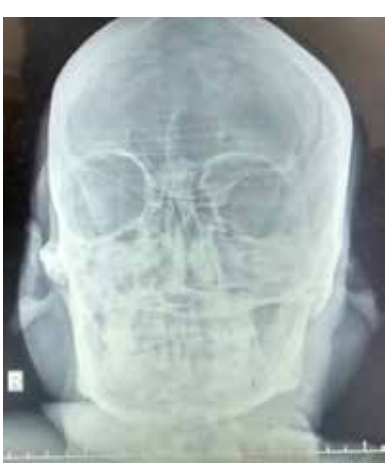
Lipid profile – within normal limits

HBA1c – 4.7

HIV – negative, HBsAg – negative, HCV – negative

X ray of Skull and Spine – normal





Xray of Shoulder – lytic[3] lesion involving the right glenoid. Periosteal reaction in the medial aspect of the right humeral shaft.

CT SCAN Brain – chronic non haemorrhagic infarct at left MCA territory.

MRI Brain – chronic non haemorrhagic infarct at left MCA territory.

CECT Right Shoulder – large expansile lytic lesion with marginal sclerosis, multiple enlarge axillary and supraclavicular lymphnode in right side.

CT guided FNAC Right Shoulder – mixed inflammatory cells and stromal fragments, no features of malignancy

NCV – chronic demyelinating motor sensory neuropathy, lower limb > upper limb

Discussion:
POEMS Syndrome acronyms stands for Polyneuropathy, Organomegaly, Endocrinopathy ,Monoclonal gammopathy and Skin changes.There is a vast diversity in presentation and have a diagnostic criteria which has been laid down by some authors for diagnostic assistance –

Major criteria – (Both essential)

1. Monoclonal Plasma cell Proliferative Disorder

2. Polyneuropathy
Other major criteria (any one)
- Castleman's disease[4]
- Sclerotic bone lesion
- Elevated VEGF

Minor criterias (any one)

Organomegaly –Hepatomegaly, Splenomegaly, Lymphadenopathy.

Endocrinopathy – Adrenal, Thyroid, Parathyroid, Pituitary, Gonads.

Skin changes – Hyperpigmentation, Hypertrichosis, Plethora, White nail.

Papilloedema

Extra vascular volume overload – Ascites, Peripheral edema, Pleural effusion.

Thrombocytosis or Polycythemia

Monoclonal Plasma cell proliferative Disorder[5]
POEMS Syndrome is seen in the setting of a plasma cell dyscrasia. Although many plasma cell disorders have been reported in patients with POEMS syndrome, most patients are seen with osteosclerotic myeloma or monoclonal gammopathy of unknown significance.

The M proteins most frequently found are the immunoglobulin A (IgA)–gamma and immunoglobulin G (IgG)–gamma light chains. This is in contrast to most paraproteinaemic neuropathies, in which the paraprotein is usually an IgM antibody.

Classic Multiple Myeloma has not been associated with the disease.

In a case report of one patient with POEMS Syndrome, serum electrophoresis demonstrated an M-band with isolated IgA heavy chain but no abnormal light chain, which could suggest abnormal secretion of monoclonal protein or the rare possibility of coincidental heavy-chain disease in association with POEMS Syndrome.

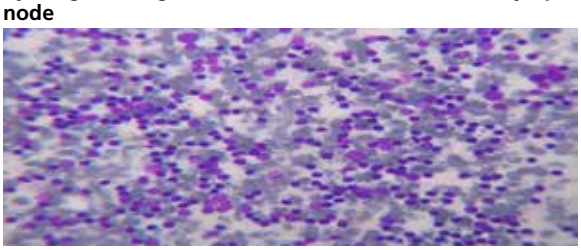
POEMS Syndrome in association with Waldenström macroglobulinemia characterized by immunoglobulin M–kappa paraproteinemia, has been reported in few patient.

On serum electrophoresis of our patient demonstrated an M-band, however the urine for Bence Jones protein was absent.

Polyneuropathy[6]-
It is the most common presentation (90%). It closely mimics CIDP. Clinically presents as peripheral symmetrical ascending sensorimotor polyneuropathy. Both demyelinating and axonal polyneuropathy are seen. Immune mediated etiology is suspected. Cranial and autonomic nerves are usually spared. Axonal degeneration and marked endoneural edema is characteristics. Our patients had chronic demyelinating motor sensory neuropathy on nerve conduction studies. Patients has both motor and sensory deficit.

Organomegaly-
Organomegaly is very common features. Liver (50%) is most common followed by spleen and then lymphadenopathy. Enlargement of the lymph nodes and spleen is secondary to changes consistent with Castleman's disease (giant angiofollicular hyperplasia, multicentric plasma cell variant) in most patients. Approximately 15% of patients with POEMS syndrome have concomitant evidence of Castleman's disease. Our patient had enlarged liver and lymphadenopathy. On histological examination of lymphnode it was consistent with Castleman's disease.

Cytological diagnosis of Castleman's disease of lymphnode

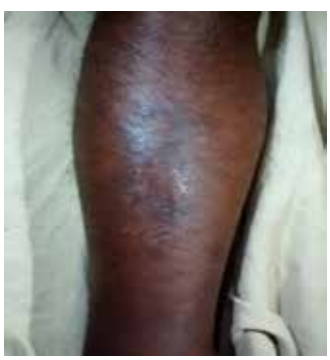


Smear showing polymorphous cell population with predominance of small lymphocytes.

Endocrinopathy[7]-
Endocrine dysfunction are common (60 – 80 %). Among those primary gonadal failure (70%) is most common followed by Diabetes mellitus (50%), thyroid dysfunction, hyperprolactinemia, adrenal insufficiency, gynaecomastia and impotency are very common. Our patient has both Diabetes mellitus and hypothyroidism.

Skin Changes[8]-
Multiple dermatological changes have been associated with POEMS syndrome. The most common changes include hyperpigmentation, skin thickening, sclerodermoid changes, and hypertrichosis. Other skin changes, including whitening of the proximal nail (Terry nails), peripheral edema, hyperhidrosis, clubbing of the fingers, Raynaud phenomenon, and angiomas, have been observed.

Our patient has white nail, hyperpigmentation, skin thickening and clubbing.


A) Ascites and generalized hyperpigmentation b) Hyperpigmentation c) White nail

Our patient full filled both the **major essential diagnostic criteria (2/2),** i.e polyneuropathy and monoclonal gammopathy.

Among **other major criterias** our patient had both **(2/3)** features of sclerotic bone lesion and Castleman's disease. Unfortunately VEGF[9] estimation was not available at our center.

Among the **minor criterias** our patient fulfill **(6/6)** all the six minor criterias i.e Organomegaly (Hepatomegaly and Lymphadenopathy), Endocrinopathy (Diabetes mellitus, Hypothyroidism and Parotid enlargement), Skin changes (diffuse hyperpigmentation, clubbing, white nails). In addition he also has ascites, pedal edema, papilloedema, thrombocytosis and polycythemia.

Keynotes –
The POEMS Syndrome is a multisystem disorder characterized by polyneuropathy, Organomegaly, Endocrinopathy, Plasma cell dyscrasia and Skin changes. Along with many other manifestations this rare syndrome may also include macroangiopathy and acute vascular occlusion. Acute ischemic strokes in patients with POEMS syndrome have rarely been reported, and the pathophysiologic mechanism of this disease is unknown. In the literature such vascular problems have received only little attention and most case reports refer to involvement of the coronary[10] and lower limb[11] arteries. Fibrinogen, increased VEGF is reported to be an independent risk factor for cerebrovascular disease. The possibility of POEMS syndrome should be considered in a patient presenting with cerebrovascular accident without any risk factor in the presence of peripheral neuropathy, multiple lymph nodes and monoclonal gammopathy.

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