

## CASE REPORTS

# POEMS Syndrome in a Patient with Castleman Disease: A Case Report

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### Abstract:

*POEMS syndrome is a rare multisystem disorder that clinically manifests as a paraneoplastic syndrome and monoclonal plasma cell dyscrasia. Its acronym is derived from its principal characteristics: polyneuropathy, organomegaly, endocrinopathy, M proteins, and skin changes. Here, a case of POEMS syndrome was reported also having features of Castleman disease. A 43-year-old man was admitted with weakness of all four limbs, tingling, heaviness, muscle cramps along with headache for the last 6 months; examination revealed flaccid quadriparesis, generalized areflexia with flexor plantar response, papilloedema, cervical lymphadenopathy, hepatomegaly, tender mass at the left parieto-occipital region, pitting edema and testicular atrophy. Laboratory tests revealed thrombocytosis, high blood sugar, hepatomegaly, lytic lesions*

*at the left parietal bone, pelvis, and intraosseous mass in the Pareto-occipital region; nerve conduction study showed the demyelinating motor neuropathy without conduction block. Intraosseous mass biopsy showed solitary plasmacytoma and immunohistochemical markers positive for CD138 and Ki-67 MUM-1 and lambda/kappa >10:1, suggesting plasma cell dyscrasia with lambda chain restriction. Biopsy from the cervical lymph node revealed features of Castleman disease. With these clinical and laboratory parameters, this case was finally diagnosed as POEMS syndrome in association with Castleman disease which is a common accompaniment with the syndrome.*

**Keywords:** Castleman disease, Solitary plasmacytoma, POEMS syndrome, Plasma cell dyscrasia.

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### Introduction:

POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes) syndrome is a rare and disabling multisystemic disorder characterised by peripheral neuropathy and a monoclonal plasma cell disorder.<sup>1</sup> Additional manifestations include papilloedema, extravascular

volume overload, sclerotic and/or lytic bone lesions and thrombocytosis. Nonetheless, clinical presentation varies greatly in each individual case, and may not present all the criteria in an individual patient. Estimated prevalence of the disease is 0.3 for 100,000 people.<sup>2</sup> In this disorder, plasma cell proliferation occurs as a solitary or multiple plasmacytomas may manifest as a sclerotic and/or lytic bone lesions. Another rare disorder that has been associated with this syndrome is Castleman disease, which is a pathological entity, characterized by non-malignant vascular proliferation with hyalinization and profuse lymphocytic infiltration. Its rarity and diversity usually implies a delayed, or even sub-diagnosis. Early diagnosis and appropriate treatment may ease the symptoms and restore the quality of life. The objective of this article is to describe a rare clinical case including its diagnostic approach and the brief therapeutic options. That will help to recognize POEMS syndrome early in a patient with chronic polyneuropathy.

### Case Report:

A 43 years old man was admitted with the complaints of bilateral symmetrical progressive weakness and wasting of all 4 limbs more marked in distal part of lower limbs with heaviness, tingling and muscle cramps but

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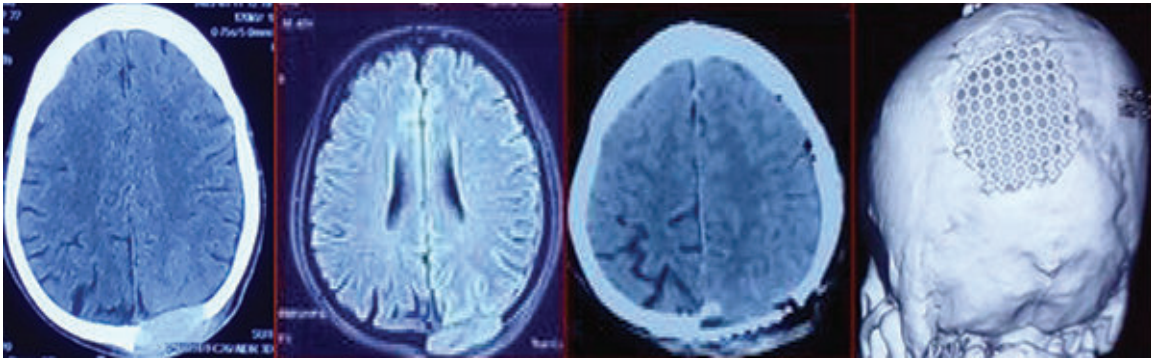
no diurnal variation and spontaneous muscle twitching for 6 months. He has global headache more marked in left parieto-occipital region for 1 month and history of loss of libido, occasional low grade irregular fever, associated with profuse night sweats, but no itching. Weight loss occurred about 8 kg within this last 6 months. All of his complaints became more marked for the last 1 month. He was diabetic for the last 6 months, treated with insulin and oral antidiabetic drug, his blood pressure was controlled with medication. His past medical history was unremarkable with no history of smoking, alcohol use, HIV infection, tuberculosis, tumor.

On examination, he has cervical lymphadenopathy involving anterior, posterior chain and right supraclavicular glands, multiple in number, variable in size, largest one was about 2×1.5 cm, discrete, rubbery in consistency, non tender, free from overlying and underlying structures, with no discharging sinus; there was a swelling at the left parieto-occipital region which was tender, soft in consistency, fixed to the underlying structure, bilateral pitting edema in lower extremities, hepatomegaly about 4cm from 9<sup>th</sup> costal cartilage along the right midclavicular line, firm in consistency, non-tender, upper border of liver dullness in right 5<sup>th</sup> ICS and testicular atrophy with soft in consistency. Neurological examination revealed papilloedema, without any visual disturbance, other cranial nerves were intact; power 4/5 in upper limbs, 3/5 proximally and 2/5 distally in the lower limb, generalized areflexia with intact all sensory modalities and flexor plantar response bilaterally.

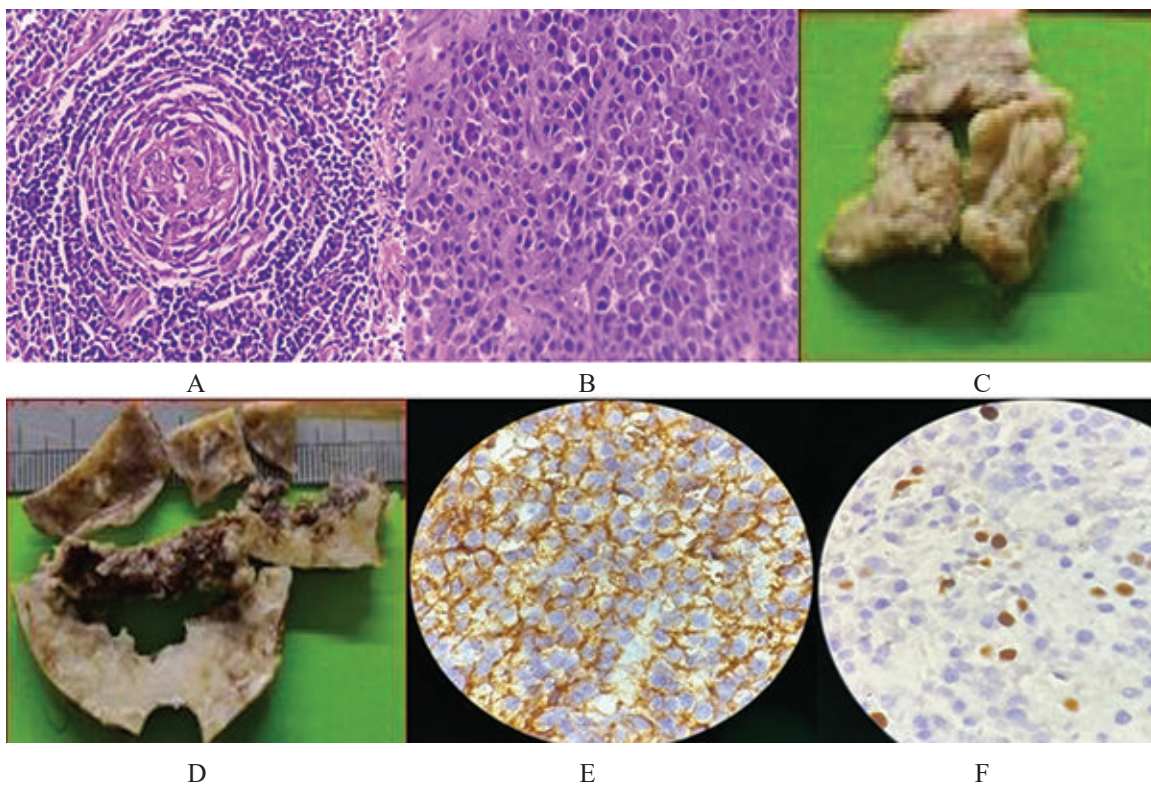
Routine blood examination revealed thrombocytosis ( $464 \times 10^9$  platelets/L; normal =  $(150-450) \times 10^9$  platelets/L), random blood sugar was 8.4mmol/l, HbA1c was 10.7%, serum protein electrophoresis revealed mildly elevated gamma fraction, most likely polyclonal hypergammaglobulinemia, no monoclonal band was seen. Serum calcium, TSH, FT4, PTH, testosterone, estrogen, cortisol, PSA, ANA, S.Albumin, Total protein, SGPT, and Creatinine were within normal limits. X-ray of the skull and Pelvis revealed an irregular osteolytic lesion in the left parieto-occipital region, and multiple lytic lesions at the right ilium, greater trochanter of right femur, and also in right ischium respectively [Figure 1]. Ultrasonic examination showed hepatomegaly, CT scan of the head and MRI of the brain revealed lytic lesion and intraosseous mass at left posterior parieto-occipital location abutting dura respectively [Figure-2] Lumbar puncture was performed and cerebrospinal fluid testing revealed increased protein (288mg/dl), raised pressure levels (300mm of water), and total WBC count 02/cumm. A Nerve conduction study confirmed demyelinating peripheral motor neuropathy without conduction block. Lymph node biopsy (from left anterior cervical chain) revealed a hyaline vascular variant of Castleman disease (high vascular proliferation, hyalinization of vessel wall, and lymphocytic infiltration) [Figure 3]. Intraosseous mass was extended to subcutaneous tissue attached with diploic space of parietal bone that was seen during surgical intervention. It was removed surgically. Tissue was taken from this



**Fig-1:** X-ray of skull and Pelvis revealed an irregular lytic lesion at left parieto-occipital region, and multiple lytic lesions at right ilium, greater trochanter of right femur and also in right ischium respectively



**Fig.-2:** (A) CT scan of head and (B) MRI of brain revealed lytic lesions and intraosseous mass at left posterior parieto-occipital location abutting dura respectively. post operative CT of head (C) & (D) revealed duroplasty done with "G" patch, and cranioplasty done with Titanium mesh under G/A



**Fig. 3 and 4:** (A) Castleman disease (B) Solitary plasmacytoma (C) grey white pieces of soft tissue (D) Left parieto-occipital bone (E) CD-138 plasma cells (F) Ki-67 plasma cells

mass and sent for histopathology and Immunohistochemistry. Histopathology report revealed solitary plasmacytoma [Figure 4]. Immunohistochemical markers were positive for CD138, Ki-67 (8% cells are positive), MUM-1, and lambda/kappa >10:1, suggesting plasma cell dyscrasia with lambda chain restriction.

Initially, the patient was treated conservatively with I/V methylprednisolone without any improvement. After completion of the diagnostic procedure, this patient was transferred to the National Institute of Cancer Research & Hospital, Mohakhali, Dhaka for further management.

### Discussion:

POEMS syndrome was first reported by Scheinker in 1938.<sup>3</sup> Crow described the first clinical case in 1956.<sup>4</sup> Accordingly, It is also known as ‘Crow-Fukasa syndrome’, Takatsuki syndrome; Osteosclerotic myeloma are another eponyms of this disorder. Systemic inflammatory responses mediated by the cytokines, released by plasma cells are observed in POEMS<sup>5,6,7</sup>. Osteosclerotic myeloma without bony pain, occurs in <3% of all patients of myeloma are observed in this syndrome. Both of these findings were observed in this patient. The initial presenting feature often as in this patient is chronic peripheral neuropathy. Because of the insidious nature, protein electrophoresis, immunoelectrophoresis and skeletal survey is recommended in patients who present with unexplained polyneuropathy. The characteristic plasma cell disorder includes monoclonal proteins (paraproteins) composed of a single heavy (M, G or A) and light chain (kappa or lambda). From a key aspect of POEMS, it is composed of lambda light chains in 95% of cases, and associated to IgA or IgG heavy chains.<sup>89,101</sup> in this patient though the initial protein electrophoresis missed monoclonal gamopathy but subsequent immunohistochemistry demonstrated the plasma cell dyscrasia, which is a major criteria for disease diagnosis. Furthermore, protein electrophoresis can be up to 30% false negatives.<sup>111</sup> The monoclonal protein in POEMS usually <2g/dl, may not be detectable using immunofixation in up to 10% of cases.

In the POEMS syndrome both polyradiculoneuropathy and monoclonal plasma cell disorder observed in 100% condition, sclerotic bone lesions in 27-97% , elevated VEGF in 95%, organomegaly in 45-85%, extravascular volume overload (edema, pleural effusion, or ascites) in 29-87%, endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic) in 67-84%, skin changes , Papilledema in 29-64%, and thrombocytosis/polycythemia in 54-88%.<sup>12</sup> This patient had almost all the features of POEMS syndrome, furthermore, cervical lymph node biopsy revealed features of Castleman disease, which may be present in 11-25% condition. Castleman disease (or angiofollicular lymph node hyperplasia) is also a rare lymphoproliferative disorder. It has two clinical categories: unicentric and multicentric<sup>13</sup>. Multicentric Castleman disease (MCD) is generally the plasma cell type, but the hyaline vascular

type has been described in some patients. Unicentric Castleman’s disease usually presents as masses in young adults (20–30 years of age) but MCD develops in old patients (40–50 years of age). Systemic symptoms are rare in unicentric but common in MCD. Not only lymph node organs involvement is frequent.<sup>14</sup>

The pathogenesis of POEMS syndrome remains unclear. A previous study confirmed that elevated levels of tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin-6 (IL-6), and Vascular endothelial growth factor (VEGF) in patients of POEMS syndrome are correlated with disease activity.<sup>15</sup> However, it was beyond of scope to assess TNF- $\alpha$ , IL-6, or VEGF in this patient.

*[Figure 3 and 4] (A) Castleman disease (B) Solitary plasmacytoma (C) grey white pieces of soft tissue*

(D) Left parieto-occipital bone (E) CD-138 plasma cells (F) Ki-67 plasma cells

Therapy for POEMS syndrome should include radiotherapy, chemotherapy, autologous blood stem cell transplantation targeting therapy, intravenous gamma-globulin therapy, plasmapheresis, corticosteroids etc.<sup>16</sup> The clinical course of POEMS syndrome is also chronic. A previous study revealed that the median survival time of this syndrome is 165 month.<sup>171</sup> Another study showed that the prognosis of MCD patients was poor, and median survival time is 30 months.<sup>181190</sup> Due its rarity and association with multi systemic disorders, the diagnosis of POEMS syndrome is often delayed. High degree of suspicion is required for early diagnosis. This patient is treated with chemotherapy (eg, Melphalan) under specialized guidance.

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