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CASE REPORT

POEMS Syndrome - A Diagnostic Dilemma with Challenging Presentation

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Abstract

Polyneuropathy, Organomegaly, Endocrinopathy, M-protein, Skin changes (POEMS) syndrome is a rare disorder with multiple presentations and a constellation of symptoms. We present a 62 year-old female who presented to the Emergency Department for acute dyspnea. Chest Xray showed sclerotic lesions in the ribs and thoracic spine. Further imaging studies with computed tomography (CT) and positron emission tomography (PET) scans were suggestive of a benign process. Improvement was seen with supportive management. A few months later, patient developed neurological symptoms with reduced exercise tolerance. Mixed demyelinating and axonal polyneuropathy was diagnosed by electromyography. Further work up with bone marrow biopsy and immunochemistry testing revealed lambda and kappa plasma cell disorder, with elevated vascular endothelial growth factor (VEGF). Patient was diagnosed with POEMS and initiated on chemotherapy. POEMS syndrome is commonly missed due to its rarity and varied clinical presentations. VEGF plays a crucial role in the diagnosis. Management requires a multidisciplinary approach.

Keywords: POEMS syndrome, Polyneuropathy, Plasma cell disorder, VEGF, Vascular endothelial growth factor, Organomegaly, Endocrinopathy, M-protein, Skin changes syndrome, Demyelinating, Neuropathy

1. Introduction

POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes) syndrome is a rare constellation of clinical signs and symptoms involving multiple systems. The mandatory criteria for diagnosis include polyneuropathy and plasma cell disorder.[1] Patients commonly present with varied symptoms which make up the acronym "POEMS" and other nonspecific signs and symptoms including ascites, pleural effusion, and thrombocytosis. Due to its nonspecific presentation, diagnosis is often missed or delayed. Patients can sometimes be diagnosed with a primary neurologic disorder such as Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP).[1] The exact prevalence in the US remains unknown despite reported cases in the literature. The pathophysiology of POEMS remains unclear. Elevated levels of vascular endothelial growth factor (VEGF) have been implicated in the majority of cases and. is currently used as a marker to aid diagnose and monitor disease activity.[2,3] We describe a case of POEMS and our approach to diagnosis and management.

2. Case

A 62 year-old female with a past medical history of hypertension and asthma presented to the Emergency Department with acute dyspnea. Chest Xray showed sclerotic foci of T11 vertebrae, right first rib, and left 5th rib. Treatment for asthma exacerbation was provided and advised to follow up on an out-patient basis. Further evaluation with a Computed Tomography (CT) scan showed multiple sclerotic lesions scattered throughout the spine and

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pelvis with increased uptake in the femur concerning for metastatic disease. Positron Emission Tomography (PET) scan showed similar findings with subtle increased metabolic activity suggestive of a benign process (Fig. 1). Close monitoring with repeat imaging a year later showed stable lesions. Approximately six months later, the patient developed slow progressive tingling and numbness in both feet as well as reduced exercise intolerance. Further clinical evaluation by the neurology service revealed an underlying peripheral neuropathy. Electromyography (EMG) showed severe mixed demyelinating-axonal sensorimotor polyneuropathy with asymmetric active denervation, findings of conduction block and temporal dispersion (Fig. 2).

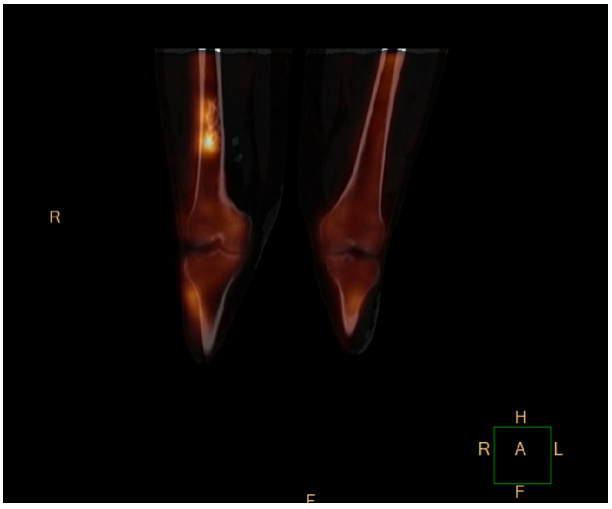

Fig. 1. Positron emission tomography (PET) scan with increased metabolic activity to the right femur.

Comprehensive motor sensory neuropathy laboratory panel was positive for perinuclear anti-cytoplasmic neutrophil antibodies (pANCA) (titer-1:160) and elevated rheumatoid factor (28 IU/ml (range - <14 IU/ml). Cerebrospinal fluid (CSF) analysis showed elevated myelin basic protein without oligoclonal bands, although four paired bands were observed. CSF immunofixation electrophoresis did not show any monoclonal bands. Magnetic resonance imaging (MRI) of the brain showed diffuse dural enhancement and thickening (Fig. 3). Further rheumatological laboratory workup was unremarkable. Oral prednisone was initiated for possible inflammatory neuropathy. Some improvement in ambulation was noted. Bone marrow aspirate showed trilineage hematopoiesis, megakaryocytic hyperplasia, mild plasmacytosis (10% by immunohistochemistry), mild excess in lambda expressing plasma cells, and thickened bone trabeculae consistent with osteosclerosis. Immunoglobulin G subtype 4 (IgG4) immunoperoxidase stain was negative. Serum immunofixation showed a normal immunoglobulin panel and elevated free kappa (23.6 mg/L (range 3.3–19.4mg/L) and lambda chains (32.0 mg/L (range 5.7–26.3 mg/L). Kappa-to-lambda ratio was normal. Biopsy of the T11 thoracic vertebral sclerotic lesion showed osteosclerosis. VEGF was elevated 1380 pg/ml (normal 0–115 pg/ml). Diagnosis of POEMS was established based on known criteria.[1] No evidence of endocrinopathy was seen upon further testing. Abdominal computed tomography (CT) imaging showed mild splenomegaly. Echocardiography showed normal ejection fraction of 60%, grade 1

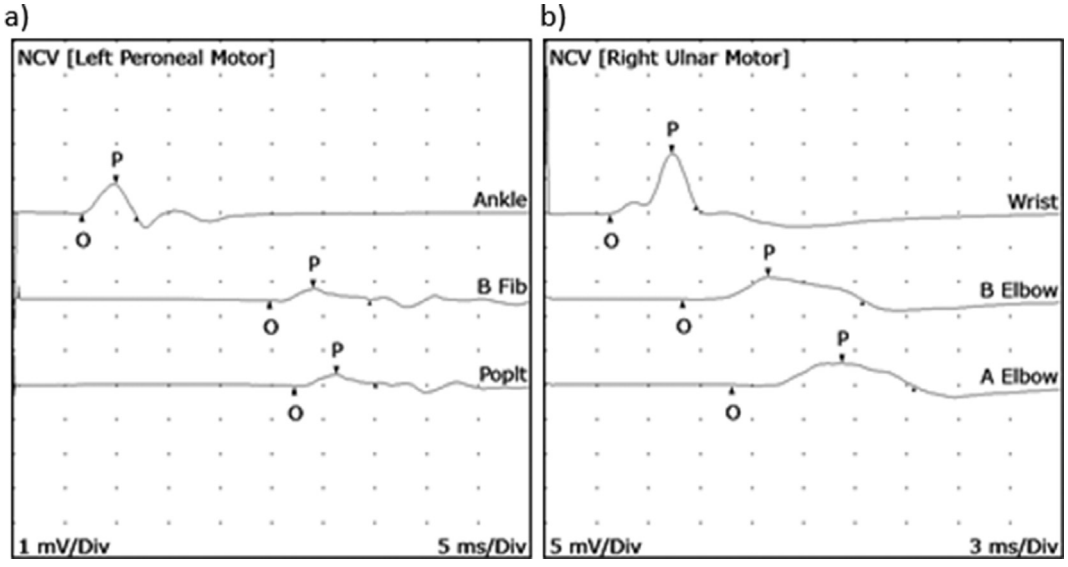

Fig. 2. Nerve Conduction Study illustrating a) temporal dispersion of the left peroneal nerve b) conduction block in the right ulnar motor nerve.

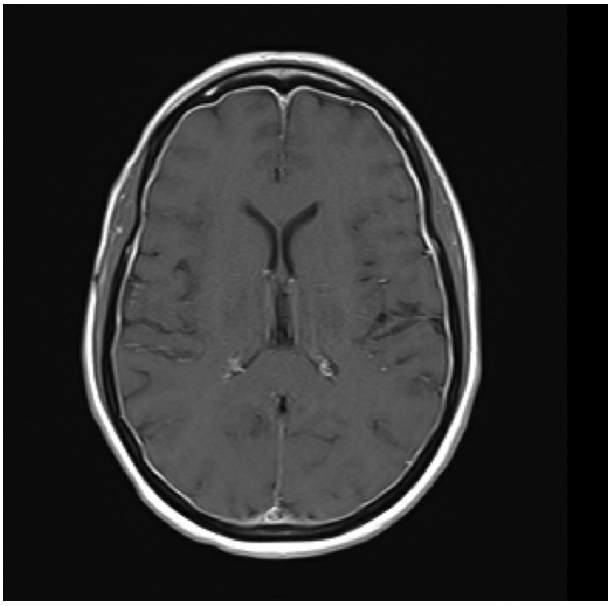

Fig. 3. Magnetic Resonance Imaging (MRI) brain showing diffuse thickening and enhancement of the dura.

diastolic dysfunction and no wall abnormalities. Pulmonary function test showed mild obstructive ventilatory defect consistent with asthma. Oncology evaluation was performed. Chemotherapy using daratumumab, lenalidomide, and dexamethasone was initiated. Some improvement in neurological symptoms ensued. Autologous stem cell transplantation has been planned.

3. Discussion

Diagnosis of POEMS syndrome remains challenging due its rarity and associated multiple clinical presentations. It is often misdiagnosed or diagnosed later in the disease course. Based on previous literature and as seen with our patient, diagnosis can be achieved approximately one to two years after initial symptom presentation.[4,5] Common misdiagnosis include CIDP, Monoclonal Gammopathy of Undetermined Significance (MGUS) or multiple myeloma.[6]

In our patient, brain imaging findings were nonspecific and revealed diffuse dural thickening and enhancement. In a retrospective study of MRI brain findings in patients with POEMS, approximately seventy percent of patients had asymptomatic pachymeningeal involvement.[7] This finding may help to differentiate POEMS from other neurological disorders and may be an important diagnosis criterion to be added.

POEMS should be suspected in patients with findings of osteosclerosis along with progressive polyneuropathy. Many patients will in fact present with only few signs and symptoms included in the established diagnosis criteria.[6] Most patients present in the fourth to fifth decade of life with male predominance though a wide age range has been previously reported.[8] As seen in our patient, sclerotic lesions can be found in up to 95% of patients with POEMS with a lower prevalence in patients from China.[9,10] Contrary to our patient, further evaluation with a bone marrow biopsy can sometimes help reach a definitive diagnosis as monoclonal plasma cells may be seen.[11,12] Although not necessary to establish a diagnosis of POEMS, other previously reported clinical features include: thrombocytosis, polycythemia, and skin changes. As noted in a recent retrospective study of 108 patients with POEMS, these features were less frequently reported.[13]

The pathophysiology of POEMS remains unclear. VEGF has been described as a marker of disease activity.[14] Markedly elevated levels are seen in patients with POEMS syndrome. Moreover, when used in combination with clinical symptoms, VEGF levels can be used to distinguish POEMS from other plasma cell dyscrasias or other conditions in which it can be elevated.[15] Early diagnosis remains important as treatment of POEMS significantly differs from other mimicking diseases. Depending on the extent of the disease, as with patients with a solitary plasmacytoma, radiation therapy remains the first line of treatment. Patients with diffuse sclerotic lesions receive chemotherapy and if eligible, stem cell transplant.

In conclusion, diagnosis of POEMS syndrome requires a high index of clinical suspicion. With advancement in management, early diagnosis can help to reduce or prevent disabling symptoms, morbidity, and mortality.[16] Incidental finding of sclerotic bone lesions should raise suspicion and prompt further workup to lead to an earlier diagnosis of POEMS syndrome, more so when polyneuropathy is also present.

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Conflcits of interest

None.

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