The Peripheral Neuropathies of POEMS Syndrome and Castleman Disease

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KEYWORDS

• POEMS syndrome • POEMS neuropathy • Castleman disease
• Castleman neuropathy • Monoclonal gammopathy

KEY POINTS

- Polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell-proliferative disorder, skin changes (POEMS) syndrome often presents with a peripheral neuropathy that is motor predominant with prominent lower limb weakness and atrophy.
- POEMS syndrome should be considered in patients with a diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy that is resistant to standard therapy.
- Frequent neuropathic pain and absence of cranial nerve involvement in POEMS syndrome are helpful in distinguishing clinical characteristics from chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).
- Peripheral neuropathy can occur in multicentric Castleman disease and is often a mild distal sensory neuropathy.

INTRODUCTION

Monoclonal gammopathies affect 3% to 4% of the population older than 50 years and affect more than 5% of the population older than 70 years.[1] They reflect a diverse group of disorders that share the secretion of monoclonal immunoglobulin produced by the bone marrow. These disorders include multiple myeloma; polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes (POEMS) syndrome; Waldenström macroglobulinemia, light-chain amyloidosis; and monoclonal gammopathy of undetermined significance (MGUS). The most common neurologic complication is peripheral neuropathy. Monoclonal protein type and neuropathy pattern as well as the presence of other associated clinical features can aid in this determination. POEMS syndrome often presents with a subacute motor polyradiculoneuropathy, and the associated systemic features can be easily overlooked. The monoclonal protein is lambda in greater than 95% of cases, and its presence is a clue in patients who present with treatment-refractory chronic inflammatory

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demyelinating polyradiculoneuropathy (CDIP). Castleman disease (CD) can be associated with POEMS syndrome but can also be present independent of POEMS syndrome. CD can be classified as unicentric or multicentric, with the latter associated with peripheral neuropathy. In contrast to POEMS syndrome, the neuropathy of CD is often a mild distal sensory neuropathy. The neuropathies associated with POEMS and CD are reviewed in detail.

POLYNEUROPATHY, ORGANOMEGALY, ENDOCRINOPATHY, MONOCLONAL PLASMA CELL-PROLIFERATIVE DISORDER, SKIN CHANGES (POEMS) SYNDROME

General

POEMS syndrome is a clonal plasma cell disorder that is described by the acronym in its name: polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell-proliferative disorder, and skin changes. Other names used for POEMS syndrome include Takatsuki syndrome, Crow-Fukase syndrome, or osteosclerotic myeloma. There are many features associated with the syndrome, and the diagnostic criteria are listed in **Table 1**.[2] Monoclonal plasma cell-proliferative disorder and peripheral neuropathy are required for the diagnosis. One other major criterion, elevated vascular

Table 1
Criteria for the diagnosis of polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes syndrome[a]

Mandatory major criteria	1. Polyneuropathy (typically demyelinating) 2. Monoclonal plasma cell-proliferative disorder (almost always lambda)
Other major criteria (one required)	3. CD[a] 4. Sclerotic bone lesions 5. Vascular endothelial growth factor elevation
Minor criteria	6. Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy) 7. Extravascular volume overload (edema, pleural effusion, or ascites) 8. Endocrinopathy (adrenal, thyroid,[b] pituitary, gonadal, parathyroid, pancreatic[b]) 9. Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, white nails) 10. Papilledema 11. Thrombocytosis/polycythemia[c]
Other symptoms and signs	Clubbing, weight loss, hyperhidrosis, pulmonary hypertension/restrictive lung disease, thrombotic diatheses, diarrhea, low vitamin B_{12} values

The diagnosis of POEMS syndrome is confirmed when both of the mandatory major criteria, one of the 3 other major criteria, and one of the 6 minor criteria are present.

[a] There is a CD variant of POEMS syndrome that occurs *without* evidence of a clonal plasma cell disorder that is not accounted for in this table. This entity should be considered separately.

[b] Because of the high prevalence of diabetes mellitus and thyroid abnormalities, this diagnosis alone is not sufficient to meet this minor criterion.

[c] Approximately 50% of patients will have bone marrow changes that distinguish it from a typical MGUS or myeloma bone marrow.[8] Anemia and/or thrombocytopenia are distinctively unusual in this syndrome unless CD is present.

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