Oncology, Nuclear Medicine and Transplantology
(eISSN 3105-8760)

Original Article

POEMS Syndrome as a Mask of Multiple Myeloma: A Case Report with a Significant Response to Daratumumab Therapy

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Received: Mar 27, 2026
Accepted: Jul 09, 2026

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Citation: Madieva A, Karabekov AB, Tursyn AB, Kemaikin VM, Zhambulaev RU, Aynabay AM, et al. POEMS Syndrome as a Mask of Multiple Myeloma: A Case Report with a Significant Response to Daratumumab Therapy. Oncology, Nuclear Medicine and Transplantology. 2026;2(3):onmt022.
https://doi.org/10.63946/onmt/19021

ABSTRACT

Introduction: POEMS syndrome is a rare paraneoplastic disorder associated with plasma cell dyscrasia and characterized by a combination of organomegaly, peripheral polyneuropathy, endocrinopathies, osteosclerotic lesions, monoclonal shedding, and typical skin changes. Diagnosis is challenging due to the nonspecific clinical presentation and minimal bone marrow infiltration. Currently, treatment approaches remain nonstandard, and the use of anti-CD38 therapy is limited.

Objective: To demonstrate the complexity and duration of diagnosis of POEMS syndrome and evaluate the clinical effect of anti-CD38 therapy.

Materials And Methods: A retrospective analysis of clinical, laboratory, and imaging data from a 38-year-old patient seen at the National Cancer Research Center was conducted. Diagnostic evaluation included serum enzyme-linked immunosorbent assay, vascular endothelial growth factor (VEGF) levels, PET/CT, bone marrow examination, and assessment of compliance with the Dispenzieri 2019 criteria. Treatment efficacy was assessed based on clinical symptoms and laboratory findings.

Results: The patient was diagnosed with polyneuropathy, organomegaly, extravascular fluid overload, endocrinopathy, monoclonal IgG-λ secretion, and significantly elevated VEGF levels. Minimal plasma cell infiltration was noted in the bone marrow. POEMS syndrome was diagnosed. Treatment with Daratumumab-Lenalidomide-Dexamethasone (Dara-RD) resulted in significant clinical improvement, decreased edema, and stabilization of laboratory parameters.

Conclusion: This case demonstrates the complexity of diagnosing POEMS syndrome with minimal bone marrow infiltration, severe systemic manifestations, and problems with long-term diagnostic verification, lasting for 5 years (from 2019 to 2025). Daratumumab-Lenalidomide-Dexamethasone (DaraRD) therapy has demonstrated significant clinical benefit and can be considered a progressive treatment option for severe forms of the disease.

Keywords: POEMS Syndrome; VEGF; Plasma Cell Dyscrasia; Anti-CD38 Antibodies

Introduction

POEMS syndrome is a rare paraneoplastic disorder associated with plasma cell dyscrasia, characterized by a combination of polyneuropathy (P), organomegaly (O), endocrinopathies (E), monoclonal gammopathy (M), and skin changes (S). The disease is associated with λ-light chain-secreting clones, localized osteosclerotic lesions, and elevated vascular endothelial growth factor (VEGF) levels.

Optimal therapy for POEMS syndrome has not been standardized, and the use of anti-CD38 monoclonal antibodies remains a subject of investigation. We present a rare case of IgG-λ multiple myeloma associated with POEMS syndrome, demonstrating a marked clinical and laboratory response to daratumab-based therapy [1].

Case Description

A 38-year-old man presented with progressive abdominal distension, severe generalized edema, gait disturbance, numbness of the lower extremities, hyperpigmentation and scaling of the skin, general weakness, and a weight loss of 30 kg over five years.

The disease began in 2019 with gradual distal muscle weakness and pain in the lower extremities. The patient was initially tested for polycythemia, but a JAK2 mutation was not detected. In 2020–2021, electromyography (EMG) revealed severe demyelinating sensorimotor polyneuropathy. The patient subsequently developed splenomegaly, lymphadenopathy, pleural effusion, and an osteosclerotic lesion of the right eighth rib. Immunosuppressive therapy with glucocorticosteroids and intravenous immunoglobulins provided only temporary improvement.

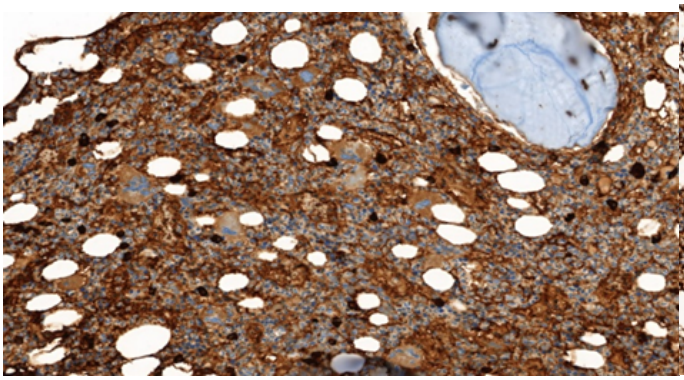

Figure 1.1. Free light chains Lambda_40.0x.

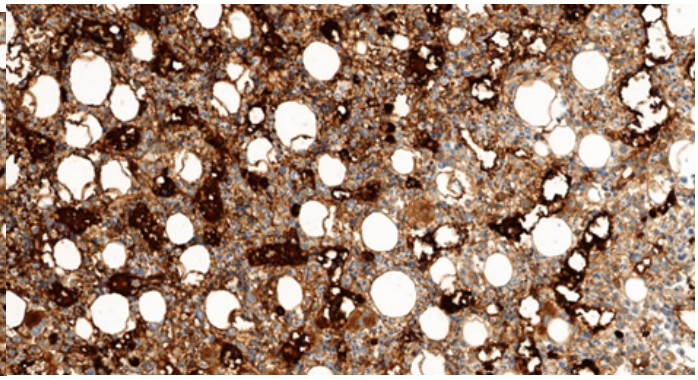

Figure 1.2. Free light chains Kappa_40.0x. Immunohistochemical analysis of a tumor tissue specimen (bone marrow).

In October 2025, the patient's condition deteriorated sharply, manifesting as massive ascites, generalized edema, respiratory failure, and acute kidney injury. Laboratory testing revealed a monoclonal IgG-λ protein with an M-spike of 1.98 g/L.

Immunohistochemical analysis of the plasmacytoma showed approximately 1% cells positive for κ-light chains and 2% positive for λ-light chains (Figures 1.1; 1.2). The plasma cells were positive for CD138, CD38 (7–10%), and CD117 (3–5%) (Figure 2).

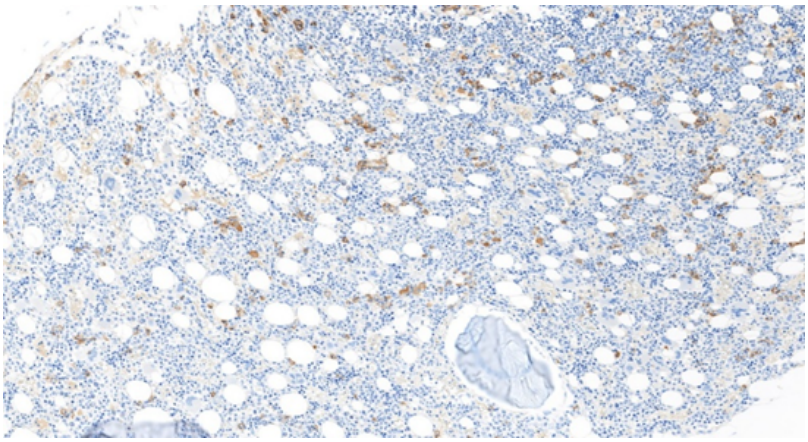

Figure 2. CD138+ (about 5-10% of cells are positive).

Bone marrow biopsy confirmed low-grade plasma cell infiltration (0.15%) with a restriction of the λ chain. The β2-microglobulin level was 18.64 mg/L, and the VEGF level exceeded 2000 pg/mL. A PET/CT scan revealed a hypermetabolic plasmacytoma in the right eighth rib. The patient met the updated 2019 Dispenzieri diagnostic criteria [1, 2]. Based on these data, a diagnosis of POEMS syndrome associated with IgG-λ plasma cell dyscrasia was made.

Treatment

Given the patient's severe systemic involvement and the presence of plasmacytoma, a daratumab-lenalidomide-dexamethasone regimen was prescribed [3-7]. Daratumab is pathogenetically justified because POEMS-associated plasma cells express CD38 similarly to multiple myeloma cells. Inhibition of this clone reduces the production of proinflammatory cytokines and VEGF [8].

Several studies have reported the efficacy of daratumab-containing regimens in POEMS. Gavriatopoulou et al. (2020) reported successful clinical and laboratory responses with this combination, and Zhao et al. observed a significant reduction in VEGF levels and clinical improvement during daratumab therapy [4, 9].

After two cycles of therapy, our patient experienced a significant decrease in monoclonal protein levels, resolution of ascites and peripheral edema (Figs. 3.1; 3.2), stabilization of renal function, and partial improvement of neurological symptoms. According to the 2019 NCCN/Dispenzieri response criteria, a partial hematological and organ response was achieved (Figs. 4; 5) [2].

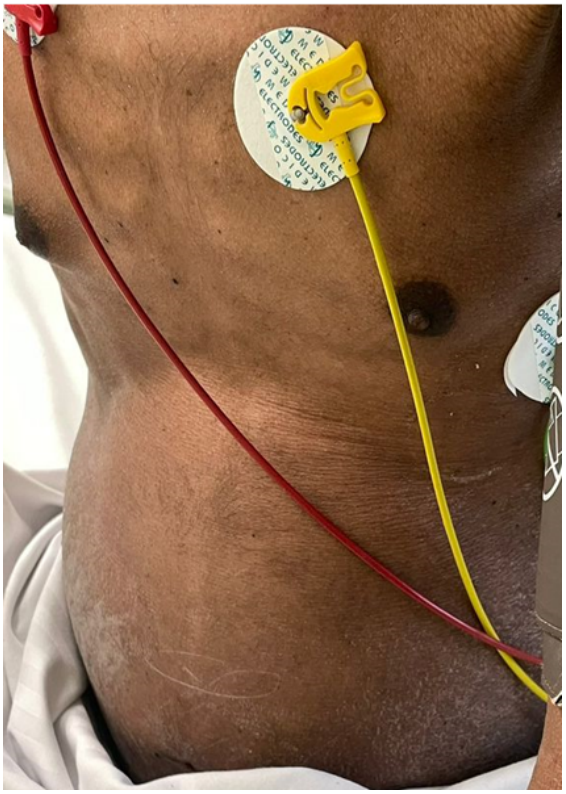

Figure 3.1. Ascites volume 1500-1800 ml.

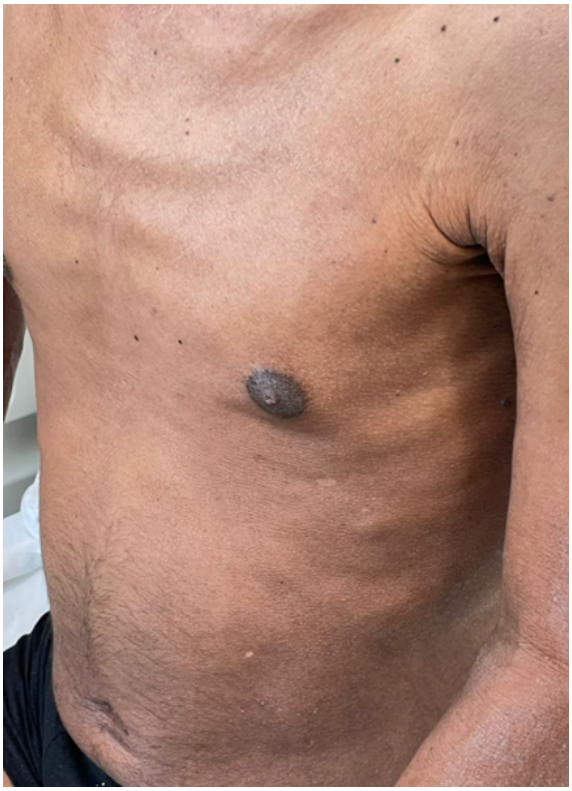

Figure 3.2. Ascites regression (February 26, 2026) (November 13, 2025)

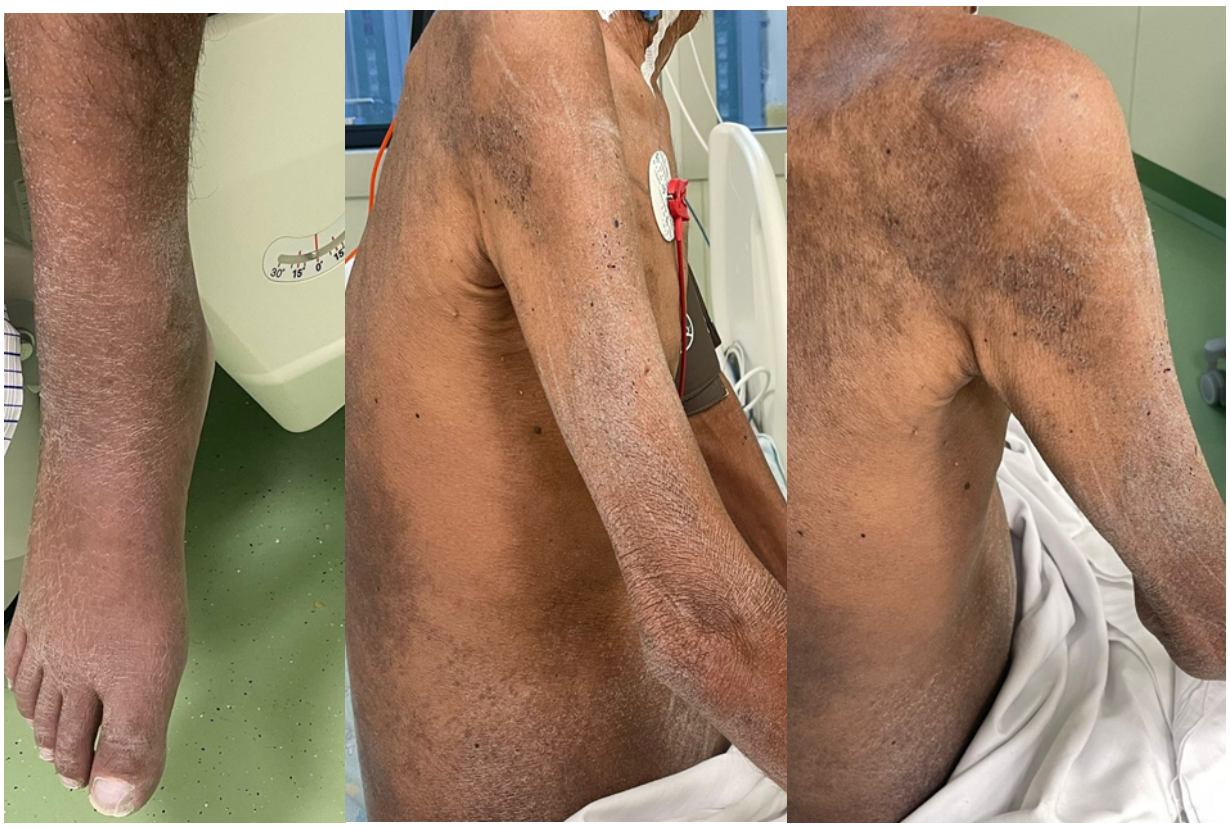

Figure 4. Before starting Dara-RD (daratumumab–lenalidomide–dexamethasone) therapy.

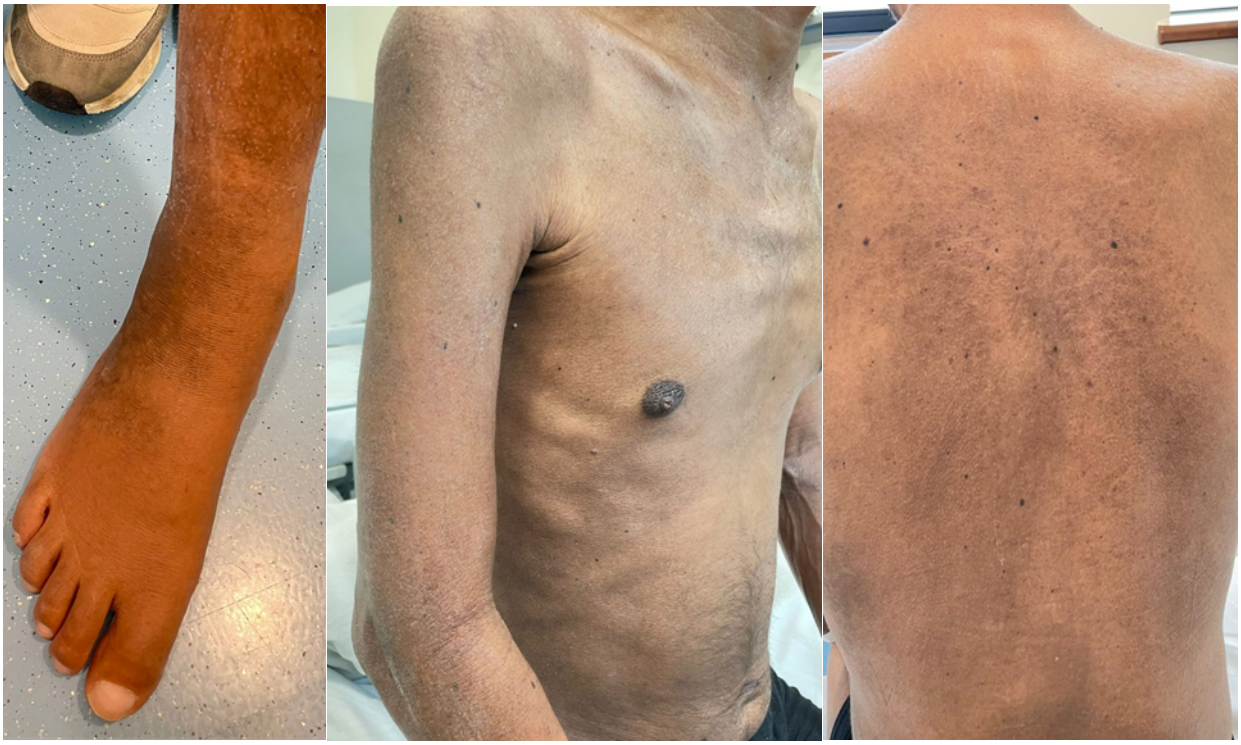

Figure 5. After 2 courses of the Dara-RD (daratumumab–lenalidomide–dexamethasone) regimen.

Discussion

The presented clinical case demonstrates a significant diagnostic delay of approximately five years, characteristic of POEMS syndrome. Similar diagnostic delays have been described widely reported and are associated with both the rarity of the disease and the heterogeneity of clinical manifestations. According to a large retrospective analysis by A. Dispenzieri et al., which included more than 90 patients, the median time from the onset of the first symptoms to diagnosis ranged from 13 to 33 months, but in individual cases this period can exceed 5 years [10].

POEMS syndrome is an extremely rare paraneoplastic disease. Its exact prevalence is unknown. However, according to epidemiological studies, the disease is much less common than multiple myeloma and is described mainly in small clinical series or cohort observations [1,3]. In the largest published series, the number of observed patients rarely exceeds 100-200 cases, which highlights the limited clinical experience available. The difficulty of diagnosing POEMS syndrome is due to the fact that the initial clinical manifestation of the disease is predominantly isolated polyneuropathy, which is most often interpreted as chronic inflammatory demyelinating polyneuropathy. Several reviews show that a significant proportion of patients turn to neurologists at an early stage and receive immunosuppressive therapy without significant clinical effect [11,12,13].

A similar diagnostic error was observed in the presented case, where the patient received a long course of glucocorticosteroids and intravenous immunoglobulins.

An additional diagnostic challenge is minimal or absent bone marrow infiltration with plasma cells. Unlike classical multiple myeloma, in POEMS syndrome, the plasma cell content in the bone marrow often remains low, and the pathological clone may be localized predominantly as a solitary or localized plasmacytoma (Dispenzieri, 2019). In the presented case, the plasma cell level was less than 1%, consistent with disease characteristics described in the literature.

The key pathogenetic factor in POEMS syndrome is considered to be hyperproduction of vascular endothelial growth factor (VEGF). Elevated VEGF concentrations correlate with the severity of vascular hyperpermeability, the development of extravascular fluid overload, edema, ascites, and pleural effusions [14, 15, 16].

In the patient's case, VEGF levels exceeded 2000 pg/ml, which was accompanied by severe edema and massive ascites.

Thus, the presented case illustrates the typical features of POEMS syndrome: a long diagnostic process, minimal bone marrow infiltration, and pronounced systemic manifestations caused by cytokine-mediated mechanisms.

Conclusion

POEMS syndrome can present with minimal bone marrow infiltration and significant systemic involvement, leading to diagnostic difficulties and delays in treatment.

Daratumumab-lenalidomide-dexamethasone therapy has demonstrated significant clinical and laboratory responses and can be considered as an effective treatment option for severe forms of POEMS syndrome with systemic manifestations.

Further clinical observations are needed to determine the role of anti-CD38 therapy in the treatment algorithm for this rare disease.

Acknowledgements

Author Contributions: All authors made significant contributions to the study concept, data collection and analysis, manuscript preparation and editing, approved the final version of the article, and are responsible for its content.

Funding: The study was conducted without financial support.

Disclosure: The authors declare no conflicts of interest.

Disclosure of AI use: No artificial intelligence technologies were used in the preparation of this manuscript.

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