VEGF-Refractory Castleman-Variant POEMS Without Monoclonal Protein: Navigating Therapeutic and Access Gaps in a Rare Clinical Entity

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Introduction

Castleman-variant POEMS syndrome without a monoclonal component represents a **rare and underrecognized subtype** of a multisystemic disorder where conventional diagnostic and therapeutic frameworks often fail.

While VEGF is central to disease pathogenesis, **treatment guidance beyond anti-IL-6 therapy is sparse**, and disease monitoring becomes particularly challenging in the **absence of a measurable clonal marker**.

In such scenarios, clinicians are left navigating **off-label regimens, reimbursement barriers**, and the **disconnect between biomarker trends and clinical function**.

Objectives

To present a VEGF-refractory case of Castleman-variant POEMS without monoclonal protein.

To highlight therapeutic challenges and access barriers in rare disease management.

Case description/Methods

64-year-old male with Castleman-variant POEMS

Criterion Category	Diagnostic Criterion	Patient	Details
Mandatory major criteria	**Polyneuropathy**	✓	Tetramelic axonal sensorimotor polyneuropathy
	Monoclonal plasma cell-proliferative disorder	✗	
Other major criteria (one mandatory)	Castleman disease	✓	Histology: multicentric Castleman disease (mixed type)
	Sclerotic bone lesions	✗	
	Vascular endothelial growth factor elevation	✓	>2000 pg/ml
Minor criteria (one mandatory)	Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy)	✓	Splenomegaly Hepatomegaly Lymphadenopathy
	Extravascular volume overload (edema pleural effusion or ascites)	✓	Pleural effusion
	Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic)	✓	Autoimmune thyroiditis
	Skin changes (hyperpigmentation, hypertrichosis, glomuleroid hemangiomata, plethora, acrocyanosis, flushing, white nails)	✓	Hyperpigmentation
	Papilledema	✗	
	Thrombocytosis/polycythemia	✓	Thrombocytosis
Other symptoms and signs	Clubbing, weight loss, hyperhidrosis, pulmonary hypertension/restrictive lung disease, thrombotic diatheses. diarrhea. low vitamin B12 values	✓	Weight loss, hyperhidrosis

Table 1. POEMS Diagnostic Criteria Fulfilled in This Patient. Patients meet one of the mandatory major criteria, two of the other major criteria and 5 of the minor criteria, making him the **Castleman variant of POEMS syndrome**.

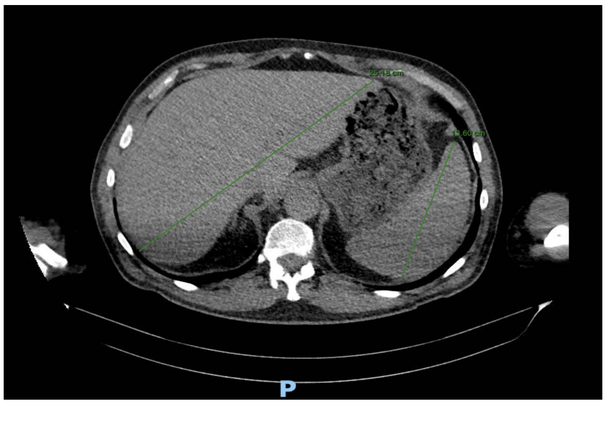
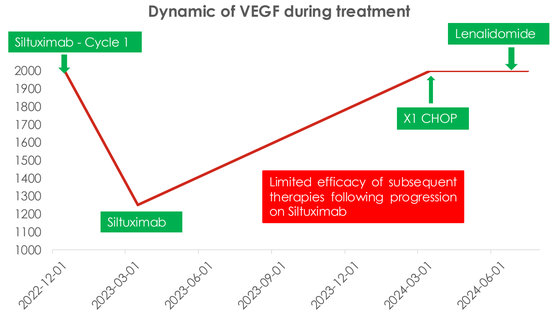


Image 1. CT scan of the abdomen at diagnosis showing hepatomegaly and splenomegaly

Results

- Initial treatment with **siltuximab** yielded a **transient VEGF reduction to 1253 pg/mL**, but after 19 cycles, the patient showed **clinical progression** with worsening hepatosplenomegaly (liver 25.6 cm, spleen 19.6 cm), recurrent pleural effusion, and severe polyneuropathy.
- Following guidelines, **CHOP chemotherapy** was administered. A **rapid functional improvement** in mobility and fatigue occurred, but was **not sustained**.
- The patient was switched to **lenalidomide (10–25 mg)**, rationalized by literature suggesting VEGF responsiveness and possible neuropathy benefit. Hepatomegaly regressed modestly (–2 cm), and the patient improved from **wheelchair-dependent to walking with support**, yet **VEGF remained >2000 pg/mL**, indicating biochemical refractoriness.



Summary

Treatment timeline:

- **Siltuximab (19 cycles):** transient VEGF ↓ to 1253 pg/mL, then progression (hepatosplenomegaly, pleural effusion, severe neuropathy).
- **CHOP chemotherapy:** short-term improvement of mobility and overall general state, not sustained.
- **Lenalidomide (10–25 mg):** modest hepatomegaly regression (–2 cm), improved mobility (wheelchair → walking with support), but VEGF >2000 pg/mL.

Discussion

This case illustrates the **limits of current therapeutic algorithms** in Castleman-variant POEMS. While VEGF is the core pathogenic mediator, response is rarely binary: the patient experienced **transient organ and neurologic gains**, but **VEGF failed to reflect these improvements**, and later **diverged from the clinical course**.

Moreover, **no access to clinical trials**, and the **need for self-funded lenalidomide**, underscore a systemic gap in rare disease care.
Neuropathy remains the dominant driver of morbidity, affecting quality of life and autonomy.

References

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