WHEN THE DIAGNOSIS REMAINS ELUSIVE: A CASE OF SUBACUTE-ONSET POLYNEUROPATHY

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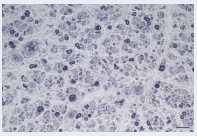
OBJECTIVES

Chronic polyneuropathies with subacute onset and unclear etiology represent a **diagnostic and therapeutic challenge**. The purpose of this report is to describe the diagnostic pathway and therapeutic strategies in such a complex scenario.

CASE PRESENTATION

We present the case of a **47-year-old Albanian man** who developed **rapidly progressive acral pain and motor weakness** in **August 2024**. Symptoms initially involved the lower limbs, extending to the upper limbs, resulting into complete loss of ambulation within weeks. GBS was first considered, and treatment with **IVIg and plasmapheresis** were initiated. In **February 2025**, due to clinical worsening, he was admitted to our neurology unit in Milan. Upon admission, examination revealed severe symmetric **distal tetraparesis, areflexia, distal tactile hypoesthesia and hypopallesthesia**.

INVESTIGATIONS AND RESULTS

ENMG	Severe axonal motor-sensory polyneuropathy with active denervation
Spinal MRI	Dorsal vertebral lesions and cauda equina root enhancement
Cerebrospinal fluid	Isolated hyperproteinorrachia
Whole-body CT scan	Vertebral lesions and lymphadenopathy
Sural nerve biopsy	Nonspecific axonal loss compatible with Inflammation (figure A)  *Figure A. Sural nerve toluidine blue-stained semithin section showing moderately severe loss of myelinated nerve fibers, axonal degeneration and increased endoneurial fibrous tissue. Scale bar: 25 µm.*
Extensive blood tests	Infectious, autoimmune and genetic etiologies ruled out
PET/CT, testicular ultrasound, bone marrow biopsy	No evidence of malignancy

TREATMENT

High-dose steroids and rituximab failed to yield significant improvement. The patient underwent rehabilitation; yet two months later, he required re-hospedalization due to fever of unknown origin.

SECOND HOSPITALIZATION

An **extensive diagnostic work-up** was performed, including laboratory tests, transthoracic echocardiography, whole-body CT scan, fundoscopy, vertebral biopsy, bone marrow aspirate, abdominal fat pad biopsy.

The constellation of findings was consistent with **POEMS syndrome diagnosis** (figure B).

POEMS syndrome diagnostic criteria

Major

Polyneuropathy	☑
Monoclonal plasma cell disorder	☑
Sclerotic bone lesions	☑
Elevated VEGF levels	☑
Castleman disease	☐

Minor

Organomegaly (liver, spleen, lymph nodes)	☑
Extravascular volume overload (edema, effusions, ascites)	☑
Endocrinopathy (excl. isolated diabetes or hypothyroidism)	☐
Skin changes (hyperpigmentation, hypertrichosis, angiomas etc.)	☐
Papilledema	☑
Thrombocythosis / Polycythemia	☑

Figure B. According to current diagnostic standards, three major criteria are required (polyneuropathy and a clonal plasma cell disorder are mandatory), in addition to at least two out of four minor criteria.

Following multidisciplinary discussion, off-label therapy with **daratumumab**, **lenalidomide**, and **corticosteroids** was initiated.

CONCLUSIONS

This case highlights the **complexity** of chronic polyneuropathies with subacute onset and uncertain etiology; it also highlights the need for a **systematic re-evaluation** and **multidisciplinary** team involvement.

Moreover, despite common assumptions, bone marrow biopsy findings in POEMS syndrome are **often nonspecific** and insufficient alone to establish plasmacytoma diagnosis.

References:

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