Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Plasma Cell Disorder, and Skin Changes (POEMS) Syndrome Presenting after Immune Thrombocytopenic Purpura and Complicated by Sinusoidal Obstruction Syndrome

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KEY WORDS: polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma-cell disorder, and skin changes (POEMS syndrome), immune thrombocytopenic purpura (ITP), chronic inflammatory demyelinating polyneuropathy (CIDP), vascular endothelial growth factor, sinusoidal obstruction syndrome (SOS)

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Polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma-cell disorder, and skin changes (POEMS syndrome) is a rare multisystem paraneoplastic disorder driven by a plasma-cell dyscrasia and cytokine overproduction. It is often misdiagnosed as chronic inflammatory demyelinating polyneuropathy (CIDP) due to overlapping neuropathy [1]. Although thrombocytosis is typical, immune thrombocytopenia is a rare and underrecognized presentation. We describe a patient with longstanding immune thrombocytopenic purpura (ITP) that evolved to POEMS, developed sinusoidal obstruction syndrome (SOS) after an autologous stem-cell transplantation (ASCT), and remained cytopenic due to hypersplenism, highlighting diagnostic and therapeutic challenges.

PATIENT DESCRIPTION

A 60-year-old woman with a remote history of deep vein thrombosis and pulmonary embolism while on oral contraceptives (treated with 18 months of anticoagulation) developed progressive neuropathic symptoms between 2012 and 2014, including paresthesias, distal sensory loss, and left foot drop. Electrophysiologic studies were consistent with demyelinating polyneuropathy, and a diagnosis of CIDP was made. She was initially treated with corticosteroids but became steroid-dependent, with clinical deterioration on tapering. Trials of azathioprine and plasmapheresis were ineffective. Intravenous immunoglobulin (IVIG) led to partial stabilization, allowing eventual discontinuation of corticosteroids.

During this period, she developed persistent thrombocytopenia (platelets 30–40 × 10^9/L) without alternative hematologic abnormalities and was diagnosed with ITP. Thrombocytopenia fluctuated in parallel with neurological symptoms and responded partially to IVIG.

By late 2016, her clinical picture evolved with systemic manifestations including generalized pruritus, progressive edema, ascites, pleural and pericardial effusions, and unintentional weight loss (~15 kg). Imaging demonstrated marked splenomegaly (up to 20.5 cm), ascites, and sclerotic bone lesions. Bone marrow biopsy revealed approximately 10% monoclonal lambda-restricted plasma cells, and ^{18}F-fluorodeoxyglucose positron-emission tomography/computed tomography showed hypermetabolic sclerotic lesions. Serum vascular endothelial growth factor (VEGF) levels were within the normal range, although measured during corticosteroid therapy. Despite the absence of elevated VEGF and overt endocrinopathy, the combination of demyelinating neuropathy, monoclonal plasma-cell disorder, sclerotic bone lesions, organomegaly, and extravascular volume overload fulfilled diagnostic criteria for POEMS syndrome.

In February 2018, she underwent ASCT. The post-transplant course

was complicated by SOS, requiring treatment with defibrotide, and was further complicated by prolonged aplasia, septic shock, and significant fluid retention requiring extended diuretic therapy. She gradually recovered but remained chronically cytopenic, attributed to persistent hypersplenism. Over the following years, platelet counts ranged from 30–40 × 10^9/L, with neutropenia (500–1000/μL) and stable hemoglobin levels (11–12 g/dl).

Two years later, a new metabolically active lesion was identified at the L2 vertebral body. As a biopsy was not feasible, empiric radiation therapy was administered, resulting in complete radiologic resolution. Serial ^{18}F-FDG PET/CT imaging showed no evidence of disease relapse.

Given persistent severe thrombocytopenia and neutropenia, splenectomy was considered to improve cytopenias. However, due to concerns regarding exacerbation of portal hypertension and increased risk of splanchnic thrombosis in the context of prior thrombotic events and endothelial dysfunction, a multidisciplinary decision was made to defer surgical intervention.

At the time of this publication, her management included periodic IVIG (30 grams every 5 weeks) for neuropathy, in addition to supportive therapy. She remains under close multidisciplinary follow-up.

COMMENT

Misdiagnosis as idiopathic CIDP is common in POEMS syndrome. In some series, up to 50% of patients are initially labeled as CIDP prior to the emergence of systemic features [2]. Electrophysiologically, up to 70% of patients fulfill formal CIDP criteria, underscoring that the resemblance is diagnostic rather than etiologic overlap. In our patient, this overlap contributed to diagnostic delay, as initial steroid responsiveness further reinforced the presumed diagnosis. However, progression to cytopenias and multisystem disease was inconsistent with idiopathic CIDP and prompted reassessment. Early recognition of this evolution is critical, as immunomodulatory therapies such as corticosteroids and IVIG often provide only transient benefit, whereas definitive disease control requires targeting the underlying plasma-cell clone [1].

ITP is an uncommon manifestation of POEMS and has rarely been reported as a preceding feature. Isolated cases describe the development of POEMS during treatment for chronic ITP, suggesting it may represent an early paraneoplastic manifestation [3]. In our patient, the coexistence of neuropathy and thrombocytopenia supported a shared underlying process. Clinically, this combination should prompt evaluation for an evolving plasma-cell disorder, particularly when systemic features emerge.

In most patients, the typical hematologic abnormality is thrombocytosis, reflecting the myeloproliferative activity and cytokine milieu characteristic of POEMS rather than peripheral platelet destruction [1]. The precise mechanism linking POEMS and ITP remains unclear, but immune dysregulation and overproduction of pro-inflammatory cytokines may have an impact.

POEMS syndrome is driven by cytokine-mediated endothelial dysfunction, with vascular endothelial growth factor (VEGF) playing a central role by increasing vascular permeability and contributing to key clinical features such as edema and extravascular volume overload [4]. Although elevated VEGF is a major diagnostic criterion, it is not required and may be falsely low in patients receiving corticosteroids or cytotoxic therapy [4]. In our patient, VEGF was measured during active steroid treatment, which likely contributed to the negative result. POEMS remains a clinical diagnosis, and normal VEGF levels should not exclude the diagnosis when suspicion is high. Repeat measurement may be warranted in appropriate settings.

ASCT is the standard therapy for eligible patients, but it carries a risk of sinusoidal obstruction syndrome (SOS), particularly in those with baseline endothelial dysfunction and fluid overload. SOS results from endothelial injury leading to portal hypertension and multiorgan complications [5]. In this case, pre-existing volume overload likely contributed to its development.

Persistent cytopenias following ASCT were attributed to hypersplenism in the context of portal hypertension, creating a therapeutic dilemma regarding splenectomy. While splenectomy may improve cytopenias, it carries a significant risk of splanchnic thrombosis, particularly in patients with prior thromboembolic events and ongoing endothelial dysfunction. Given this prothrombotic milieu, the potential risks were considered to outweigh the expected hematologic benefit, and splenectomy was deferred.

CONCLUSIONS

This case illustrates the diagnostic and therapeutic complexity of POEMS syndrome, particularly when preceded by atypical immune manifestations such as ITP and misdiagnosed demyelinating neuropathy. It highlights the need to consider PO-

EMS in patients presenting with unexplained neuropathy and cytopenias accompanied by organomegaly or fluid overload. Our patient's course underscores several key lessons:

- Immune cytopenias may represent early paraneoplastic features of POEMS and should prompt longitudinal evaluation for systemic evolution.
- Endothelial dysfunction and cytokine activation underlie both the syndrome's manifestations and its complications, including SOS after ASCT.
- Persistent hypersplenism and cytopenias post-ASCT require individualized management.

Although splenectomy can improve counts and portal hemodynamics, its thrombotic risks, particularly in patients with prior endothelial injury, may outweigh potential benefits. Ultimately, a multidisciplinary approach is essential to balance hematologic recovery, hepatic stability, and thrombotic risk in complex post-transplant POEMS cases.

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Capsule

Engineered immunosuppressive dendritic cells protect against cardiac remodeling

Li et al. showed that engineered immunosuppressive and fibrosis-targeted DCs (iCDCs) effectively protect against pathological cardiac remodeling. In mouse models of ischemia-reperfusion injury, myocardial infarction and pressure overload, iCDC therapy reduced inflammatory cardiac fibrosis, improved cardiac perfusion and preserved contractility. Mechanistically, iCDCs conferred sustained cardioprotection directly by suppressing immune and stromal cell activation or indirectly through promoting clonal expansion of regulatory T cells. Importantly, in a non-human primate model of myocardial infarction, iCDC therapy also reduced cardiac fibrosis, improved cardiac perfusion and contractile function without inducing systemic toxicity. These findings establish lesion-targeted immune modulation as a feasible strategy to control cardiac fibrosis and identify engineered dendritic cells as a promising therapeutic platform for treating cardiac remodeling and heart failure.

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Capsule

Fueling antigen presentation

Cross-presentation of extracellular antigens by dendritic cells (DCs) is a specialized function critical for eliciting CD8 T cell responses against viral and tumor antigens**. Khouili** and colleagues found that mitochondrial complex I activity supports antigen endosomal escape and promotes efficient cross-presentation by conventional type 1 DCs. Complex I activity in these cells was also necessary for optimal cross-priming of CD8 T cell responses during viral infection and tumor challenge. Loss of complex I subunits disrupted DC redox homeostasis, but restoration of the NAD^+/NADH ratio was sufficient to rescue cross-presentation capacity. These findings identify mitochondrial redox metabolism as a key regulator of antigen cross-presentation in DCs.

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