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HEART FAILURE AND CARDIOMYOPATHIES

CLINICAL CASE

POEMS Syndrome Presenting as First-Time Heart Failure Exacerbation

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ABSTRACT

We highlight the case of a 40-year-old man who presented with heart failure exacerbation and was ultimately discovered to have POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes) syndrome. (JACC Case Rep. 2025;30:102790) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A previously healthy 40-year-old male presented to our institution with 4 months of progressive fatigue, leg weakness, and weight loss. On initial evaluation in the emergency department, he was hypertensive to the 160s/90s mm Hg despite being on multiple antihypertensive medications. He was reported to have decreased breath sounds bilaterally, peripheral edema, lower extremity weakness, and jugular venous distention. Further workup revealed elevated N-terminal pro-B-type natriuretic peptide (3,126 pg/mL) and transthoracic echocardiography (TTE) showed a moderate circumferential pericardial effusion with mildly reduced left ventricular ejection fraction of 47% (**Figure 1**). Grade 3/3 diastolic dysfunction was present with E/A 1.80 (normal 0.8-2.4), medial E/e′ 18.0, and deceleration time of 124 ms with reduced global longitudinal strain and relative apical sparing pattern suggestive of an infiltrative vs hypertensive pattern (**Figure 2**). The right ventricle was mildly enlarged, with an estimated right ventricular systolic pressure of 71 mm Hg. The inferior vena cava was small with normal inspiratory collapse without findings to suggest tamponade physiology. He was admitted to a cardiology service for further management of presumed heart failure exacerbation.

LEARNING OBJECTIVES

- To consider a broad differential for patients presenting with heart failure, particularly if multiple organ systems are involved.
- To recognize that diastolic and systolic function can be impacted in POEMS syndrome, even in the absence of cardiac amyloid deposition or VEGF elevation.

PAST MEDICAL HISTORY

The patient was being treated for hypothyroidism of unknown etiology in the months leading up to presentation. He carried no other formal diagnoses.

DIFFERENTIAL DIAGNOSIS

With minimal past medical history and progressive fatigue, weakness, weight loss, and clinical findings of volume overload, heart failure, nephrotic

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ABBREVIATIONS AND ACRONYMS

CT = computed tomography

MRI = magnetic resonance imaging

POEMS = polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes

TTE = transthoracic echocardiography

VEGF = vascular endothelial growth factor

syndrome, thyroid derangements, and malignancy were highest on our differential.

INVESTIGATIONS

Laboratory work on the patient's arrival to the cardiology service showed anemia, mild leukocytosis, and thrombocytosis. In addition, potassium was elevated (6.0 mmol/L) with normal sodium. Endocrine studies revealed decreased levels of active thyroid hormones, testosterone, cortisol, aldosterone, and renin activity. Computed tomographic (CT) chest angiography showed no pulmonary embolism, dissection, or significant coronary artery disease but did show numerous sclerotic bone lesions (Figure 3). Subsequently, Hematology was consulted, and a bone marrow biopsy revealed focal IgA lambda light chain-restricted plasma cells (<5%). Vascular endothelial growth factor (VEGF) level was obtained and was within normal limits. Biopsy of a T7 sclerotic lesion was unrevealing. In addition, fluorodeoxyglucose positron emission tomography-CT showed numerous non-fluorodeoxyglucose-avid sclerotic osseous lesions without other significant findings. Given relative apical sparing on TTE, cardiac magnetic resonance imaging (MRI) was subsequently performed and demonstrated normal myocardial nulling and absence of myocardial delayed enhancement (Figure 4). There was no myocardial or pericardial edema on qualitative assessment of T2-weighted edema-sensitive images. Left ventricular ejection fraction was 49%, and end-diastolic mass index was 90 g/m^2 (normal 35-71 g/m^2). Right ventricular ejection fraction was 48% with normal size and wall thickness. Similarly to what was seen on TTE, there was a moderate-to-large circumferential pericardial effusion without findings to suggest increased ventricular interdependence. T1 and T2 mapping was not performed. Abdominal fat pad biopsy showed no evidence of amyloid deposition. The patient underwent paracentesis and thoracentesis, with results consistent with a transudative process. Electromyography was performed because of leg weakness and showed polyradicular neuropathy with mixed demyelinating and axonal features.

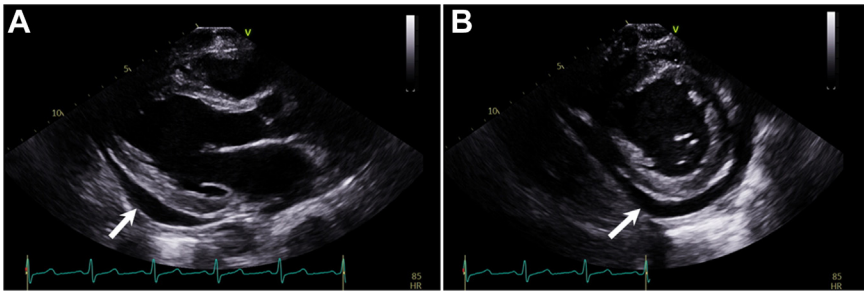
MANAGEMENT

Initial management included antihypertensive therapy, insulin, and potassium binders for his hyperkalemia, paracentesis, and thoracentesis. Despite significant peripheral edema, further diuresis was withheld owing to rapid volume depletion with initial diuresis and the small inferior vena cava with normal inspiratory collapse on TTE suggestive of low central venous pressure. He was hemodynamically stable, and his pericardial effusion did not demonstrate signs of tamponade so no pericardiocentesis was performed. After testing confirmed the diagnosis of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes) syndrome, he was transferred to the hematology service, where he received cyclophosphamide and high-dose prednisone. He improved significantly over the next 2 weeks and was discharged from the hospital. Several months later, the patient underwent melphalan induction followed by autologous stem cell transplant.

DISCUSSION

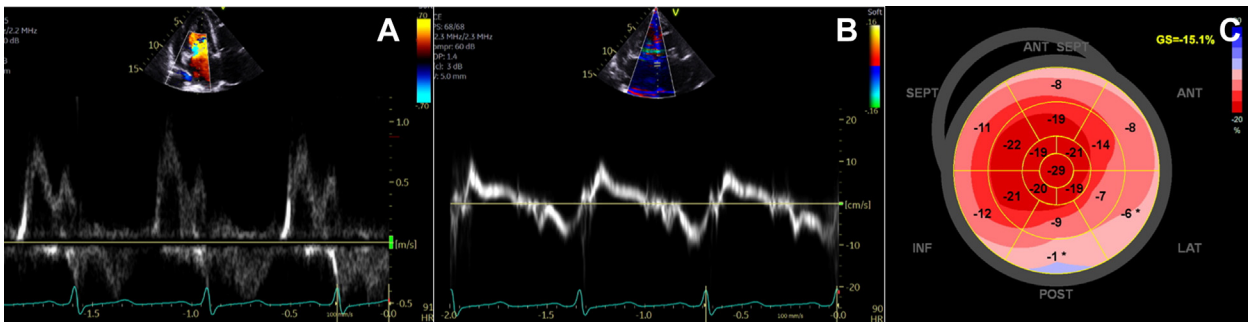
We present this uncommon case which, on first impression, appeared to be consistent with a

FIGURE 1 Transthoracic Echocardiogram on Presentation



Parasternal (A) long-axis and (B) short-axis views on transthoracic echocardiography demonstrate a moderate circumferential pericardial effusion (arrows).

FIGURE 2 **Further Characterization of Initial Transthoracic Echocardiogram**

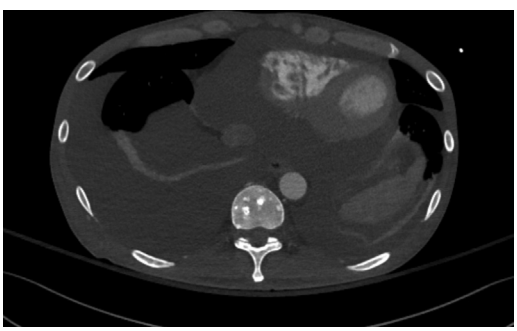


(A) Mitral valve inflow pulse-wave Doppler demonstrate an elevated E/A ratio of 1.8 with a short deceleration time of 124 ms. (B) There is also diminished mitral valve medial annular tissue Doppler velocity resulting in an elevated E/e′ ratio of 18. (C) Averaged global longitudinal strain is reduced at −15% with relative apical sparing pattern.

first-time heart failure exacerbation, possibly secondary to uncontrolled hypertension, but with further exploration proved to be part of a rare syndrome with multisystem involvement.

POEMS syndrome is a paraneoplastic syndrome secondary to underlying plasma cell neoplasm.[1] Epidemiologic data is limited owing to its rarity but one previous study estimated prevalence at 0.3 cases per 100,000 people.[2] To make the diagnosis of POEMS syndrome, 2 mandatory major criteria must be met, accompanied by at least 1 other major criterion and 1 minor criterion (**Table 1**). In this patient's case, he had evidence of polyneuropathy on electromyography and monoclonal plasma cell expansion on bone marrow biopsy, satisfying the mandatory major criteria. Sclerotic bone lesions on CT fulfilled an additional major criterion, and volume overload, endocrinopathy, and thrombocytosis fulfilled the minor criteria.

FIGURE 3 **CT Chest Angiogram**



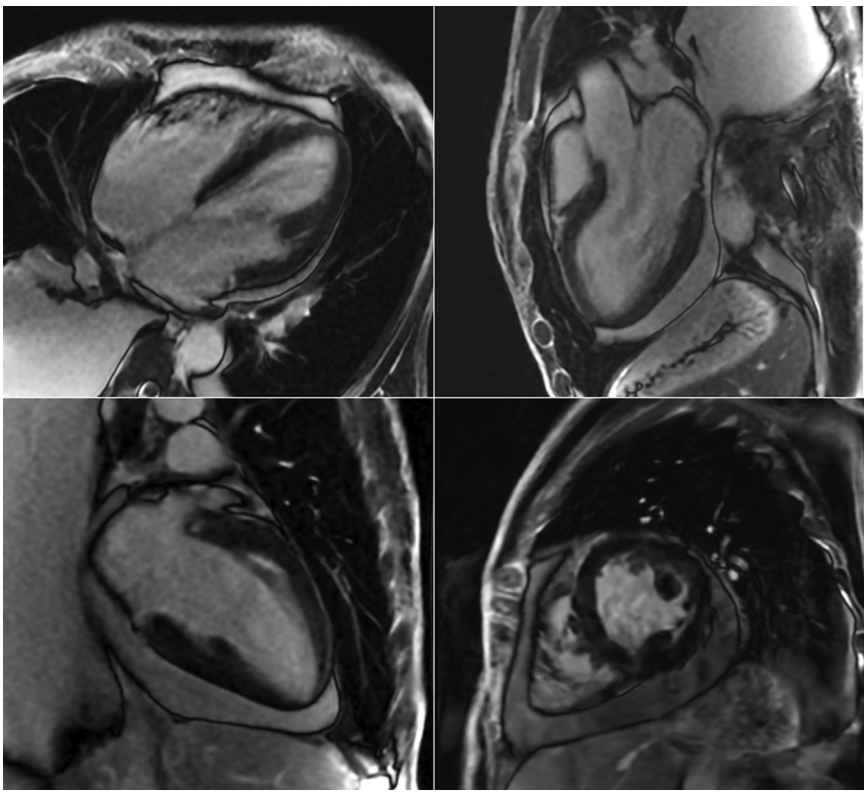
Computed tomographic scan of the chest demonstrates bilateral pleural effusions and multiple sclerotic osseous lesions, as can be visualized involving the T12 vertebral body.

Heart failure is a rare finding in patients with POEMS syndrome. A previous review identified 3 instances of heart failure among 99 patients with POEMS syndrome.[3] It is not known precisely how POEMS syndrome leads to heart failure, but one hypothesis is that an elevated VEGF level may contribute to or mimic heart failure owing to increased vascular permeability and extravascular fluid accumulation.[4,5] Notably, the VEGF level of our patient was within normal limits. Another possibility is light chain amyloid deposition in cardiac muscle tissue leading to diastolic dysfunction.[6,7] Although no cardiac biopsy was performed in our case, cardiac MRI did not show any evidence of an infiltrative process (**Figure 4**).

The absence of either elevated VEGF or infiltrative process on cardiac MRI led us to wonder what else may have contributed to his heart failure. It is well documented that effusions—both pleural and pericardial—can lead to significant diastolic dysfunction,[8] and his TTE on presentation did show severely impaired diastolic function with increased filling pressures. Thus, we could reasonably attribute his diastolic heart failure at least in part to these fluid collections. Poorly controlled hypertension likely played a major role in his presentation, particularly with the apical sparing that was seen on global longitudinal strain imaging. It is possible that hypertensive cardiomyopathy also may have contributed to the mildly reduced ejection fraction.

Another explanation that we considered is his laboratory-proved hypothyroidism, adrenal

FIGURE 4 Cardiac MRI



Cardiac magnetic resonance imaging again demonstrates the moderately sized pericardial effusion and lack of myocardial delayed enhancement.

TABLE 1 Criteria for Diagnosis of POEMS Syndrome

Mandatory major criteria	1. Polyneuropathy (typically demyelinating)
	2. Monoclonal plasma cell-proliferative disorder (almost always lambda)
Other major criteria (1 required)	3. Castleman disease
	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, pituitary, gonadal, parathyroid, pancreatic)
	9. Skin changes (hyperpigmentation, hyperkeratosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, white nails)
	10. Papilledema
	11. Thrombocytopenia/polycythemia
Other symptoms and signs	Clubbing, weight loss, hyperhidrosis, pulmonary hypertension/restrictive lung disease, thrombotic diatheses, diarrhea, low vitamin B12 values

insufficiency, hypoaldosteronism, and low renin activity. In previous non-POEMS-related studies, both hypothyroidism and adrenal insufficiency have been highlighted as possible factors leading to reduction in left ventricular systolic function.[9,10]

FOLLOW-UP

The patient underwent repeated TTE 4 months after discharge from the hospital. This showed slightly improved left ventricular ejection fraction of 54%, grade 1/3 diastolic dysfunction, and an estimated right ventricular systolic pressure of 31 mm Hg. His pericardial effusion had resolved, as had his pleural effusions and ascites. He achieved successful engraftment after his stem cell transplant. He continued to have hypertension, which is being managed with felodipine and carvedilol, but was able to discontinue his thyroid and adrenal replacement medications. He is reportedly back to 80% to 90% of

his original baseline and has been able to resume his favorite activity, hiking, without issue.

CONCLUSIONS

Cases of POEMS syndrome are exceedingly rare, and it is uncommon that it presents with heart failure. Heart failure in previous cases has been linked to cardiac amyloid deposition or VEGF-mediated mechanisms. Through this case, we highlight that heart failure can be present even in the absence of cardiac amyloidosis or VEGF elevation. We postulate that his presentation was mostly driven by poorly controlled hypertension with pleural and pericardial effusions contributing further to his diastolic impairment. The underlying endocrinopathy also may have played a role in his presentation. Furthermore, this case highlights that with prompt identification and treatment of the underlying POEMS syndrome, both systolic and diastolic dysfunction can markedly improve within months of treatment initiation.

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