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CASE REPORT
Cardiac imaging

POEMS syndrome causing left ventricular hypertrophy, myocardial dysfunction, and pericardial effusion: a case report

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Background POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes) is a paraneoplastic syndrome caused by a plasma cell proliferative disorder. Characteristics of POEMS syndrome include elevated pro-inflammatory and angiogenic cytokine levels that lead to multi-organ dysfunction. Patients have a variety of initial symptoms, but cardiac involvement is not common.

Case summary We report a case of a 31-year-old Chinese woman with chief complaints of chest pain and dyspnoea who was diagnosed with POEMS syndrome. The cardiovascular system in the case study patient was characterized by pericardial effusion, enlarged left atria, abnormal myocardial segmental deformation, left ventricular hypertrophy, pulmonary hypertension, and increased glucose metabolism in the left and right ventricular myocardium. The pericardial effusion diminished, while cardiac function, left ventricular wall thickness, and pulmonary hypertension gradually returned to normal with dexamethasone and bortezomib treatment.

Discussion This case suggests that cardiovascular system damage may be related to systemic diseases. Cardiovascular system damage caused by POEMS syndrome is recoverable after chemotherapy treatment. Echocardiography readily visualizes the changes in the heart of a patient with POEMS syndrome, clearly reflecting the changes in the structure and function of the heart before and after treatment.

Keywords POEMS syndrome • Pericardial effusion • Myocardial hypertrophy • Cardiac • Case report

ESC Curriculum 2.2 Echocardiography • 2.1 Imaging modalities

Learning points

- Cardiovascular system damage may be related to systemic diseases.
- POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes) is a paraneoplastic syndrome that leads to multi-organ dysfunction, although cardiac involvement is not common.
- Appropriate chemotherapy can recover the cardiovascular system damage caused by POEMS syndrome.

Introduction

POEMS syndrome is a rare disease associated with plasma cell dyscrasia IgA or lambda-restricted IgG, which have been confirmed to be related to elevated pro-inflammatory cytokine levels.[1,2] The diagnosis of POEMS syndrome is made based on a combination of the following conditions: polyneuropathy, sclerotic bone lesions, castleman's disease, organomegaly, endocrinopathy, elevated M-protein level, skin changes, and elevated vascular endothelial growth factor (VEGF) level.[3] Pulmonary hypertension is more common in patients

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with POEMS syndrome, and studies have shown that about 25–30% of patients have it.[4] Multiple organ involvement is also characteristic of this disorder, although cardiac involvement is rare. Treatment options include autologous stem cell transplantation, radiotherapy, chemotherapy, corticosteroids, and therapies targeting VEGF.[1] Bortezomib is a proteosome inhibitor, which can be used as one of the chemotherapy drugs for induction therapy of POEMS syndrome. We report a case of cardiovascular system damage caused by POEMS syndrome that was successfully treated with dexamethasone and bortezomib.

Timeline

Time	Events
12 months before	Patient developed oedema of her lower limbs.
Day 0	Upon admission, patient presented with obvious chest pain and dyspnoea.
Day 1	Transthoracic echocardiography showed pericardial effusion, enlarged left atria, abnormal myocardial segmental deformation, left ventricular hypertrophy, and pulmonary hypertension.
Day 10	Impression: POEMS syndrome diagnosed at clinic based on: polyneuropathy, monoclonal plasmaproliferative disorder, sclerotic bone lesions, elevated vascular endothelial growth factor (VEGF), organomegaly, oedema, endocrinopathy, and skin changes.
	Treatment: Bortezomib, dexamethasone, and diuretics
Day 18	Patient is discharged
One-month follow-up	Patient's cardiac function had markedly improved, body weight had decreased by 10 kg, and oedema was obviously decreased.
Three-month follow-up	Echocardiography showed that the pericardial effusion was diminished, while cardiac function, left ventricular wall thickness, and systolic pulmonary artery pressure gradually returned to normal. Serum VEGF was significantly decreased, accompanied by the marked recovery of impaired nerve conduction. Serum and urinary light chain and M-protein levels became negative.

Case presentation

A 31-year-old Chinese woman was admitted to hospital with obvious chest pain and dyspnoea. She had developed oedema of the lower limbs 1 year before admission. She had no history of hypercholesterolaemia, hypertension, coronary heart disease, alcohol consumption, or drug abuse, and her family history was unremarkable. Physical examination revealed skin hyperpigmentation and minimal oedema of the lower extremity. Electrocardiography showed sinus tachycardia, ventricular premature beat, and left deviation of the electrocardiogram axis (*Figure 1*). Transthoracic echocardiography revealed a moderate amount of pericardial effusion, enlarged left atria, pulmonary hypertension (systolic pulmonary artery pressure of ~46 mmHg), thickness of the left ventricle of 1.3 cm, hypokinesis of the left ventricular posterior wall, decreased left ventricular diastolic function (*Videos 1–3*), and global longitudinal strain of 12.3% (*Figures 2A and 3A*; *Table 1*). The patient received intravenous diuretics and underwent pericardial effusion drainage. Coronary computed tomographic angiography excluded coronary artery disease. Computed tomography of the chest and abdomen revealed bilateral pleural effusion accompanied by bilateral inferior pulmonary atelectasis, pericardial effusion, bilateral axillary, and slightly enlarged mediastinal lymph nodes (*Figure 4A*), hepatosplenomegaly, ascites, and spinal segmental degeneration (*Figure 4B*). Positron emission tomography–computed tomography (PET-CT) revealed increased left ventricular radioactivity uptake (SUVmax: 20.8), increased right ventricular radioactivity uptake (SUVmax: 7.45), increased glucose metabolism in enlarged axillary lymph nodes (SUVmax: 1.32), splenomegaly with increased glucose metabolism (SUVmax: 1.52), pericardial effusion, ascites, and pleural effusion (*Figure 5*). The patient had no neurological symptoms, although electromyography suggested polyneuropathy.

Laboratory tests revealed that N-terminal-pro B-type natriuretic peptide concentrations were markedly elevated to 9841 pg/mL (normally <300 pg/mL). Serum cardiac troponin T levels were within normal limits. Infection, tuberculosis, and malignancy were excluded by biochemical and cytological analysis of pericardial effusion. Blood coagulation tests showed increased plasma D-dimer level and increased activated partial thromboplastin time. A routine urine exam showed a urine protein level of 2+. Furthermore, 24-h urinary protein quantitation result was 0.25 g (normally <0.15 g/24 h). The patient also had renal dysfunction. Serum immunofixation electrophoresis revealed increased production of M-protein. The increased production of M-protein may be related to immunoglobulin light-chain amyloidosis (AL) or POEMS syndrome. Further evaluation was performed to determine the aetiology of increased M-protein production. Serum and urinary light chain levels were increased, while serum autoimmune antibodies were negative. Endocrine tests confirmed hypothyroidism and increased prolactin value. Serum VEGF level was significantly increased (800 pg/mL, normal range: 0–142 pg/mL). Bone marrow and periumbilical adipose tissue biopsy results showed that bone marrow nucleated cell proliferation was active, with proliferation of collagen fibres in the dermis. The remainder of observations were unremarkable and crystal violet and Congo red staining results were negative. The final diagnosis of POEMS syndrome was made based on the combination of the following findings: polyneuropathy, plasmaproliferative disorder, elevated VEGF level, organomegaly, oedema,

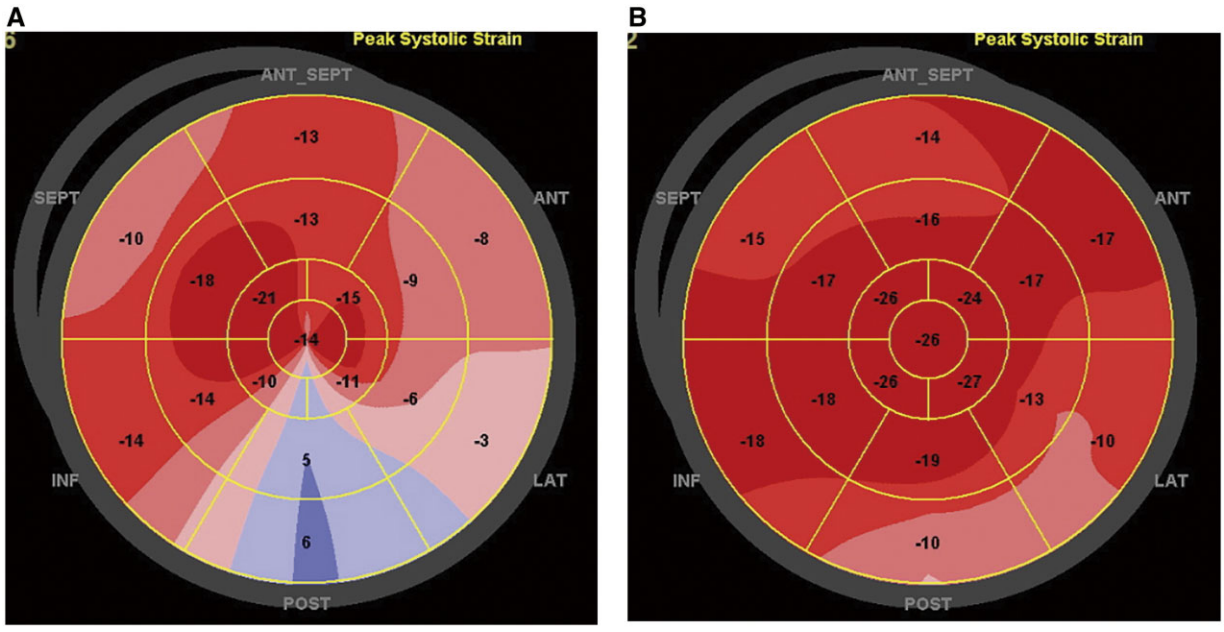


Figure 1 Electrocardiography showed sinus tachycardia, ventricular premature beat, and left deviation of the electrocardiogram axis.

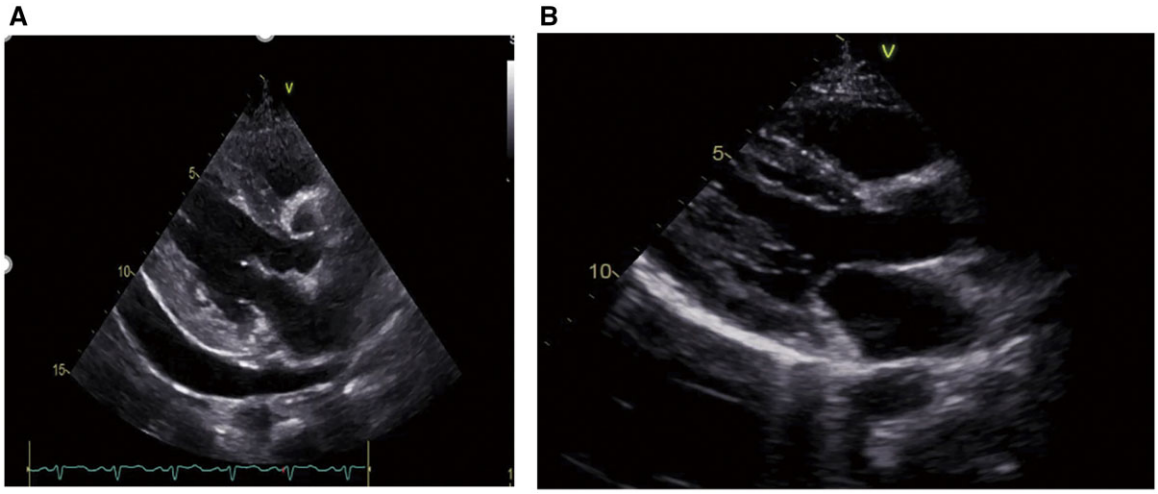


Figure 2 Bull's eye plots. (*A*) Global longitudinal strain (-12.3%) before treatment. (*B*) Global longitudinal strain (-19.1%) after treatment.

endocrinopathy, and skin changes. Pulmonary hypertension was thought to be secondary to POEMS syndrome. Upon obtaining written informed consent under the approval of the institutional review board, the patient was treated with bortezomib and dexamethasone.

Thirty days after the treatment, her cardiac function had markedly improved, her body weight had decreased by 10 kg, and oedema was obviously decreased. After 3 months, echocardiography showed no pericardial effusion. The thickness of the left ventricle was within normal limits and left ventricular systolic and diastolic function was significantly improved (Supplementary Videos 4–6). Global longitudinal strain of 19.1% was significantly higher than before (*Figures 2B and 3B*; *Table 1*). Serum VEGF was significantly decreased, accompanied by the marked recovery of impaired nerve conduction. Serum and urinary light chain and M-protein levels became negative.

Discussion

POEMS syndrome is a rare paraneoplastic syndrome, and its diagnostic criteria are based on the current Dispenzieri diagnosis. It needs to meet the mandatory major criteria (monoclonal plasma proliferative disorder, polyneuropathy), one of the other required major criteria

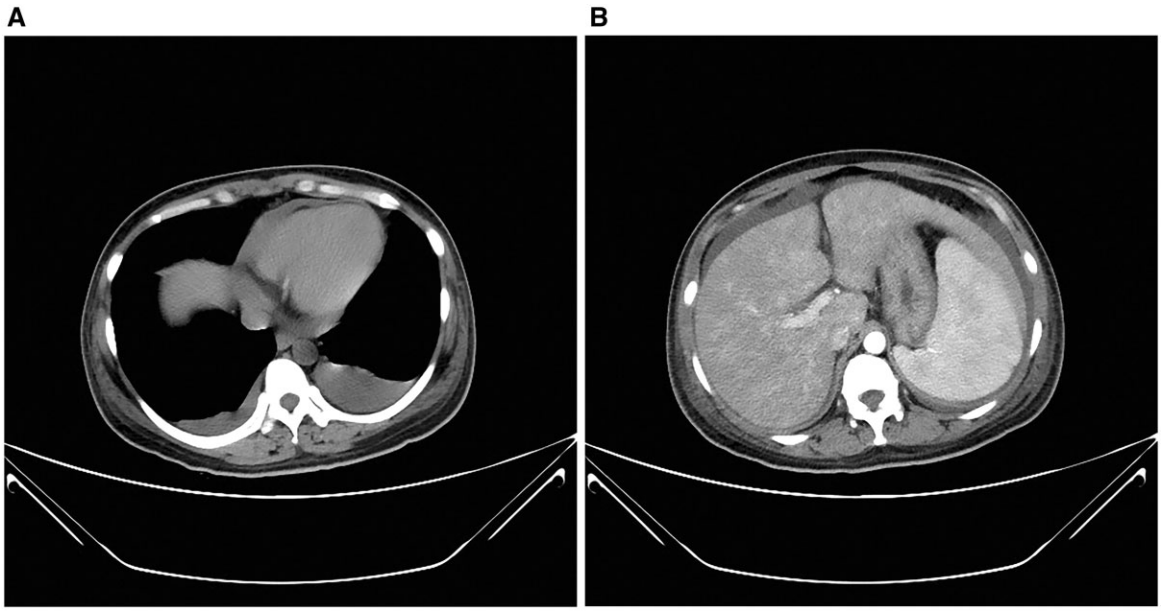


Figure 3 Echocardiography performed before and after dexamethasone and bortezomib therapy. (*A*) Echocardiography revealed left ventricular hypertrophy, a moderate amount of pericardial effusion and enlarged left atrial diameter from para-sternal long-axis view. (*B*) Echocardiography revealed normal myocardial thickness and the diameter of left atrium from para-sternal long-axis view.

Table 1 Echocardiographic characteristics of the patient before and after treatment

Characteristics	Before treatment	After treatment
LAA (cm^2)	21.5	15.3
EDV (mL)	96.3	84.3
ESV (mL)	46	29.6
LVEF (%)	52.2	64.9
IVSd (mm)	13	9.0
LVPWd (mm)	13	9.0
LVd mass index (g/m^2)	181.6	97.5
FAC (%)	39	45
TAPSE (mm)	19.2	23
E/*E*′	14	8.1
GLS-Avg	-12.3%	-19.1%
PASP (mmHg)	46	21

EDV, end-diastolic volume; ESV, end-systolic volume; FAC, fractional area changes; GLS-Avg, global longitudinal strain-average; IVSd, inter-ventricular septum thickness at end-diastole; LAA, left atrium area; LVEF, left ventricular ejection fraction; LVPWd, left ventricular posterior wall thickness at end-diastole; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid annular plane systolic excursion.

including sclerotic bone lesions, Castleman's disease, elevated VEGF, and one of the required minor criteria including organomegaly, oedema, endocrinopathy, skin changes, papilloedema, and thrombocytosis/polycythaemia.

The prevalence of abnormal myocardial segmental deformation and left ventricular hypertrophy in POEMS syndrome is estimated to be between 3% and 6%, A retrospective study found that out of 99 cases of POEMS syndrome, three cases were associated with changes in heart structure and function at presentation.[5] The cardiovascular system in the case study patient was characterized by pericardial effusion, enlarged left atria, abnormal myocardial segmental deformation, left ventricular hypertrophy, pulmonary hypertension, and increased glucose metabolism in the left and right ventricular myocardium. We considered that changes in the heart structure and function were POEMS syndrome-related because the patient had no coronary artery stenosis and no history of cardiomyopathy or hypertension.

Takahashi *et al.*[6] have reported that the changes in cardiac extracellular oedema were visualized using 3 T magnetic resonance imaging in POEMS syndrome. Although the precise mechanisms causing excessive VEGF production and consequent cardiac extracellular oedema in patients with POEMS syndrome remain to be elucidated, we suspect that extracellular oedema is the cause of left ventricular hypertrophy.[7] The elevated VEGF level was responsible for coronary microvascular hyperpermeability, which may cause acute myocardial segmental deformation dysfunction.[5] Clinical improvement in most patients with POEMS syndrome is accompanied by a significant decrease in serum VEGF level.[8] In this case, myocardial hypertrophy was accompanied by hypokinesis of the left ventricular posterior wall, which may indicate acute microcirculation disturbance. Serum cardiac troponin T levels were within normal limits, which indicate that cardiac extracellular oedema does not cause cardiomyocyte death.

Both AL amyloidosis and POEMS syndrome are associated with an underlying plasma cell proliferative disorder. They can lead to elevated serum M-protein level and cause ventricular hypertrophy. AL amyloidosis is an acquired disease caused by the deposition of

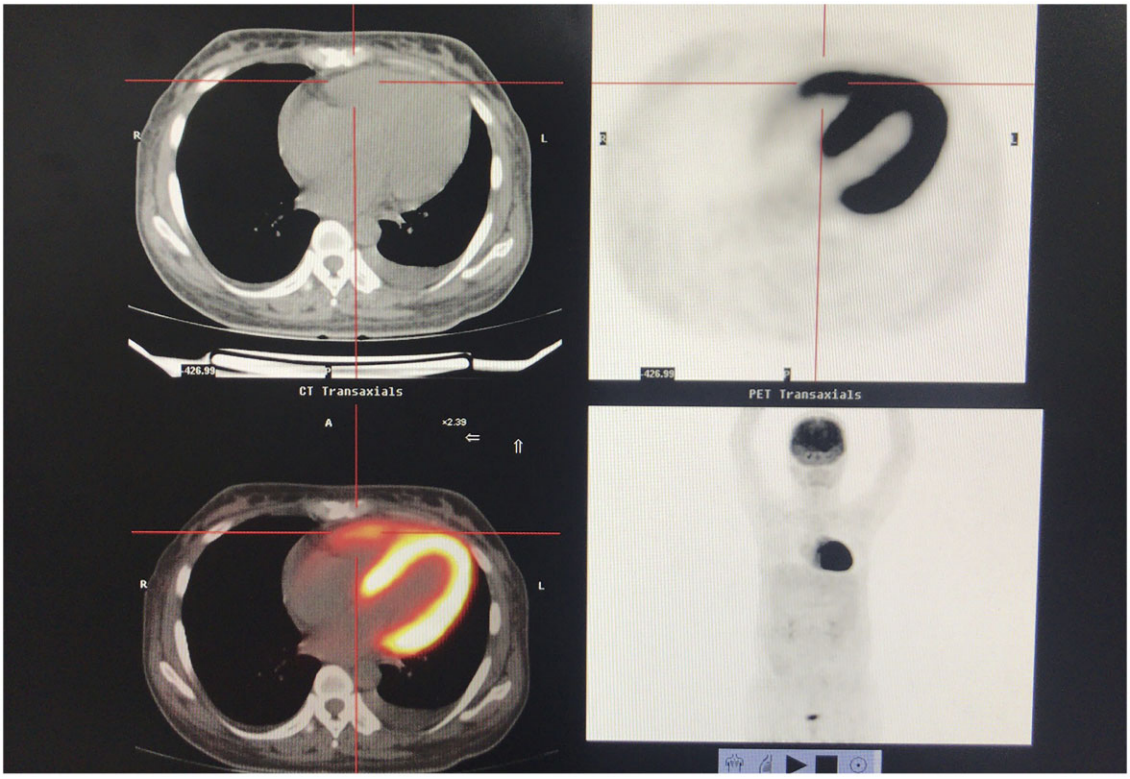


Figure 4 (*A*) Computed tomography of the chest revealed bilateral pleural effusion accompanied by bilateral inferior pulmonary atelectasis, pericardial effusion. (*B*) Computed tomography of the abdomen revealed hepatosplenomegaly and ascites.

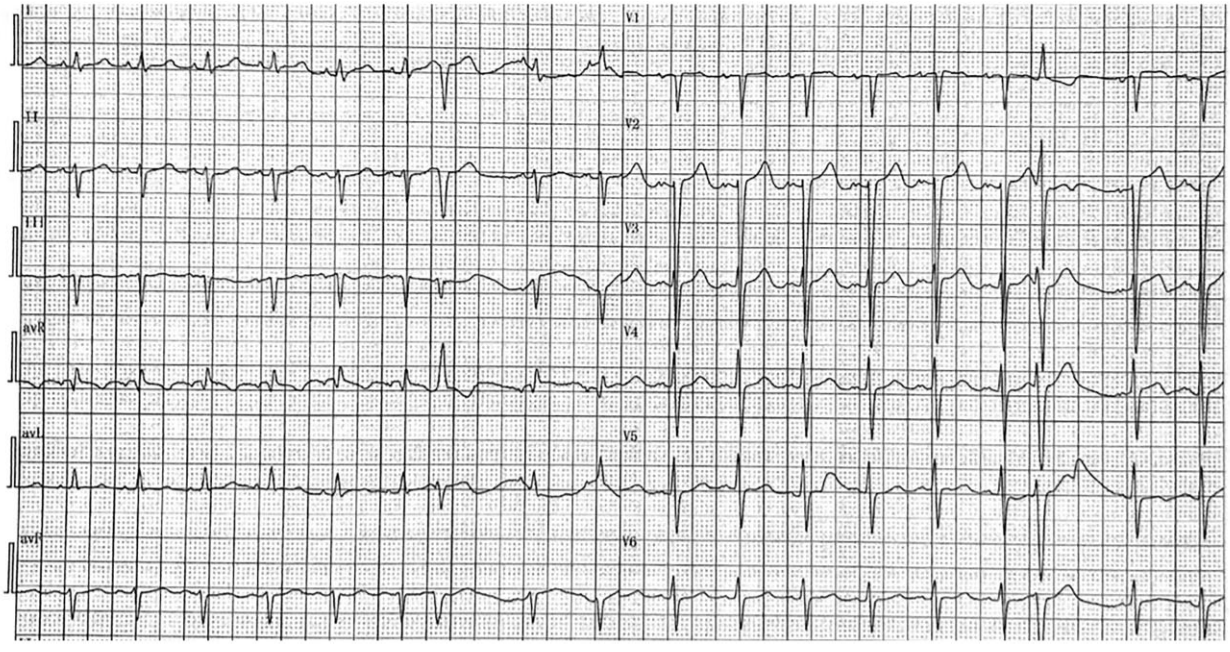
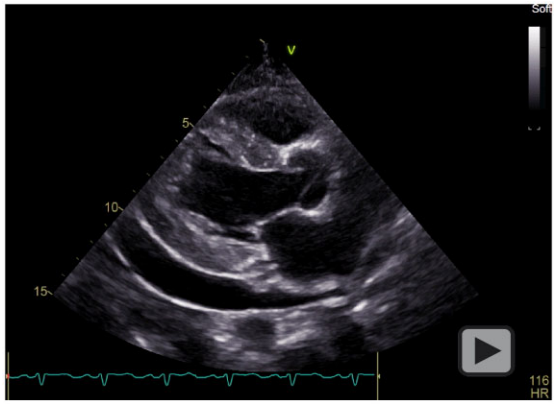
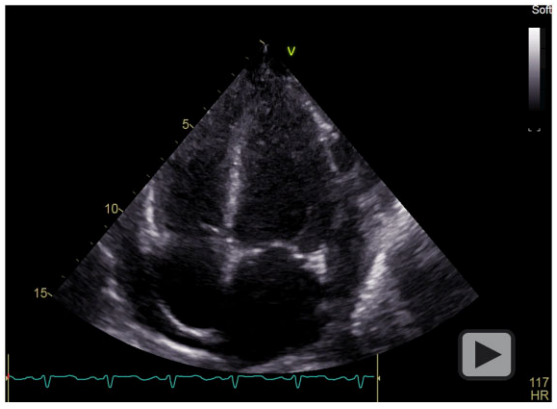


Figure 5 Positron emission tomography–computed tomography: increased left ventricular radioactivity uptake (SUVmax: 20.8) and increased right ventricular radioactivity uptake (SUVmax: 7.45).



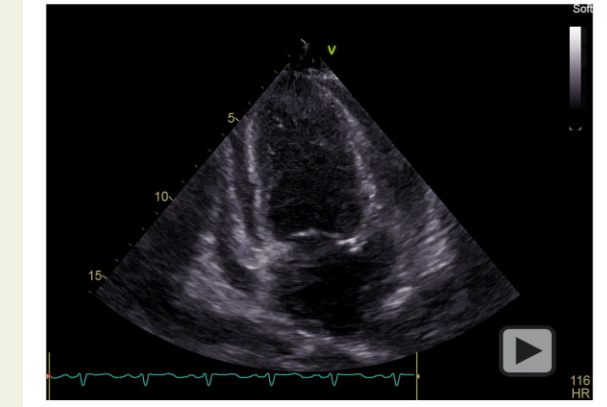
Video 1 Transthoracic echocardiography-parasternal long-axis view: ventricular hypertrophy, a moderate amount of pericardial effusion, enlarged left atria diameter and hypokinesis of the left ventricular posterior wall before dexamethasone and bortezomib therapy.



Video 2 Transthoracic echocardiography-apical four-chamber view: ventricular hypertrophy, a moderate amount of pericardial effusion and enlarged left atria diameter before dexamethasone and bortezomib therapy.

immunoglobulin light chains produced by plasma cells in the tissues. Congo red staining demonstrated amyloid deposition. However, POEMS syndrome is not an immunoglobulin deposition disease.[9] Prognosis is poor for patients with cardiac AL amyloidosis. However, appropriate chemotherapy treatment can result in a good prognosis for POEMS patients with heart involvement. Inoue *et al.*[5] study of the cardiac biopsy in patients with POEMS syndrome showed that it was non-specific damage to the myocardium rather than myocarditis, AL amyloidosis, sarcoidosis, and cardiomyopathy. Appropriate radiographic evaluation, detection of VEGF, and detailed neurological examination help to distinguish POEMS syndrome from other conditions like AL amyloidosis, sarcoidosis, and cardiomyopathy.

This case report is limited by our inability to provide cardiac magnetic resonance results because there were metal foreign bodies in the patient's body. Nevertheless, this case describes the clinical features, echocardiography results, and PET-CT features of POEMS syndrome. Positron emission tomography–computed tomography confirmed myocardial glucose metabolism in patients with POEMS syndrome was increased. Whether the increased myocardial glucose metabolism is related to myocardial extracellular oedema has yet to be elucidated. To the best of our knowledge, this is the first case of evaluating myocardial metabolism in a patient with POEMS syndrome using PET-CT. Cardiovascular system damage caused by POEMS syndrome is recoverable. Echocardiography readily visualizes the changes in the heart of a patient with POEMS syndrome, clearly reflecting the changes in the structure and function of the heart before and after treatment.



Video 3 Transthoracic echocardiography-apical two -chamber view: ventricular hypertrophy, a moderate amount of pericardial effusion and enlarged left atria diameter before dexamethasone and bortezomib therapy.

Lead author biography

Shanshan Wang (MD) is a fellow cardiologist and an echocardiographer at the Second Affiliated Hospital of Soochow University.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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