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CASE REPORT
Heart failure

A novel case report of isolated cardiac myxedematosus

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Background Cardiac mucinous deposits are a rare entity only previously described in the setting of scleromyxedema, a disorder characterized by cutaneous and systemic mucin deposits, fibroblastic proliferation, and monoclonal gammopathies.

Case summary A 41-year-old woman was transferred to our hospital after a month-long hospitalization with worsening cardiogenic shock requiring ionotropic support. Cardiac magnetic resonance imaging revealed a left ventricular ejection fraction of 23%, prior right coronary artery infarct, full-thickness late gadolinium enhancement in the left ventricle basilar wall, global abnormal parametric mapping parameters of both native T1, T2, and extracellular volume, and severe biventricular dysfunction concerning for infiltrative cardiomyopathy. Endomyocardial biopsy demonstrated heavy deposits of interstitial mucin, confirmed by electron microscopy; a Congo red stain was negative for amyloid. She was treated with an aggressive decongestive strategy, oral guideline-directed medical therapy, and intravenous immunoglobulin (IVIg); she was discharged home off inotropic support. Subsequently, she had three additional hospitalizations for heart failure exacerbation in a span of 6 months, and her overall prognosis remains guarded.

Discussion We report a first known case of isolated cardiac myxedematosus associated with a severe systolic and diastolic cardiomyopathy. Our patient did not have any clinical evidence of systemic scleromyxedema or paraproteinemia, both of which have been reported in association with cardiac mucin deposits. Mucinosus has been described in patients with systemic lupus erythematous; however, cardiac deposits have not been reported. While IVIg has been used as a treatment in previously reported cases of cardiac scleromyxedema, its clinical benefit remains unclear in isolated cardiac myxedematosus.

Keywords Scleromyxedema • Cardiac mucin • Endomyocardial biopsy • Case report

ESC curriculum 2.3 Cardiac magnetic resonance • 6.2 Heart failure with reduced ejection fraction • 6.5 Cardiomyopathy • 7.3 Critically ill cardiac patient

Learning points

- Mucinous cardiac deposits are a rare entity described previously only in the setting of systemic scleromyxedema or paraproteinemia. However, isolated cardiac myxedematosus can occur as seen in our patient.
- Cardiac mucinosus is poorly understood, and without clear treatment, guidance portends a poor prognosis.
- Endomyocardial biopsy can be of high clinical utility and should be considered in cases of refractory cardiogenic shock.

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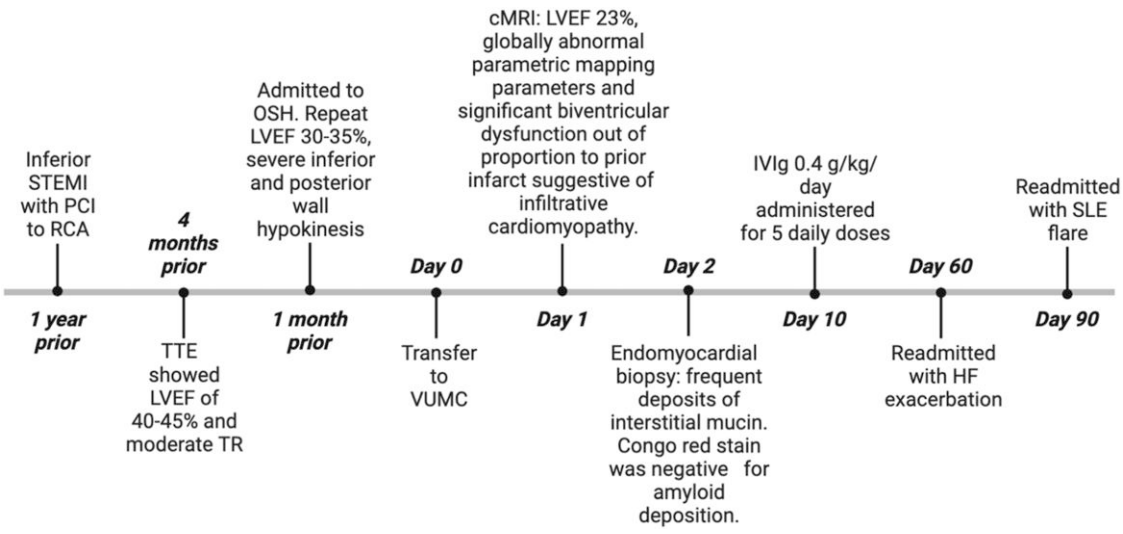
Introduction

Mucinous cardiac deposition is a rarely reported phenomenon, only previously described in the setting of systemic scleromyxedema. Scleromyxedema is a rare mucinous dermatologic condition characterized by cutaneous mucin deposits and fibroblastic proliferation.[1] The pathogenesis is poorly understood but has clinical overlap with scleroderma and scleredema. Systemic mucinous infiltration can involve various organs, including the heart, kidney, lungs, pancreas, and adrenal glands.[1] To date, only a few cases of cardiomyopathy associated with infiltrative cardiac scleromyxedema have been reported.[2–5] In all of these cases, the presentation was accompanied by dermatologic findings consistent with scleromyxedema or systemic paraproteinemia. Herein, we present a case of a 41-year-old woman with isolated cardiac myxedematosus without dermatologic or systemic manifestations of scleromyxedema or paraproteinemia. To our knowledge, this is the first reported case of an isolated cardiac myxedematosus.

Summary figure



Case presentation

A 41-year-old woman with insulin-dependent type 2 diabetes, hypertension, dyslipidaemia, and tobacco use was transferred to our hospital with worsening cardiogenic shock on ionotropic support. She had an inferior ST elevation myocardial infarction (STEMI) ~1 year earlier and received percutaneous coronary intervention (PCI) to the right coronary artery (RCA) at that time. Transthoracic echocardiogram (TTE) that was performed 3 months prior to her incident hospitalization at an outside hospital showed a left ventricular ejection fraction (LVEF) of 40–45% with moderate concentric left ventricular hypertrophy. She was admitted to an outside facility 5 weeks prior to the transfer with worsening dyspnoea on exertion, lower extremity oedema, paroxysmal nocturnal dyspnoea, pre-syncope, and weakness. Initial workup at the outside hospital demonstrated a N-terminal pro-brain natriuretic peptide (NT-proBNP) of 40 201, high-sensitivity troponin of 357 (upper limit of normal 14), and non-specific electrocardiogram changes. Repeat TTE done at the outside facility showed worsening LVEF of 30–35% with severe inferior and posterior wall hypokinesis. Intravenous (IV) diuresis was performed with bumetanide, and she was empirically started on milrinone for ionotropic support. Days later when the milrinone was attempted to be weaned off, worsening renal function (creatinine of 2.04 mg/dL) and lactic acidosis (4.7 mmol/L) were encountered. Subsequent right heart catheterization (RHC) off milrinone showed an estimated Fick cardiac output and index of 2.71 and 1.69, respectively. Therefore, the ionotropic support was re-instituted with dobutamine. Due to worsening renal failure and development of nephrotic range proteinuria, she underwent autoimmune workup, which revealed positive anti-nuclear antibody (>1:1280), anti-nuclear ribonucleoprotein, smith immunoglobulin G (IgG), and double-stranded DNA (>1000). Additional workup included normal thyroid-stimulating hormone, negative anti-neutrophilic cytoplasmic antibody, negative beta-2 glycoprotein IgG/IgM, low complement component 3 (48 mg/dL, lower limit 79), normal complement component 4, negative phospholipid IgG, negative rheumatoid factor and cyclic citrullinated peptide, high ferritin level of 3600 ng/mL, and a positive direct anti-globulin test IgG. Serum protein electrophoresis was negative for monoclonal proteins. She was newly diagnosed with systemic lupus erythematosus (SLE), and on Day 20 of admission, she was started on hydroxychloroquine. Four days later, she then underwent a renal biopsy, which demonstrated diffuse acute tubular injury, tubular basement membrane immune complex deposits, and mild arteriolonephrosclerosis consistent with a diagnosis of lupus nephritis. Given her need of inotropic support, she was transferred to our facility for a higher level of care, including for a potential workup for advanced heart failure therapies.

Initial vitals at our hospital showed temperature of 99.4°F, pulse 112, blood pressure 127/84, and respiratory rate 27. Exam was notable for jugular venous distention to the ear, an S3 heart sound, distended abdomen, 2 + lower extremity oedema, and normal skin findings. Decongestion attempts were continued with IV bumetanide. Repeat TTE at our facility demonstrated aneurysmal formation of the basal inferior wall, thinning and dyskinesia of the basal inferoseptal wall, LVEF of 30–35%, elevated filling pressures, and moderately dilated right venticle (RV) with moderate to severely reduced function (see Supplementary material online). Cardiac magnetic resonance imaging (MRI) was

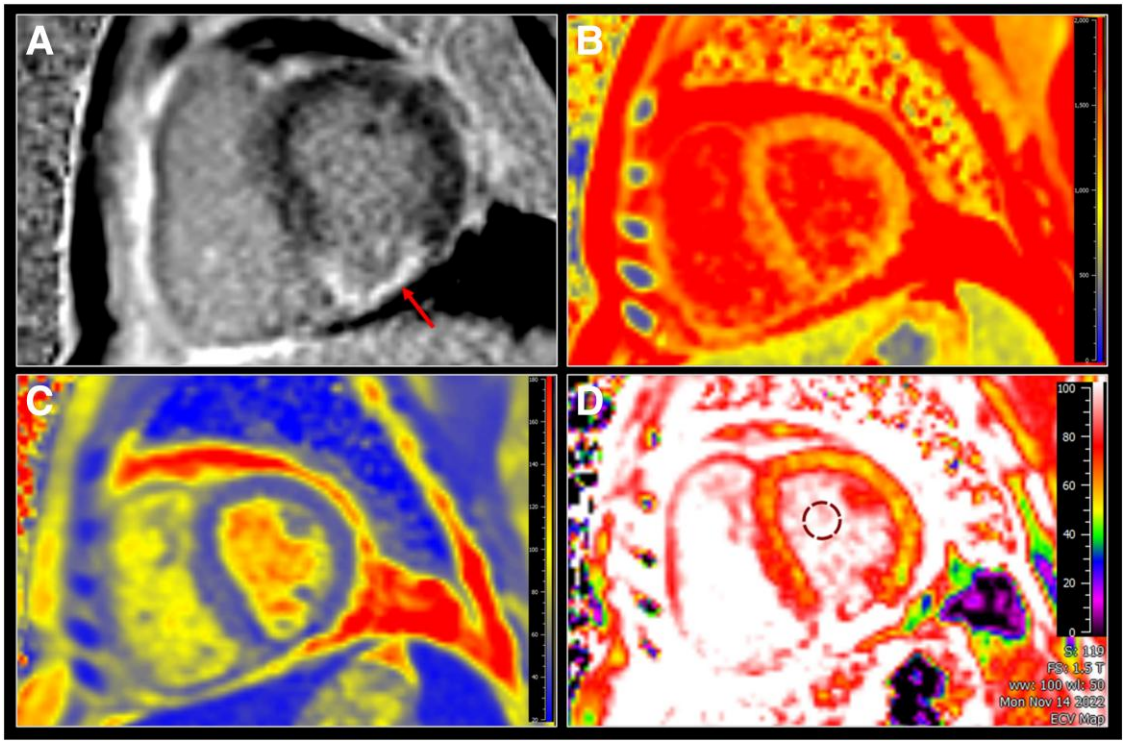


Figure 1 Cardiac magnetic resonance imaging with transmural inferior basal late gadolinium enhancement and abnormal mapping parameters on T1, T2, and extracellular volume imaging. (*A*) Full-thickness late gadolinium enhancement in the left ventricular inferoseptal and inferior basal wall (corresponding to segments 3, 4, 9, and 10), as designated by the arrow. (*B*) Globally abnormal native T1 imaging (1330–1430 ms, normal 940–1030 ms). (*C*) Globally abnormal native T2 imaging (56 ms, normal 40–50 ms). (*D*) ECV elevation of 55%, normal <31%.

performed to evaluate non-ischaemic aetiologies contributing to her presentation, which revealed LVEF of 23%, prior RCA infarct, full-thickness late gadolinium enhancement in the left ventricular inferoseptal and inferior basal wall (corresponding to segments 3, 4, 9, and 10), global abnormal parametric mapping parameters of both native T1 (1290 ms, normal 940–1030), T2 (56 ms, normal 40–50), and ECV (55%, normal <31%), and severe biventricular dysfunction concerning for infiltrative cardiomyopathy (*Figure 1* and see Supplementary material online). Two days later, she underwent right and left heart catheterization (LHC) with endomyocardial biopsy. Left heart catheterization revealed non-obstructive coronary artery disease and patent RCA stent (see Supplementary material online). Right heart catheterization showed severely elevated right-sided filling pressures (right atrial pressure of 16 mmHg, pulmonary capillary wedge pressure of 16 mmHg) with Fick cardiac output of 3.9 L/min and index of 2.2 L/min/m^2 on inotropic support. Endomyocardial biopsy revealed frequent deposits of interstitial mucin (*Figure 2*), later confirmed by electron microscopy; a Congo red stain was negative for amyloid deposition. There were no signs of active myocarditis or scarring to suggest prior episodes. A diagnosis of isolated cardiac myxedematosus was made.

She underwent aggressive decongestion, oral guideline-directed medical therapies were introduced, and she was gradually weaned off inotropic support based on stable vitals and end-organ function. The rheumatology team was consulted and recommended IV immunoglobulin (IVIg) based on published reports of scleromyxedema, recognizing the lack of data guiding the treatment of isolated cardiac myxedematosus. She received five daily doses of 0.4 g/kg/day of IVIg (740 g/day) and was discharged upon completion of this treatment. At discharge, her heart failure therapy included metoprolol succinate 12.5 mg daily, sacubitril–valsartan 49–51 mg twice a day, spironolactone 12.5 mg daily, empagliflozin 10 mg daily, and oral bumetanide 2 mg daily. She was given cyclophosphamide therapy for SLE by rheumatology in the outpatient setting. Unfortunately, she had three additional hospitalizations over the course of the next 6 months due to heart failure exacerbations and presumed lupus flares, and her overall prognosis remains guarded.

Discussion

The complexity in this patient's case herein lay in the aetiology of her mucinous cardiac deposits. She had a known diagnosis of SLE, which is known to cause endothelial damage, immune dysregulation, and pro-atherogenic state leading to accelerated coronary atherosclerosis, which, along with multiple other cardiovascular risk factors that she had, could have contributed to the STEMI event that she suffered at the age of 40.[6] Mucinosus is a well-described phenomenon of SLE; however, the isolated cardiac depositions have not been reported before. Instead, myocarditis is commonly seen in SLE patients, which is best detected with cardiac MRI. This patient's cardiac MRI suggested an infiltrative cardiomyopathy as opposed to myocarditis. Additionally, her endomyocardial biopsy did not show evidence of active myocarditis nor scarring to suggest prior episodes of myocarditis.

Scleromyxedema is a rare systemic fibromucinous condition commonly associated with monoclonal gammopathies, specifically, IgG lambda.[1,3] Systemic mucinous infiltration has been reported in the

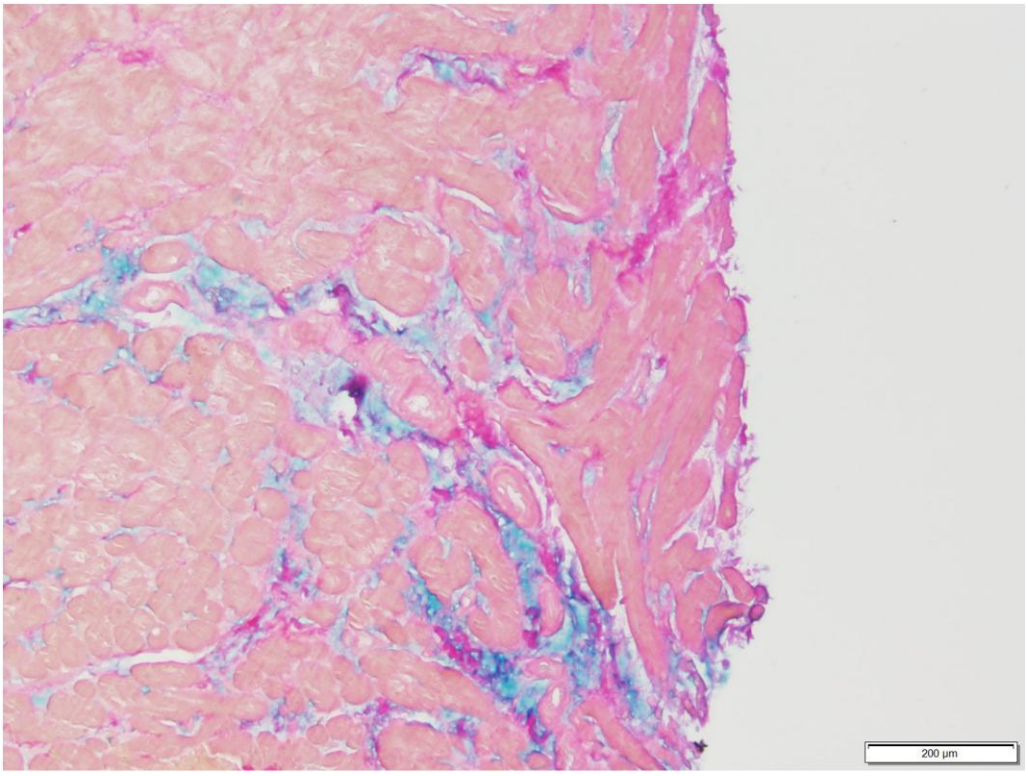
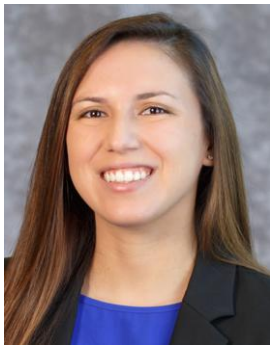


Figure 2 Endomyocardial biopsy with colloidal iron staining highlighting mucinous tissue.

lymphatic and neurologic systems, as well as the heart, kidney, lungs, pancreas, and adrenal glands, and occurs in upwards of 70% of patients.[1] Cardiac involvement specifically has been described in up to 20% of patients in case series reports.[7] In all reported cases, patients had evidence of dermatologic disease consistent with scleromyxedema, and a majority of patients had associated monoclonal gammopathy. Without evidence of classic dermatologic findings or paraproteinemia, and with the absence of mucinosus on kidney biopsy, we did not believe she met the clinical criteria for systemic scleromyxedema. The absence of the cutaneous manifestation of scleromyxedema and the lack of paraproteinemia further refute their involvement as potential sources of mucinosus. Instead, we hypothesize that the isolated cardiac mucinous deposits were of a different immunological phenomenon, aetiology of which is poorly understood. Similar to the reported cases of scleromyxedema cardiomyopathy, the prognosis of these patients remains guarded, which emphasizes the need of further research to understand the pathophysiology and specific treatment.

An additional clinical question lies in the predominant contributor to her worsening cardiomyopathy. While she had known RCA infarction, her LHC did not reveal new coronary artery disease and TTE and cardiac MRI demonstrated global LV dysfunction, not consistent with her prior infarct. Additionally, while SLE can have cardiac manifestations, she had no imaging or pathologic evidence of current or prior myocarditis. This patient's clinical picture would suggest against focal RCA disease or typical SLE cardiac involvement as the main exacerbating factors to her presentation. While the mucinous deposits found on her endomyocardial biopsy were hypothesized to contribute to her presentation, a causal association between the two cannot be made on these findings alone, particularly with no additional cases to compare to. This case exemplifies the clinical importance of endomyocardial biopsy in refractory and unexplained cases of cardiogenic shock. Additionally, the collaboration of a multi-disciplinary team including cardiology, pathology, and rheumatology allowed for a brisk diagnosis and coordinated management plan. However, due to the lack of data to explain the pathophysiology and treatment, the prognosis of these patients remains poor.

Lead author biography



Brittany Saldivar Murphy is a cardiology fellow at Vanderbilt University Medical Center. She completed her medical school at the University of Florida and Internal Medicine Residency at Vanderbilt University Medical Center.

Supplementary material

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

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Data availability

The data used in preparation of this manuscript will be shared upon reasonable request to the corresponding author.

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