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Case Report

Diffuse Cutaneous Systemic Sclerosis Complicated by Serum Amyloid A Protein Cardiac Amyloidosis and Cardiogenic Shock

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Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by progressive fibrosis of the skin and internal organs. The leading causes of death in patients with systemic sclerosis include interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), cardiac complications (such as heart failure, arrhythmias, and myocardial fibrosis), and renal crisis. AA amyloidosis is a rare form of amyloidosis, secondary to the accumulation of serum amyloid A (SAA) protein due to chronic inflammatory or infectious diseases, with cardiac involvement occurring in approximately 2% of cases. Here, we present the case of a 65-year-old female patient with AA amyloidosis secondary to systemic sclerosis, complicated by cardiogenic shock. To our knowledge, this case is the first one confirmed through endomyocardial biopsy (EMB). Rapid recognition of the condition through clinical, noninvasive, and invasive evaluation, together with aggressive immunosuppressive and immunomodulatory treatment. is crucial to determine prognosis.

A 65-year-old female patient with a history of permanent atrial fibrillation (AF), and Raynaud's phenomenon that began approximately 2 years prior, presented to the emergency department with progressively worsening dyspnea, epigastric pain, and fatigue. Her heart rate was 120 beats per minute; her blood pressure was 85/50 mm Hg; her oxygen saturation of peripheral blood (SpO_2) was 96% on room air; and her respiratory rate was 30 breaths per minute. On physical examination, a systolic murmur was detected at the mesocardium, and breath sounds were absent in the mid-basal lung segments.

The electrocardiogram showed AF with a mean ventricular rate of 95 beats per minute, low-voltage QRS complexes, and QS complexes in almost all leads (Supplemental Fig. S1). Arterial blood gas analysis revealed the following: PH, 7.6; partial pressure of carbon dioxide (pCO_2), 40 mm Hg; partial pressure of oxygen (pO_2), 75 mm Hg; lactate, 2.1 mmol/L; potassium, 3.1 mEq/L; sodium, 132 mEq/L; and bicarbonate, 36.6 mEq/L.

Laboratory tests in the emergency department revealed reduced hemoglobin levels (9.5 g/dL), normal renal and

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Novel Teaching Points

- Early diagnosis of systemic chronic inflammatory diseases is fundamental to preventing rare but potentially fatal complications, such as AA systemic amyloidosis.
- cMRI is the best noninvasive imaging technique for early diagnosis and screening of cardiac involvement in inflammatory disease and has prognostic value also.
- Despite advances in multimodality imaging, EMB remains the diagnostic gold standard for conditions such as inflammatory cardiomyopathies and amyloidosis.

hepatic function, and elevated levels of high-sensitivity troponin I (800 pg/mL; normal value (n.v., 36-116) and N-terminal pro-B type natriuretic peptide (NT-proBNP) (13,594 pg/mL; n.v., 0-125).

The cardiovascular point-of-care ultrasound revealed severe biventricular dysfunction, with a left ventricular ejection fraction (LVEF) of 30%, a tricuspid annular plane systolic excursion (TAPSE) of 12 mm and a tricuspid annular S′ velocity of 8 cm/s, severe mitral regurgitation, torrential tricuspid regurgitation, and bilateral pleural effusion.

The patient was then admitted to the cardiac intensive care unit with diagnosis of cardiogenic shock and was promptly started on norepinephrine (0.2 μg/kg/min) and dobutamine (6 μg/kg/min), along with high-dose intravenous diuretic therapy with furosemide (125 mg/d), leading to a gradual stabilization of the clinical condition. The following day, under hemodynamic support with dobutamine and norepinephrine, the patient underwent invasive coronary angiography, which was negative.

Considering the history of Raynaud's phenomenon, the patient underwent rheumatologic evaluation that identified cutaneous sclerosis, facial telangiectasias, flexion contractures of the fingers, melanodermic patches on the upper and lower limbs, and mild dysphagia for solid foods. Laboratory tests revealed positivity for antinuclear antibodies (ANA) and anti-Scl70 antibodies, hypocomplementemia (C3), hypogammaglobulinemia, elevated C-reactive protein level (4 mg/dL; n.v., < 0.5) and ferritin level (138 ng/mL; n.v., 4-61), reduced albumin level (3 g/dL; n.v., 3.8-4.6), and mild proteinuria (43 mg/dL). Finally, following the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2013 criteria, a diagnosis of diffuse cutaneous systemic sclerosis (dcSSc) was made, and considering the severe cardiac involvement, the patient was started on an empirical treatment with intravenous injection of methylprednisolone (500 mg/daily for 3 days, followed by gradual tapering) and cyclophosphamide (500 mg/wk).

To confirm potential inflammatory cardiac involvement secondary to dcSSc (scleroderma cardiomyopathy), the patient underwent cardiac magnetic resonance imaging (cMRI), which revealed biatrial dilation, moderate-to-severe mitral and tricuspid valve regurgitation, left ventricular hypertrophy with global hypokinesia, and moderate reduction of global function (left ventricular ejection fraction, 40%, n.v., $> 55\%$; stroke volume index (Svi) 28 mL/m^2, n.v., 36-60); normal right ventricular volumes with mild reduction in ejection fraction (right ventricular ejection fraction, 45%, n.v., $> 50\%$; stroke volume (SV) 31 mL/mq, n.v., 34-58), moderate circumferential pericardial effusion, and bilateral apical-parietal-basal pleural effusion (Video 1, view video online) that may have been overestimated by supine position. Tissue characterization sequences showed no signal increase on short tau inversion recovery (STIR) imaging, but late gadolinium enhancement (LGE) sequences demonstrated diffuse subendocardial enhancement in both the atria and ventricles, with a nonischemic pattern, and difficulty in nullifying the myocardial signal (Fig. 1). These findings are suggestive of cardiac amyloidosis.

The patient subsequently underwent right ventricular EMB that demonstrated cloud-like deposits of amyloid protein within the interstitial space, also evident in the vascular walls. Immunotyping was positive for serum amyloid A (SAA) protein, thus allowing the diagnosis of AA cardiac amyloidosis (Fig. 2). At the same time, a right heart catheterization was performed, revealing post-capillary pulmonary hypertension with low cardiac output (mean wedge pressure, 21 mm Hg; mean pulmonary artery pressure, 28 mm Hg; cardiac index, 1.72 L/min/m^2; pulmonary vascular resistance, 2.6 Wood units).

After 2 weeks of hospitalization, the response to immunosuppressive therapy was inadequate, troponin and NT-proBNP levels remained stable over time, and weaning from inotropic and vasopressor support remained challenging. A hemodynamic response with symptomatic improvement was achieved after a 24-hour intravenous infusion of levosimendan. The patient was subsequently discharged with a plan for rheumatologic follow-up and monthly levosimendan cycles as destination therapy. Within a few months, due to clinical deterioration, she was transitioned to an end-of-life palliative care program.

SSc is a chronic autoimmune disease characterized by progressive fibrosis of the skin and internal organs, as well as vascular dysfunction. The diagnosis is based on a thorough clinical evaluation, the presence of characteristic signs, such as skin sclerosis, Raynaud's phenomenon, and the detection of specific autoantibodies according to ACR/EULAR 2013 criteria.[1] The pathogenesis of SSc involves a complex interplay of immunologic, vascular, and fibrotic mechanisms, which can lead to significant cardiac involvement. This process can affect various components of the heart, including the myocardium, pericardium, valvular structures, coronary arteries, and the conduction system. According to the European Alliance of Associations for Rheumatology Scleroderma Trials and Research (EUSTAR), cardiac causes play a significant role in the mortality of SSc patients, accounting for 26% of deaths. The main cardiac-related issues leading to mortality are heart failure and arrhythmias. Monitoring and managing these cardiac complications are crucial in improving the prognosis and outcomes for individuals with SSc.[2]

Our patient presented with cardiogenic shock requiring immediate hemodynamic support with inotropes and vasopressors. Thanks to a prompt clinical and laboratory evaluation, a diagnosis of dcSSc was made.

The differential diagnosis includes all potential causes of severe biventricular dysfunction, such as acute myocardial infarction in the presence of left main disease or severe multivessel disease, fulminant myocarditis, scleroderma-related cardiomyopathy, and scleroderma—PAH with severe

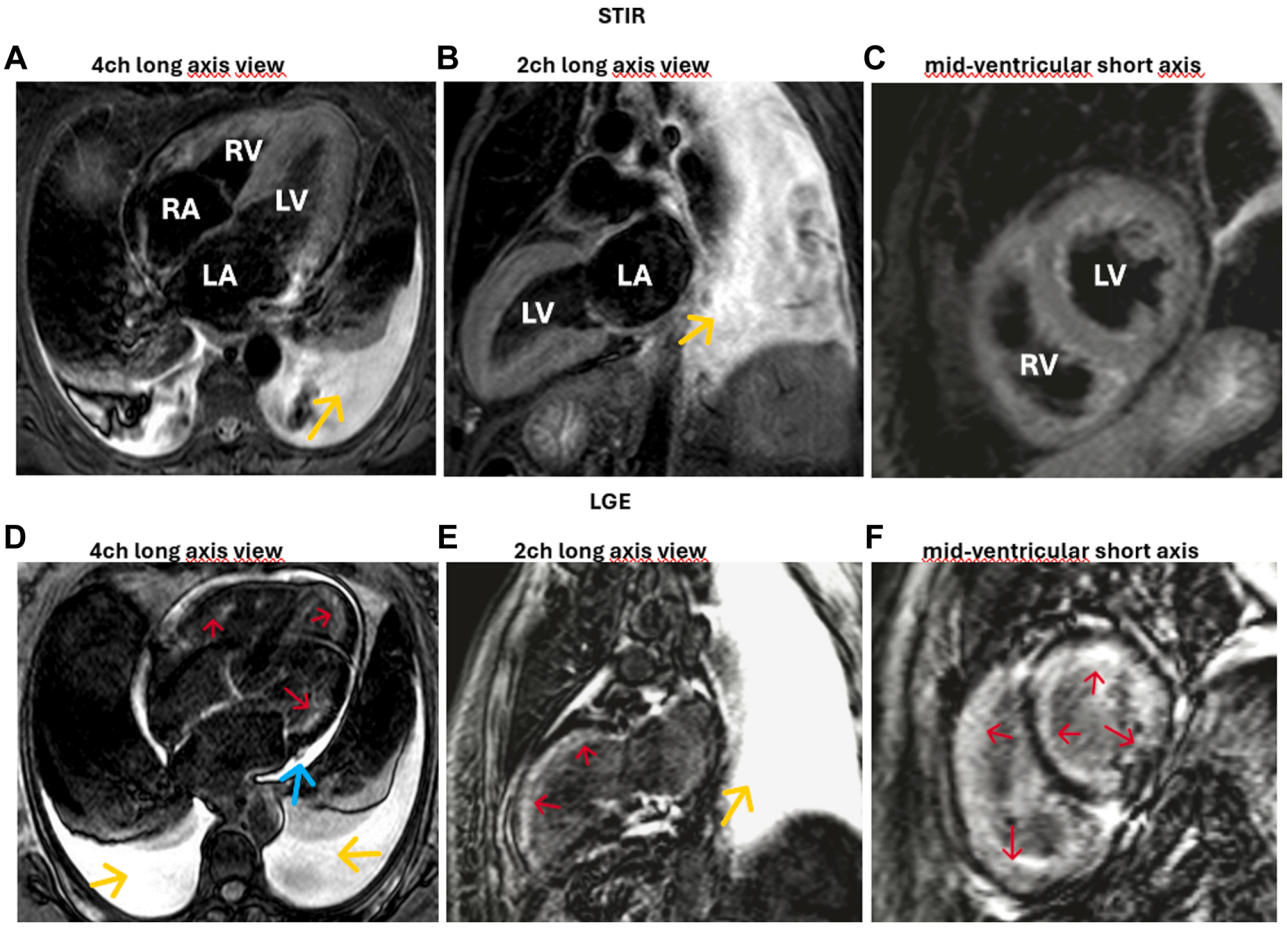

Figure 1. Cardiac MRI. (**A-C**) Short tau inversion recovery T2 weighted (STIR): there are no areas of increased myocardial or pericardial signal compatible with edema; (**D-F**) Magnitude inversion recovery late gadolinium enhancement: **red arrows** show diffuse subendocardial signal intensity increases in both ventricles, extending to the atria, compatible with nonischemic necrosis. At the basal level, high degrees of transmurality are reached. T1 mapping was not available. Therefore, measurement of native T1 values or extracellular volume was not possible. Nevertheless, the findings were consistent with suspected cardiac amyloidosis. The **yellow arrows** indicate the pleural effusion, and the **blue arrow** indicates the pericardial effusion. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. 2ch, 2 chambers; 4ch, 4 chambers.

pulmonary hypertension with right ventricular dysfunction; once cardiac amyloidosis was suspected, the differential diagnosis focused on the specific subtypes of cardiac amyloidosis.

Current therapeutic evidence for SSc with cardiac involvement remains scarce and is limited largely to case reports.[3] In this case, an empiric approach with methylprednisolone and cyclophosphamide was undertaken in an attempt to attenuate myocardial inflammation.

Although no definitive cMRI criteria are available to reliably describe cardiac involvement in SSc, a certain finding is that fibrosis is common even in asymptomatic patients. Fibrosis tends to exhibit various patterns of distribution (subendocardial, midwall, interventricular insertion points) and shows a progressive base-to-apex gradient. Left ventricular systolic dysfunction is rarely observed, whereas diastolic dysfunction is more frequently detected at an earlier stage.[4]

In this case, cMRI revealed moderate biventricular dysfunction, absence of inflammation, and the presence of extensive subendocardial/transmural fibrosis diffusely affecting both ventricles and the atria, in a pattern typically described in cardiac amyloidosis[5]; EMB confirmed the diagnosis of AA amyloidosis.

AA amyloidosis is a rare form of amyloidosis, secondary to the accumulation of SAA protein due to chronic inflammatory or infectious diseases.[6] The condition is characterized primarily by renal involvement, with a clinical picture dominated by renal failure, proteinuria, hepatomegaly, and gastrointestinal issues. Cardiac involvement occurs in approximately 2% of cases. In the Western world, the occurrence of AA amyloidosis has become less frequent, owing to better control and treatment of chronic infections and immunologic disorders.[7]

To our knowledge, this case is the first confirmed through EMB of AA amyloidosis secondary to SSc. The significance of this case lies in the consideration that a rare complication of a systemic disease, if left unrecognized and untreated over time, can lead to rapid and fatal complications. In this regard, the patient's clinical history was relatively short, with the onset of Raynaud's phenomenon just 2 years prior, followed by acute heart failure that was refractory to all treatments. Therefore, dcSSc remains a condition that requires particular attention, as in some cases it can be progressive and rapidly fatal. cMRI is the best noninvasive imaging technique for early diagnosis and screening of this condition. Aggressive immunosuppressive and immunomodulatory treatment should be initiated as soon as possible.

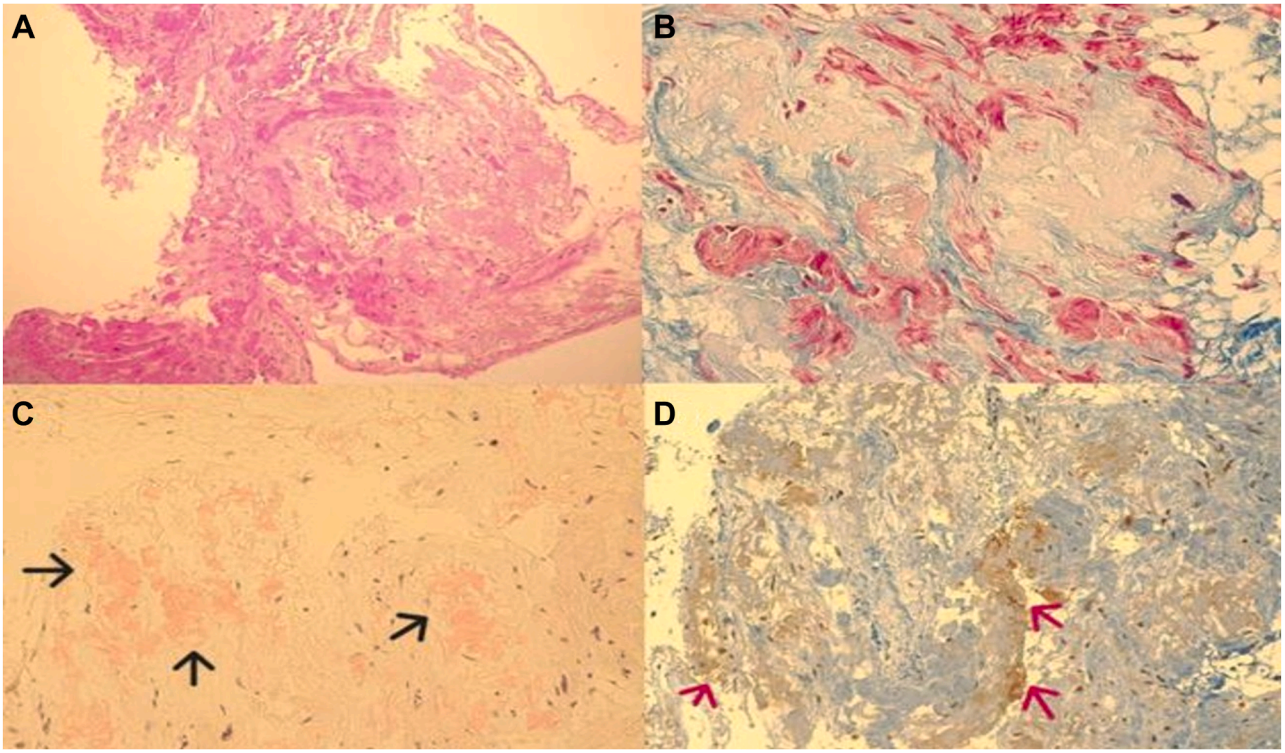

Figure 2. Endomyocardial biopsy. (**A**) 10X hematoxylin-eosin and (**B**) 40X Masson's trichrome stains showing mild myocyte hypertrophy and attenuation, along with a moderate perimyocytic interstitial fibrous network. (**C**) 20X Congo red stain showing amyloid deposits (**black arrows**). (**D**) 20X immunohistochemistry with anti-serum amyloid A antibody showing infiltration of myocardium (**red arrows**).

Ethics Statement

The research reported has adeared to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This is a retrospective case report using de-identified data; therefore the institutional review board did not require consent from the patient.

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Disclosures

The authors have no conflicts of interest to disclose.

References

1. Van den Hoogen F, Khanna D, et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2013;72:1747-55.
2. Tyndall AJ, Bannert B, et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Ann Rheum Dis 2010;69:1809-15.
3. Batani V, Dagna L, De Luca G. Therapeutic strategies for primary heart involvement in systemic sclerosis. Rheumatol Immunol Res 2024;5:72-82.
4. Gargani L, Todiere G, Guiducci S, et al. Early detection of cardiac involvement in systemic sclerosis: the added value of magnetic resonance imaging. JACC Cardiovasc Imaging 2019;12:927-8.
5. Maceira AM, Joshi J, Prasad SK, et al. Cardiovascular magnetic resonance in cardiac amyloidosis. Circulation 2005;111:186-93.
6. Li Z, Cui X, Yao Z, et al. Systemic AA amyloidosis with cardiac involvement in a patient with a history of tuberculosis. JACC 2024;83(13_Suppl):2787.
7. Mirioglu S, Uludag O, Hurdogan O, et al. AA amyloidosis: a contemporary view. Curr Rheumatol Rep 2024;26:248-59.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2025.11.003