Complete Heart Block in Systemic Sclerosis with Characterization on Cardiac MRI

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ABSTRACT: Cardiac involvement of infiltrative disease, such as systemic sclerosis, carries significant morbidity and mortality. All parts of the heart may be affected, although the conduction system is less commonly involved. We report a rare case of systemic sclerosis causing third-degree atrioventricular block and the first known reported case to use cardiac magnetic resonance imaging (CMR) as a diagnostic and prognostic instrument. It is not known whether using cardiac CMR in systemic sclerosis with cardiac involvement could lead to earlier intervention with escalation of medical therapy or earlier referral for transplant evaluation.

INTRODUCTION

Third-degree atrioventricular (AV) block or complete heart block (CHB) is due to an interruption in atrial electrical impulses transmitting to the ventricles.[1] Common etiologies of CHB are conduction system degeneration, acute myocardial infarction, congenital disorders, and metabolic disorders.[2] Very rarely, CHB can be caused by infiltrative diseases such as systemic sclerosis (SSc).[3-7] SSc is an autoimmune disorder with variable clinical manifestations and organ involvement due to a trifecta of autoimmunity, vasculopathy, and fibrosis.[8] The skin, gastrointestinal tract, and lungs are more commonly involved in SSc than the heart. When the heart is involved, the myocardium, pericardium, and, less commonly, the conduction system may be affected. Cardiac involvement in patients with SSc carries significant morbidity and mortality. With recent improvements in the prognosis of scleroderma renal crisis, the two main causes for disease-associated mortality in SSc are cardiac and pulmonary involvement.[9] In a systematic review and meta-analysis, cardiac involvement was the leading cause of mortality in these patients (29%).[10] Complete AV block is a very rare but serious complication in SSc. It has been reported in only five previous case reports. Screening for cardiac involvement of SSc has historically been limited to electrocardiograms (ECG), echocardiograms, and laboratory tests including troponin-I (Tn-I) and B-type natriuretic peptide (BNP) levels.[11] The following case describes a patient with SSc who developed CHB. This is the first known case in the literature to use cardiac magnetic resonance imaging (CMR) prior to pacemaker implantation to characterize the extent of fibrosis in this rare cause of CHB.

CASE DESCRIPTION

We describe the case of a 42-year-old Hispanic male with limited cutaneous systemic sclerosis characterized by interstitial lung disease (ILD) with 5-L oxygen dependence, biopsy-proven autoimmune necrotizing myopathy of the bilateral lower extremities, gastrointestinal dysmotility, and Raynaud's phenomenon with digital ulceration. Serologies were notable only for positive antinuclear antibody at a titer of 1 to 640 and positive anti-Ro antibodies. A diagnosis of SSc was made in October 2018, and he was started on prednisone (1 mg/kg) and mycophenolate mofetil (1500 mg, twice daily), which improved the muscle and lung manifestations of disease.

Prednisone was tapered down to 5 mg daily by July 2019. At this time, he presented to an outside hospital with dyspnea and chest pain. The patient's heart rate (HR) was 90 to 103 beats per minute (bpm) and respiratory rate was 21 respirations per minute (rpm). His Tn-I was elevated at 0.37 ng/mL and his ECG revealed sinus tachycardia with left bundle branch block. There was no prior ECG available for comparison. A code was called for the patient to be taken to the catheterization lab emergently. Left heart catheterization showed no evidence of obstructive atherosclerosis. Transthoracic echocardiogram (TTE) revealed a left ventricular ejection fraction of 50% to 55%, mild left ventricular wall thickening, trace tricuspid regurgitation, and no wall motion abnormalities. The right ventricular systolic pressure (RVSP) was 34 mm Hg. A trace pericardial effusion along the left ventricular free wall was identified. Additionally, his BNP level was 390 pg/mL. Given the lack of evidence for coronary artery disease and resolution of chest pain, no new cardiac therapy was started. He was ultimately discharged for close follow-up with his outpatient rheumatologist. Repeat pulmonary function testing showed a decrease in forced vital capacity of 18% and worsening hypoxia with rising oxygen requirements (2-4 L dependence via nasal cannula). His prednisone was increased from 5 mg/d to 20 mg/d, and plans were made to add rituximab to his medication regimen for refractory ILD and as a steroid-sparing agent.

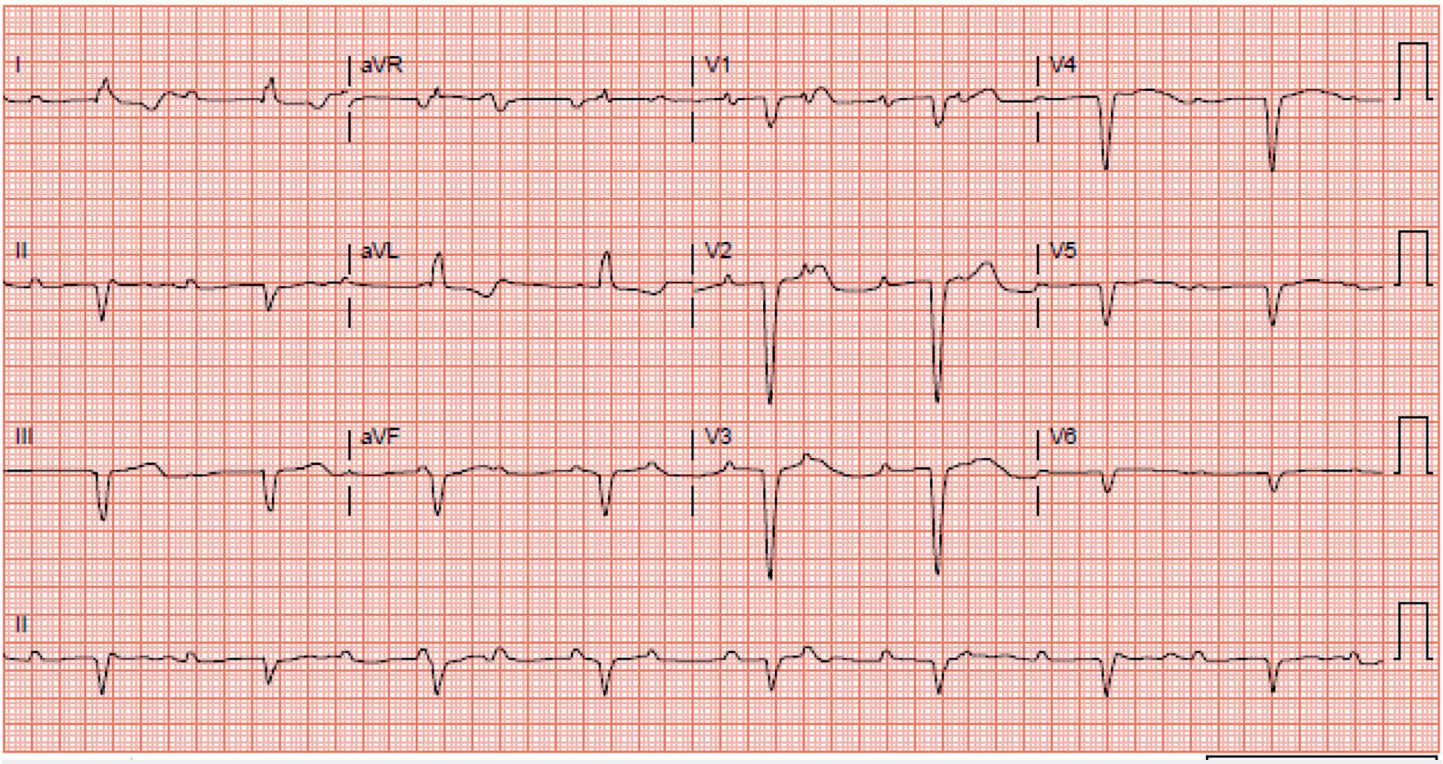

Figure 1.
Electrocardiogram revealing complete atrioventricular heart block.

In September 2019, the patient presented to our hospital with progressively worsening dyspnea and left-sided chest pain. He confirmed associated dizziness but denied syncopal episodes. On physical exam, he was tachypneic with a respiratory rate of 24 to 49 rpm. He had fine bibasilar crackles and difficulty speaking in complete sentences on 4L of oxygen by nasal cannula. His initial HR was 67 bpm, but he developed bradycardia with HR ranging from 39 to 49 bpm over the subsequent hour (his baseline HR in rheumatology clinic was 90 to 100 bpm). An ECG revealed third-degree AV heart block (Figure 1). Tn-I was elevated at 0.48 ng/mL and subsequently downtrended to 0.43 ng/mL an hour later. His BNP level, which was 390 pg/mL in July, had increased to 934 pg/mL. Notably, the patient was not taking AV nodal blocking agents at home. He had no history of conduction abnormalities on prior ECGs. Interventional cardiology was consulted for pacemaker placement. Due to concern for cardiac fibrosis secondary to SSc, the patient was temporarily transferred to another hospital with CMR capabilities. Cardiac CMR revealed diffuse subendocardial scarring, predominantly in the lateral, anterior, and inferior walls (Figure 2). The total scar burden was 35% in the left ventricle, and there was also right atrial and right ventricular involvement with mid-free-wall subendocardial scar at the basal level (Figure 2). There was slight flattening of the interventricular septum consistent with right-sided volume overload (similar findings were seen on transthoracic echocardiograms). Imaging also supported the presence of myocardial edema. A dual-chamber pacemaker was placed at that hospital, although a right atrial lead revision was needed the following day. He was discharged the next day with cardiac electrophysiology and rheumatology follow up.

Shortly after pacemaker placement, he was readmitted to our facility for worsening dyspnea on exertion. Chest computed tomography (CT), without contrast, showed interval development of diffuse ground-glass opacities on a background of fibrosis, consistent with ILD flare. He was treated with pulse dose of intravenous methylprednisolone 1000 mg for three consecutive days and received his first cycle of rituximab shortly thereafter. In addition to treating the refractory ILD, rituximab could also treat the myocarditis seen on cardiac MRI. The benefits were thought to outweigh any potential risks, such as delayed myocardial infarction, which has been associated with rituximab therapy in a few rare case reports.[12]

In October 2019, TTE revealed mild tricuspid regurgitation and an elevated RVSP of 46 mm Hg that was concerning for pulmonary arterial hypertension (PAH). There were no overt

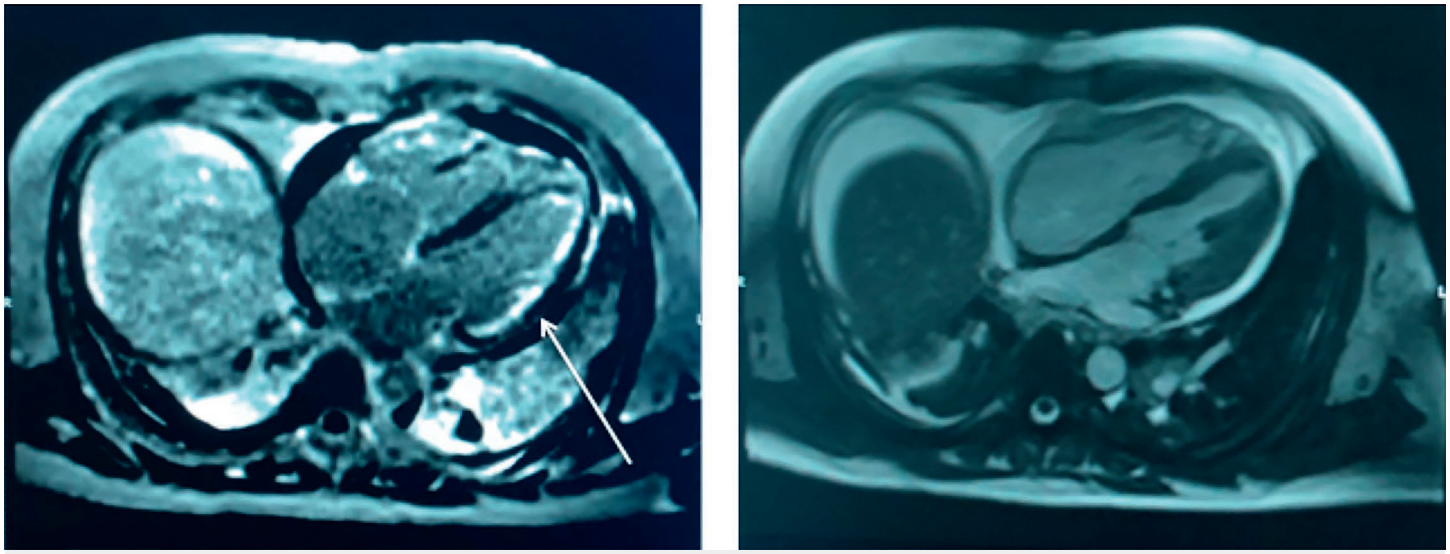

Figure 2.
Cardiac magnetic resonance imaging, four-chamber view. (Left) Delayed enhancement with enhanced area indicating subendocardial scarring (white arrow). (Right) Steady state free precession.

findings to suggest the pacing wire was impinging on the mobility of the tricuspid leaflets. A myocardial perfusion imaging study was also done and revealed no signs of any microvascular coronary disease. The patient was referred to lung transplant and pulmonary hypertension specialists for evaluation.

In January 2020, he was readmitted to the hospital for worsening dyspnea at rest and progressive hypoxia requiring high-flow nasal cannula at 30 L/min with FiO2 80%. Repeat TTE revealed a left ventricular ejection fraction of 35%, moderate to severe tricuspid regurgitation, and an RVSP of 83 mm Hg. A subsequent right heart catheterization confirmed PAH with a right atrial pressure of 12 mm Hg, mean pulmonary artery pressure of 33 mm Hg, pulmonary capillary wedge pressure of 8 mm Hg, Fick's cardiac output of 2.9 L/min, and cardiac index of 1.7 L/min/m^2. A chest CT without contrast showed progressive ILD. Unfortunately, the patient was not a candidate for heart-lung transplantation. He and his family elected to pursue home hospice, and he died peacefully at home 4 days after discharge.

DISCUSSION

Although cardiac involvement is not uncommon in patients with systemic sclerosis, second- and third-degree AV block is rare, accounting for less than 2% of SSc cases with cardiac involvement.[13] Instead, diastolic dysfunction and first-degree AV block are more frequently observed.[1] Currently, there are only five case reports in contemporary literature describing a patient with CHB as a result of SSc.[3-7] This is the first case report that we know of where CMR was used to evaluate the extent of cardiac fibrosis.

CMR techniques can be used to differentiate pathologies that are commonly associated with SSc. Myocarditis is mainly detected through diffuse increased signals on T2-weighted imaging[15] (this was not done in our patient due to poor patient compliance). In addition, T1 imaging and calculated extracellular volume can be used to assess for myocardial edema,[16] in which elevated T1 values (1100-1200 ms in our patient, where normal is ~990 ms) suggest myocarditis. In contrast, fibrosis is detected on CMR with delayed hyperenhancement as gadolinium is trapped in diseased tissue while washing away from healthy myocardium.[17]

The limited data on SSc and CMR make it difficult to understand the true utility of this advanced imaging modality. However, a systematic review of patients with cardiac sarcoidosis revealed that the presence of fibrosis on CMR was associated with an increased risk of arrhythmogenic events and all-cause mortality.[18] This study showed that CMR and delayed gadolinium enhancement can provide meaningful prognostic information in sarcoid patients, even when cardiac function was normal.

In our patient, CMR was done to better understand and confirm the suspected etiology of his CHB. A scar pattern typical of SSc was noted with diffuse subendocardial scarring (Figure 2). In a European League Against Rheumatism study, more

than half of the patients with SSc were estimated to have cardiac involvement.[19] In this subset of fibrosis patients with cardiac involvement, CMR may offer additional diagnostic value that more conventional testing cannot. Furthermore, CMR may detect myocardial disease in patients with symptomatic SSc even in the setting of a "normal" echocardiogram.[20] The use of CMR may lead to earlier intervention, whether that be escalation of medical therapy or earlier referral for cardiac (or cardiopulmonary) transplant evaluation.

The standard treatment for symptomatic CHB is permanent pacemaker implantation, as was done for this patient.[20] Since cardiac MRI was obtained just prior to the initial pacemaker implantation, the results were not yet available to cardiac electrophysiology. Unfortunately, the right atrial lead failed due to its initial placement on fibrotic tissue. It is possible that the lead revision could have been avoided had the cardiac MRI findings been available prior to the initial pacemaker placement. The cardiac MRI was, however, used by the interventional cardiologist during the right atrial lead revision to ensure placement onto healthy myocardium. The dual-chamber pacemaker subsequently functioned normally.

Because this is the first reported case of CHB in the setting of SSc to undergo CMR, the clinical utility of this imaging modality in transplant evaluation remains unknown. There is currently no consensus on a meaningful algorithm for the use of CMR in SSc patients.[21] Undoubtedly, CMR offers an in-depth evaluation of the extent of fibrosis that can be seen in patients with SSc involving the heart. Further use of CMR is needed to understand its impact on early diagnosis, patient management, and outcomes in infiltrative diseases, such as SSc.

Conflict of Interest Disclosure:
The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Keywords:
systemic sclerosis, complete heart block, infiltrative disease

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