

Progressive giant cell myocarditis presenting with inappropriate shocks from a subcutaneous defibrillator



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Introduction

Giant cell myocarditis (GCM) is a rare form of myocarditis predominantly affecting young, healthy adults. It is usually characterized by progressive cardiac failure, and ventricular arrhythmias are common.¹ Despite treatment with immunosuppression and guideline-directed heart failure therapy, implantable cardioverter-defibrillators (ICDs) are commonly inserted.² The currently available subcutaneous ICD (S-ICD; Emblem; Boston Scientific, Marlborough, MA) has a high efficacy rate for conversion of ventricular arrhythmias² and, when compared to transvenous ICDs, has a numerically lower infection rate at the expense of a higher rate of inappropriate shocks.³ We present a case of a patient who had progression of GCM leading to poor QRS complex sensing and suffered inappropriate S-ICD shocks.

Case report

A 48-year-old man was referred to our advanced heart failure institute following a diagnosis of GCM. He had initially presented to a regional hospital with chest pain and exertional dyspnea. He had a past medical history of proctocolectomy and ileoanal anastomosis for severe ulcerative colitis. At presentation he was hypotensive (90/60 mm Hg) and had features of left ventricular (LV) failure, which was managed with intravenous dobutamine and diuretics. His presenting electrocardiogram (ECG) demonstrated widespread ST-segment elevation and markedly elevated high-sensitivity troponin I (hsTnI 28,837 ng/L, reference <26 ng/L) and C-reactive protein (166 mg/L, reference <5 mg/L).

KEYWORDS Giant cell myocarditis; Subcutaneous ICD; Inappropriate shocks; Over-sensing; Conduction disease
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KEY TEACHING POINTS

- Giant cell myocarditis is associated with ventricular arrhythmias, hence implantable cardioverter-defibrillator (ICD) implantation is common. Subcutaneous ICDs (S-ICDs) may be an alternative to transvenous ICDs in patients who do not require pacing.
- S-ICDs are more prone to inappropriate ICD discharges owing to P-wave and T-wave over-sensing. Progressive giant cell myocarditis may lead to a change in QRS amplitude and morphology, which can increase the risk of inappropriate ICD discharges.
- Poor S-ICD sensing may be managed by conversion to a transvenous ICD or lead repositioning.

Transthoracic echocardiography demonstrated severe global left ventricular systolic dysfunction, with an estimated LV ejection fraction (LVEF) of 10%. Coronary angiography excluded significant coronary artery disease. Cardiac magnetic resonance imaging demonstrated diffuse transmural late gadolinium enhancement involving the apical, midseptal, and basal lateral LV segments, as well as the apical right ventricle (RV). Additionally, apical LV and RV mural thrombi were noted, for which he received therapeutic anticoagulation.

Endomyocardial biopsy demonstrated a diffuse mixed lymphocytic and eosinophilic infiltrate with occasional giant cells, consistent with GCM. At this point the patient was transferred to our institute for further treatment.

The patient was commenced on immunosuppression with a course of intravenous methylprednisolone followed by an oral taper, cyclosporine, and mycophenolate mofetil. Bisoprolol and ramipril were started; sacubitril-valsartan was trialed but was limited by symptomatic hypotension. Repeat cardiac magnetic resonance imaging 2 weeks after the initial

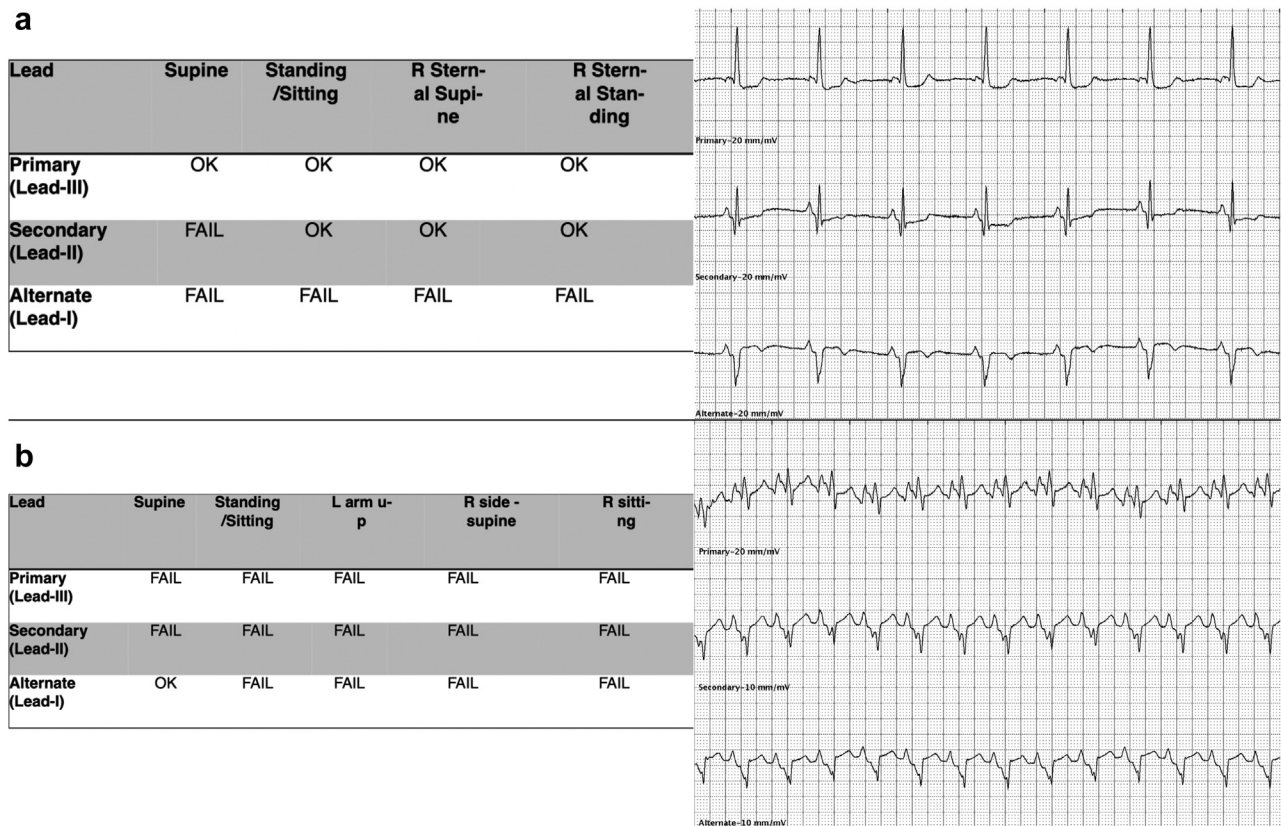


Figure 1 **a:** Preimplant subcutaneous implantable cardioverter-defibrillator screening using the Automated Screening Tool with acceptable sensing using the primary vector. The QRS complexes demonstrate a good amplitude compared to the P and T waves. **b:** Repeat screening with subsequent failure in all vectors. There is now a lower QRS amplitude and a marked change in morphology. Electrocardiograms from the supine position are shown.

scan demonstrated an improvement in LV systolic function, with an estimated LVEF of 34% and partial resolution of his LV and RV thrombi.

A primary prevention ICD was offered to the patient, given the diagnosis of GCM, elevated cardiac troponins, ventricular fibrosis, reduced LVEF, and recurrent asymptomatic nonsustained ventricular tachycardia. A decision was made to implant an S-ICD rather than a conventional transvenous ICD, given his lack of pacing requirement, intercurrent RV thrombus, and risk of infection owing to ongoing immunosuppression.

S-ICD screening was performed using the Automated Screening Tool (Boston Scientific, Marlborough, MA). Using a left sternal margin lead position, screening was successful using the primary vector in all positions. The alternate vector failed in all positions, and the secondary vector failed in the supine position but was successful in all other positions (Figure 1a). The Emblem S-ICD and a 3501 subcutaneous electrode were implanted uneventfully, with a lead impedance of 62 ohms. Defibrillation threshold testing was not performed owing to the risk of embolism of ventricular thrombus. The patient was discharged 1 month following his initial presentation. His hsTnI level normalized prior to discharge (15 ng/L, reference 16 ng/L).

The patient remained clinically stable with New York Heart Association class III heart failure symptoms. He

performed weekly remote monitoring transmissions and no concerns regarding device function were raised. His cyclosporine levels were in the therapeutic range, and he remained on mycophenolate and low-dose prednisolone. A transthoracic echocardiogram performed 3 months following the initiation of immunosuppression and heart failure therapy demonstrated ongoing severe LV systolic dysfunction, with an LVEF of 32%.

Five months following his discharge from hospital, the patient experienced multiple ICD discharges while at rest. The patient reported a moderate deterioration in his exercise tolerance over the preceding 2 weeks. His hsTnI level on admission was markedly elevated (43,064 ng/L, reference <26 ng/L). A chest radiograph demonstrated pulmonary congestion and transthoracic echocardiography showed a deterioration in his LV systolic function, with an LVEF of 15%. Of note, his presenting ECG demonstrated sinus rhythm with right bundle branch block and left anterior fascicular block, which was not present previously (Figure 2b).

Interrogation of his S-ICD revealed inappropriate shocks related to P- and T-wave over-sensing. Low-amplitude QRS complexes and intermittent QRS under-sensing was also noted (Figure 3). The SMART Pass filter (Boston Scientific, Marlborough, MA) was noted to have been automatically disabled 1 month prior to presentation. Subcutaneous electrocardiograms (S-ECGs) from the primary and

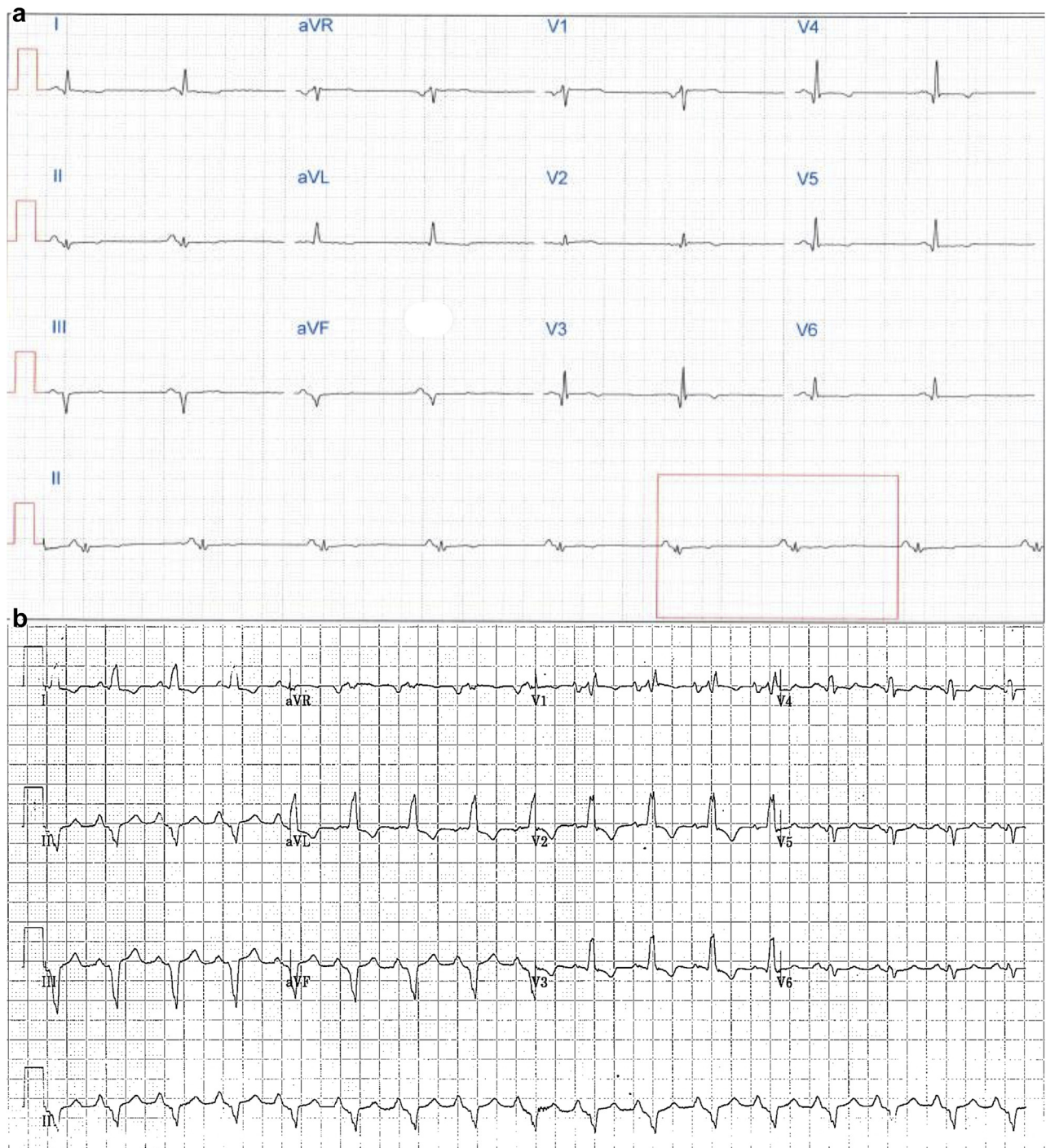


Figure 2 a: Electrocardiogram (ECG) at subcutaneous implantable cardioverter-defibrillator (ICD) screening with sinus rhythm, inferolateral Q waves, and nonspecific ST-T abnormalities. b: Presenting ECG at the time of admission for inappropriate ICD shocks showing sinus rhythm with right bundle branch block and left anterior fascicular block.

secondary vectors did not appear identical, and the alternate sensing vector did not demonstrate a flatline appearance. Inappropriate detections of atrial fibrillation were also noted owing to over-sensing. The electrode impedance was within normal limits. Chest radiography did not show a lead fracture and confirmed a similar position of the device and lead

compared to his postimplant radiograph. There had not been a significant change in the patient's body habitus. Repeat S-ICD screening demonstrated a failure of all vectors (Figure 1b).

The patient's immunosuppression was intensified and intravenous dobutamine was started owing to progressive

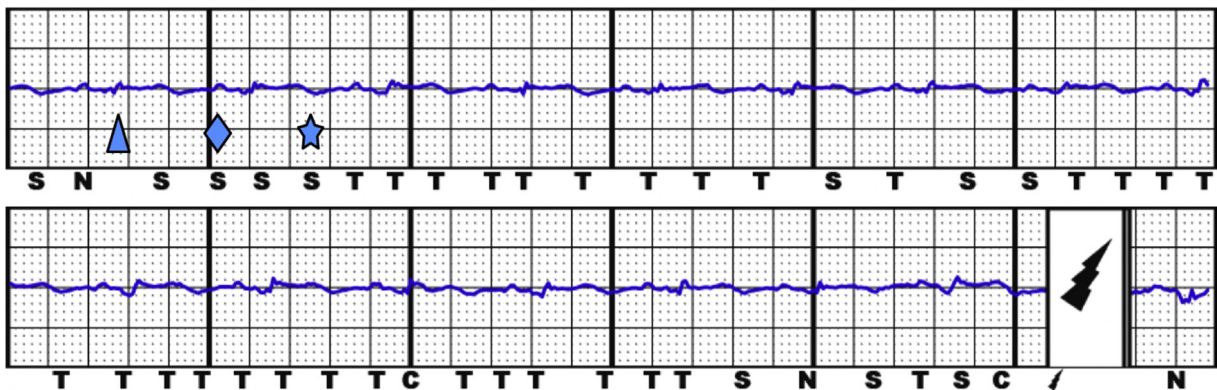


Figure 3 Interrogation of subcutaneous implantable cardioverter-defibrillator (ICD) demonstrating an inappropriate ICD shock. The arrow marker demonstrates under-sensing of the QRS complex. Diamond and star markers demonstrate P-wave and T-wave over-sensing, respectively. Note the low-amplitude QRS complexes relative to P wave and T waves. Repeated over-sensing led to fulfillment of the detection counter (T) and a subsequent inappropriate shock (lightning symbol).

cardiogenic shock. S-ICD detections were deactivated, and he was urgently listed for cardiac transplantation. Conversion to a transvenous ICD was discussed; however, the patient remained inotrope dependent and underwent orthotopic cardiac transplantation 2 weeks following this presentation. The S-ICD was explanted at the time of cardiac transplantation. To date, there has been no recurrence of GCM on surveillance endomyocardial biopsy.

Discussion

To our knowledge, this is the first case of inappropriate ICD discharges related to disease progression and poor QRS complex sensing in a patient with GCM and an S-ICD. The change in QRS morphology and amplitude impairs the ability for the device to correctly discriminate between P waves, T waves, and QRS complexes. Over-sensing of non-QRS complexes is therefore more common and may lead to inappropriate ICD discharges. Nakashima and colleagues⁴ have previously described a reduction in limb lead and chest lead QRS amplitude in patients with acute myocarditis, although this series was not specific to patients with GCM. The SMART Pass filter applies a high-pass filter to reduce over-sensing of low-frequency signals and has been shown to reduce the incidence of inappropriate shocks,⁵ but can be automatically disabled by the device if under-sensing is suspected.⁶ In our patient, the automatic disabling of the SMART Pass filter may have been an early sign of QRS amplitude reduction.

The optimum immunosuppression regimen for GCM is currently unknown. Current recommendations, based on limited data, suggest combination immunosuppression with a calcineurin inhibitor (eg, cyclosporine) with an antimetabolite (eg, mycophenolate).⁷ Despite treatment with combination immunosuppression in our patient, the presence of progressive conduction disease, symptoms of cardiac failure, and worsening LV systolic function strongly suggest progression of GCM. The significantly elevated hsTnI is also consistent with disease progression. Of note, ICD shocks have been shown to lead to an elevation in high-sensitivity

troponins,⁸ although typically not of the magnitude seen in our case.

Optimal selection of GCM patients to undergo primary prevention ICD insertion remains uncertain. To date, there are no randomized controlled trials in GCM patients to guide this decision. Current consensus guidelines recommend a primary prevention ICD in GCM when the LVEF remains less than 35% after 3 months of guideline-directed medical therapy.⁹ However, a Finnish study of 51 GCM patients demonstrated a 41% risk of sudden cardiac death or ventricular tachycardia in GCM patients at 1 year,¹⁰ which exceeds the risk seen in historical trials of nonischemic cardiomyopathy.⁹ This study identified elevated cardiac troponins and myocardial fibrosis on advanced cardiac imaging as risk factors for sudden cardiac death, and a high rate of ICD insertion was observed (62%). Our patient was offered a primary prevention ICD based on the presence of these risk factors, as well as frequent nonsustained ventricular tachycardia. A wearable cardioverter-defibrillator (LifeVest; Zoll Medical, Chelmsford, MA) as a bridge to decision for a permanent ICD⁷ is another potential option. However, in many countries, including at our institution, the LifeVest is cost prohibitive for many patients outside of clinical trials (approximately \$3000 [Australian dollars] per month of therapy). There is currently no government or insurance coverage for this device in Australia.

Other causes of device dysfunction and inappropriate ICD shocks were not seen in our patient. A normal lead impedance makes a poor header connection unlikely, and a stable position of the device on chest radiography makes significant device or lead migration unlikely. The 3501 subcutaneous electrode has been subject to a recall owing to an increased risk of lead fracture distal to the proximal sensing ring. This typically presents as a flatline appearance in the alternate sensing vectors and S-ECGs in the primary and secondary sensing vectors appearing nearly identical. Non-physiologic artefacts and high-impedance alerts may be seen¹¹; however, none of these features were present in our patient.

A transvenous ICD at the initial implant may have avoided this problem. Furthermore, owing to the chance of developing atrioventricular block and requirement for pacing, transvenous ICDs may be favored over S-ICDs by clinicians.¹ However, our patient did not have evidence of conduction disease at the time of S-ICD implantation, and the presence of RV thrombus was considered a relative contraindication to a transvenous lead owing to the risk of thrombus dislodgement and pulmonary embolism. The elevated infection risk associated with high-dose immunosuppression may also make S-ICDs an attractive alternative to transvenous ICDs when pacing is not thought to be required. Furthermore, a reduction in intracardiac R-wave sensing in GCM leading to the delivery of inappropriate shocks has also been reported.¹²

Although our patient subsequently underwent cardiac transplantation, another method for managing the problem of poor sensing may be electrode repositioning. Although not specific to GCM, Sasaki and colleagues¹³ described 2 cases of poor sensing in S-ICD systems in patients with progressive arrhythmogenic right ventricular cardiomyopathy and inappropriate shocks. In 1 case, lead repositioning under fluoroscopy was performed after mapping using the Automated Screening Tool, with an improvement in the QRS/T ratio and elimination of inappropriate shocks over a 12-month period. This solution may only be temporary as the disease continues to progress.

Earlier detection of poor sensing may be possible with regular review of a patient's 12-lead ECG and via remote monitoring. A significant change in the ECG, S-ECG, or SMART Pass filter could prompt rescreening of the patient using the Automated Screening Tool. Review of remote monitoring transmissions for inappropriate atrial fibrillation detections may also provide a mechanism for detecting over-sensing, as previously described.¹⁴ A better-informed decision could then be made on whether it is appropriate to reposition the lead or implant a transvenous ICD.

Conclusion

We describe a case of inappropriate S-ICD therapies in a patient with progressive GCM. Clinicians managing GCM patients with S-ICDs should be aware of the risk of poor sensing in disease progression, strategies for early detection of poor

sensing, and treatment options for patients who receive inappropriate ICD discharges.

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