

Atrial arrhythmias in Emery-Dreifuss muscular dystrophy: Approach to successful ablation



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Introduction

Emery-Dreifuss muscular dystrophy (EDMD) is a rare X-linked, autosomal dominant or autosomal recessive disorder characterized by the triad of (1) early-onset contractures of the elbow, ankles, and cervical spine; (2) humeroperoneal muscle wasting and weakness; and (3) cardiac involvement—for example, conduction system disease, most often heart block, and arrhythmias.^{1,2} Genes involved in EDMD include *EMD*, *LMNA*, *SYNE1*, *SYNE2*, and *FHL1*.³

EDMD is characterized by significant cardiac problems that should be diagnosed and treated promptly to improve outcomes and prolong life expectancy.^{4,5} The incidence of atrial fibrillation and atrial flutter is the highest, followed by atrioventricular (AV) block.⁶ Bradycardia at a young age followed by the development of AV block or atrial arrest has been reported.⁷ There is potential risk of ventricular tachyarrhythmias.^{5,8} Previous studies^{9,10} in EDMD patients with preserved systolic and diastolic function suggest an increase in regional and transmural ventricular repolarization heterogeneity in comparison to age- and sex-matched healthy controls; this has been linked to diffuse fibrosis and fatty acid infiltration that leads to ventricular electrical instability, resulting in malignant ventricular tachyarrhythmias and sudden cardiac death. Mapping symptomatic atrial arrhythmias can be challenging owing to the diseased substrate. We report a patient with EDMD who had symptomatic atrial flutter who was treated successfully by employing a modified mapping strategy minimizing the amount of ablation of a likely trigger, resulting in favorable long-term clinical outcome in this patient.

Case report

A 21-year-old man presented to the emergency room complaining of intermittent palpitations and chest discomfort for

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KEY TEACHING POINTS

- Emery-Dreifuss muscular dystrophy (EDMD) is a rare disease entity and there are various cardiovascular manifestations of the disease.
- Atrial arrhythmias are a significant problem requiring management in EDMD patients.
- Ablation for atrial flutter in EDMD patients presents a number of challenges.
- Three-dimensional mapping with use of lower-amplitude thresholds is an optimum technique for identifying the reentrant circuits to achieve a successful ablation in EDMD patients.
- Use of an implantable cardioverter-defibrillator should be considered for prevention of sudden death in EDMD patients.

the past 5 days. He had a past medical history of EDMD diagnosed via muscle biopsy 11 years prior. He initially received a dual-chamber permanent pacemaker, then had an episode of sustained ventricular tachycardia resulting in system upgrade to a dual-chamber implantable cardioverter-defibrillator 9 years ago. Within the past year of admission he had developed paroxysmal rapid symptomatic atrial flutter, for which he was started on rate control therapy with diltiazem, atenolol, and digoxin; however, he admittedly stopped taking all of these medications several months earlier owing to increased fatigue and did not follow up with his cardiologist. Family history was significant for EDMD in his mother and 2 brothers, who all had ICD placement. Five days prior to presentation he started feeling intermittent palpitations and received an ICD shock associated with a near-syncopal spell. He initially did not seek medical attention, but then came to the emergency room complaining of worsening palpitations and fatigue. Admission vital signs found blood pressure of 114/82 mm Hg, pulse of 99 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 96% on

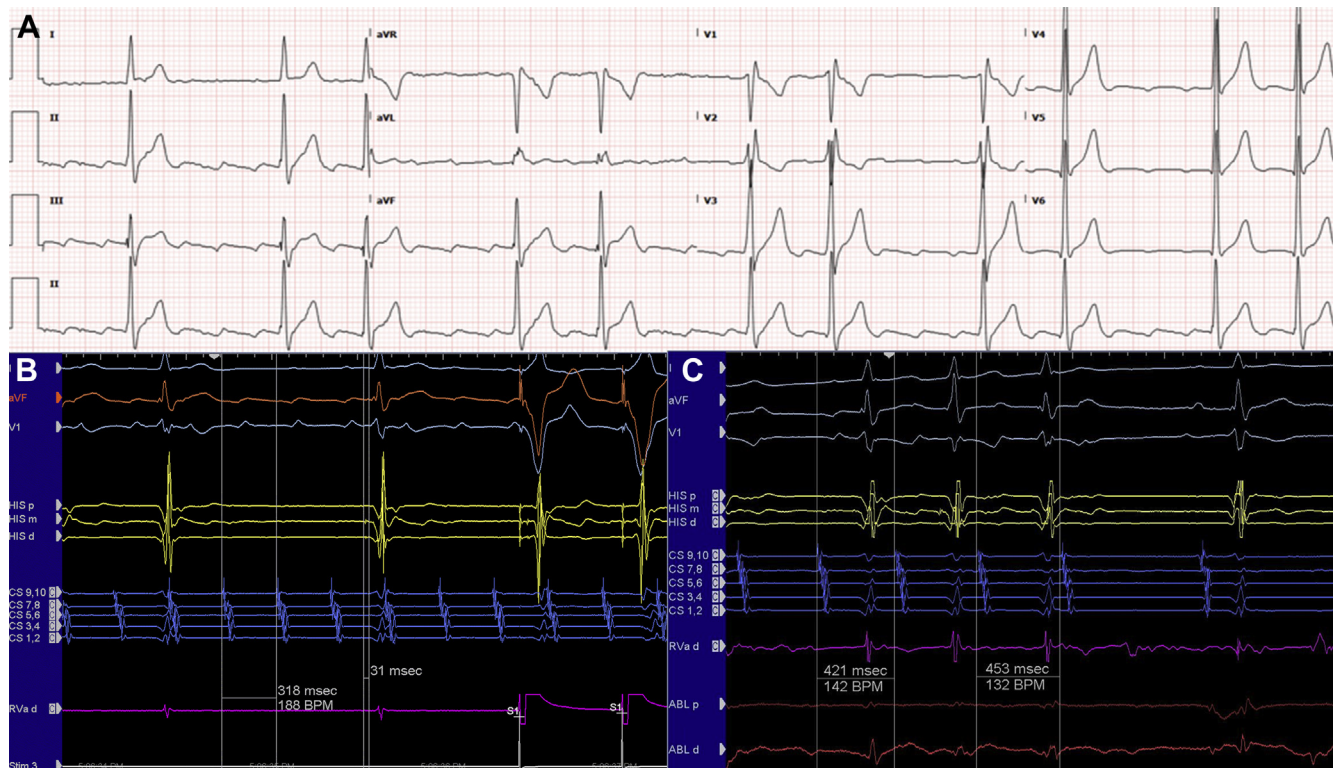


Figure 1 Surface and intracardiac electrocardiograms of atrial flutter. **A:** A 12-lead electrocardiogram demonstrated typical atrial flutter with variable atrioventricular block and narrow QRS. **B:** Intracardiac electrogram during atrial flutter with cycle length of 318 ms and normal infrahisian conduction (HV of 31 ms). CS = coronary sinus (1–2 = most distal pair, 9–10 = most proximal pair). **C:** Intracardiac electrogram demonstrating termination of atrial flutter preceded by prolongation of tachycardia cycle length.

room air. Electrocardiogram revealed rate-controlled typical atrial flutter with variable AV block (Figure 1A). Chest radiography showed no cardiomegaly, no acute cardiopulmonary disease, and an intact ICD system. Initial lab work revealed normal electrolytes, blood counts, and liver, renal, and thyroid function, with pro-BNP of 6 pg/mL and troponin T level of 0.04 mg/mL. ICD interrogation showed 27% atrial pacing, 4% ventricular pacing, 27% atrial flutter

burden over the past year, no evidence of atrial fibrillation, and 2 inappropriate ICD shocks over the past 6 months, both for 1:1 atrial flutter at cycle length of 290 ms. Transthoracic echocardiogram was performed and found normal left ventricle size and function with a left ventricular (LV) ejection fraction of 55% and top normal biauricular size. He was immediately placed on therapeutic parenteral anticoagulation on admission.

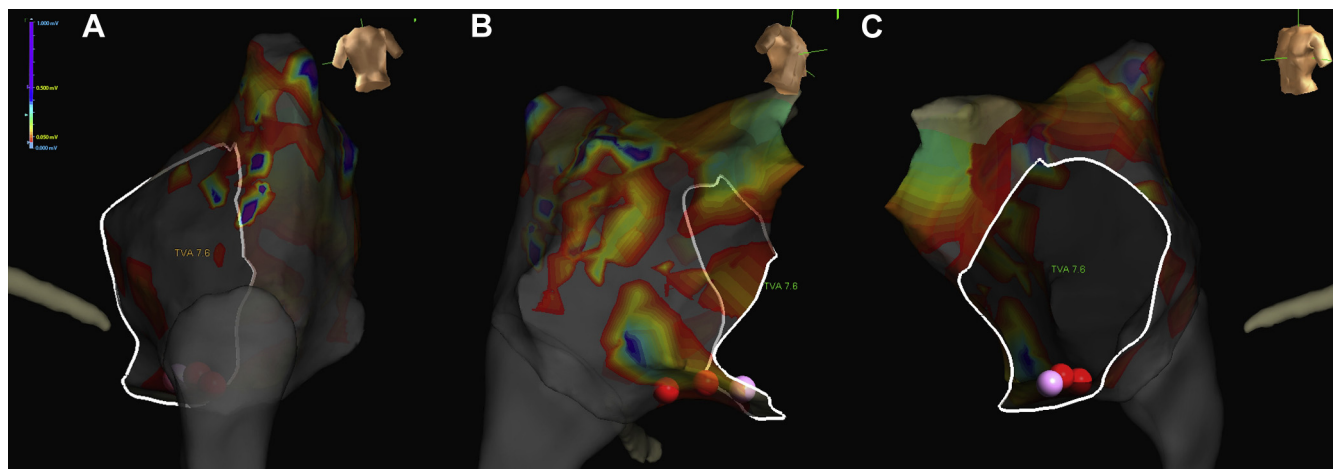


Figure 2 Three-dimensional Endocardial Solutions Inc (St Paul, MN) electroanatomic voltage map, with ablation site tags, of right atrium with lower thresholds (0.05 mV) demonstrating existing significant atrial scar. **A:** Posteroanterior view. **B:** Right anterior oblique view. **C:** Left lateral view.

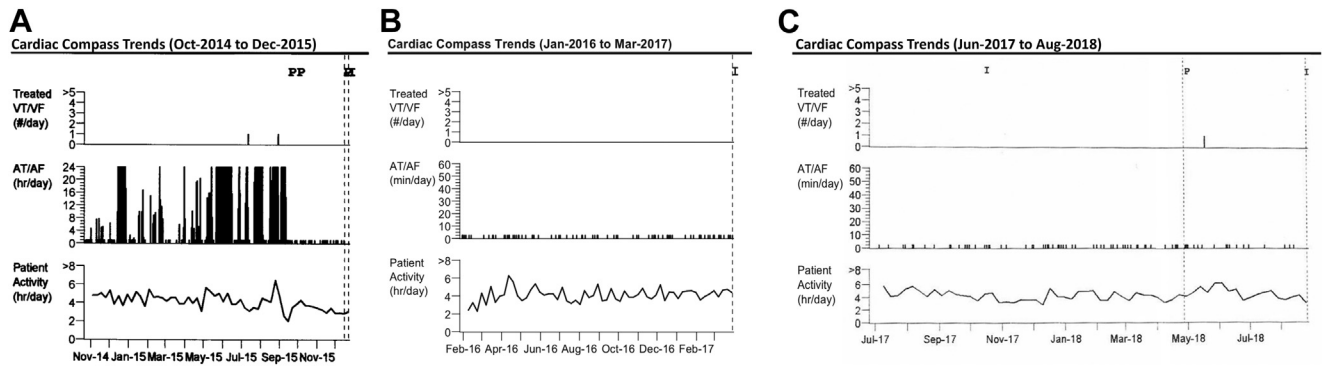


Figure 3 Cardiac compass trend from patient's implantable cardioverter-defibrillator demonstrating significant atrial arrhythmia burden prior to September 2015 cardiac ablation, and low burden post ablation. **A:** Pre- and peri-ablation. **B,C:** Thirty-five months post ablation.

A transesophageal echocardiogram was done and found no intracardiac shunt or thrombus. A comprehensive diagnostic electrophysiology study was performed and confirmed atrial flutter via intracardiac electrograms, with atrial cycle length of 318 ms (Figure 1B). Interestingly, very low-amplitude signal was present. Typical cavotricuspid isthmus-dependent counterclockwise atrial flutter was confirmed via 3D Endocardial Solutions Inc (St Paul, MN) intracardiac electroanatomic activation and propagation mapping. The entire tachycardia cycle length was mapped within the right atrium, with transisthmus conduction delay noted. On the second radiofrequency application while creating a standard cavotricuspid isthmus ablation line, the patient was noted to have prolongation and then termination of atrial flutter (Figure 1C). Voltage mapping revealed significant diffuse scar with low atrial electrogram signal amplitudes noted; only after voltage thresholds were lowered was enough viable myocardium visualized to sustain a macro-reentrant circuit (Figure 2). Bidirectional block was confirmed with transisthmus conduction times exceeding 180 ms in both directions, with clear change in activation sequence. High-dose isoproterenol was initiated without inducibility of any sustained arrhythmia.

The patient was started on apixaban for anticoagulation and metoprolol tartrate for rate control, as it was unknown at the time if further arrhythmias related to disease progression would occur. He was discharged in sinus rhythm. Three years later, there were no recurrences of sustained arrhythmia or ICD shocks, as verified by ICD interrogations (Figure 3). He remains asymptomatic after 35 months. Furthermore, the patient's quality of life and functional capacity improved dramatically with his now being able to hold a job, and both oral apixaban and metoprolol were discontinued after 6 months.

Discussion

Review of the literature identified 2 reported cases of ablation in EDMD, both with poor outcomes, 1 resulting in death and the other requiring a heart transplant. Blagova and colleagues¹¹ have described a case of atrial flutter ablation in an EDMD patient, which was initially successful, but eventually the patient had a recurrence within 4 months, compli-

cated with worsening LV systolic function ultimately necessitating a heart transplant. Carvalho and colleagues¹² have reported a case involving an EDMD patient with recurrent supraventricular tachycardia with multiple catheter ablations and pacemaker placement after AV nodal ablation, which progressed to further episodes of ventricular tachycardia and death from irrecoverable asystole. To the best of our knowledge, our experience is the first reported catheter ablation with favorable long-term clinical outcome in a patient with EDMD. Thirty-five months' follow-up post ablation revealed a significantly reduced burden of atrial flutter and fibrillation (Figure 3). This could be attributed to our patient possibly having a more benign variant of EDMD, or perhaps we achieved a more desirable outcome by employing a different ablation strategy. Stoyanov and colleagues¹³ reported 2 cases of EDMD patients with atrial electrical standstill defined by right atrial voltage <0.10 mV with lack of high-output right atrial capture, yet 1 of them was still able to perpetuate atrial flutter. No atrial ablation was attempted in either patient. We recommend catheter ablation using 3D mapping with use of lower-amplitude thresholds (0.05 mV, as we did in our case) to finely map the reentrant circuits in order to target zones of slow conduction and minimize the amount of ablation, which could advance myocardial fibrosis and promote disease progression, thereby worsening morbidity and mortality. This approach therefore could offer safer and more favorable prognostic catheter ablation for atrial arrhythmias.

A prospective study by Nigro and colleagues¹⁴ provided strong evidence for considering primary ICD implantation in *LMNA* mutation carriers with cardiac conduction disorders and preserved LV function. These patients have a high rate of progressive myocardial fibrosis resulting in atrial arrhythmias, sinoatrial conduction disease causing symptomatic bradycardia, and fatal ventricular arrhythmias resulting in mortality. Hence, a dual-chamber ICD should be the initial choice of device therapy in these patients to prevent sudden death and treat eventual high-grade AV block.¹⁵

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