ESC European Society of Cardiology

European Heart Journal - Case Reports (2022) **6**, 1–5
https://doi.org/10.1093/ehjcr/ytac324

CASE REPORT
Arrhythmias/electrophysiology

A case report of successful physiological pacing in a patient with lamin A/C cardiomyopathy

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Received 1 February 2022; first decision 8 March 2022; accepted 29 July 2022; online publish-ahead-of-print 2 August 2022

Background Lamin A/C (LMNA) mutations account for 5–8% of familial dilated cardiomyopathies, and can manifest with conduction abnormalities and ventricular arrhythmias in 78% of patients. Therefore, when suspected, it is important to implant the correct type of device.

Case summary A 52-year-old gentleman with a family history of cardiomyopathy, presented with asymptomatic atrial fibrillation and complete atrioventricular block associated with a narrow QRS interval. Investigations confirmed dilated and severely impaired left ventricular systolic function. He underwent successful conduction system pacing in combination with a primary prevention defibrillator. Genetic screening confirmed LMNA cardiomyopathy. During 3 years follow up, his left ventricular function remained unchanged with stable conduction system capture and he received appropriate therapy from his device for ventricular tachycardia.

Discussion His-bundle pacing promotes rapid and synchronous activation of the ventricles via the intrinsic conduction system of the heart. In selected individuals with LMNA cardiomyopathy, conduction system pacing is viable alternative to conventional cardiac resynchronization therapy using coronary sinus tributaries.

Keywords Case report • Physiological pacing • LMNA cardiomyopathy • Left ventricular systolic dysfunction • Inherited cardiovascular condition • Dilated cardiomyopathy

ESC curriculum 5.9 Pacemakers • 6.2 Heart failure with reduced ejection fraction • 5.11 Cardiac resynchronization therapy devices • 6.5 Cardiomyopathy • 5.6 Ventricular arrhythmia

Learning points

- Patients with lamin A/C (LMNA) cardiomyopathy present with conduction abnormalities and impairment of the left ventricle (LV).
- Conduction system pacing is a feasible alternative to traditional pacing approaches, and it mimics intrinsic activation of the LV.
- Conduction system pacing should be considered in LMNA cardiomyopathy, as it minimizes the risk of LV function deterioration when compared with the traditional means of pacing.

Introduction

Lamin A/C (LMNA) cardiomyopathy is an autosomal dominant condition and has a penetrance of 100% by 60 years of age.[1] Patients with this condition are at risk of left ventricular systolic dysfunction (LVSD), conduction abnormalities, and sudden cardiac death (SCD).[1] van Rijsingen *et al.*[2] identified four independent risk factors for SCD in patients with LMNA cardiomyopathy—left ventricular ejection fraction (LVEF) <45% at first clinical contact, non-sustained ventricular tachycardia (NSVT), male gender, and non-missense mutation of the LMNA gene.

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Handling Editor: David Duncker
Peer-reviewers: Edin Begic; Marta Cvijic; Stefan Simovic
Compliance Editor: Oliver Ian Brown
Supplementary Material Editor: Damien Farhad Nur Salekin

Conventional right ventricular apex (RVA) pacing causes a non-physiological activation of the ventricle, resulting in dyssynchrony, a broader QRS complex, and consequently impairment of the LV.[3] The dyssynchrony from RVA pacing has even more of a detrimental effect in patients already diagnosed with LVSD.[4] His-bundle pacing negates this by allowing rapid and synchronous activation of the ventricles via the intrinsic conduction system of the heart. In this report, we present a 52-year-old gentleman who underwent successful HBP for CHB secondary to LMNA cardiomyopathy.

Timeline

Dates	Events
April 2018	Patient was referred to our emergency department as he was bradycardic in the community. A 12-lead electrocardiogram (ECG) showed evidence of complete heart block (CHB) Investigations: Transthoracic echocardiogram (TTE)—Dilated left ventricle (LV) with ejection fraction (EF) of 26% Coronary angiogram—Unobstructed coronaries Cardiac magnetic resonance—Late gadolinium enhancement of the anterior, mid septum, and antero-lateral segments. Severe LV impairment with ejection fraction of 26%. Management/follow up • Commenced carvedilol, eplerenone, sacubitril/valsartan, dapagliflozin • His-bundle pacing (HBP), and an implantable cardioverter defibrillator (ICD) as findings at the time were suspicious of LMNA cardiomyopathy • 4 monthly pacing checks • Annual clinic appointments • 2 yearly echocardiogram
August 2019	Genetic screening confirmed LMNA cardiomyopathy with Desmoplakin gene mutation
December 2020	Patient presented to the emergency department with an appropriate ICD shock Management: • Carvedilol dose up-titrated • Commenced amiodarone • Remained arrhythmia free for 72 h, therefore discharged back to the community with regular outpatient follow up
October 2021	Routine TTE—EF (3D) = 44% Routine pacing check—100% HBP

Case presentation

A 52-year-old gentleman with no medical history presented with a 1-day history of left-sided neck and shoulder ache. The patient's father died at the age of 68, and the cause was felt to be due to some form of cardiomyopathy. His sister also passed away at a young age in her sleep, with a presumed diagnosis of epilepsy. In terms of clinical observations, the pulse rate was 40 b.p.m., and the blood pressure was 149/104 mmHg. Clinical examination was unremarkable.

A 12-lead ECG revealed atrial fibrillation with narrow QRS complexes (116 ms) associated with a junctional escape rhythm, suggestive of CHB (*Figure 1A*). Blood tests revealed elevated high-sensitivity troponin-I titres of 47.8 and 52.6 ng/L (upper limit is 19.8 ng/L). Connective tissue, autoimmune, and extensive virology screen were negative. A TTE revealed dilated diastolic internal diameter of 6.4 cm with a biplane LVEF of 26%. The infero-septal wall was akinetic, and the antero-lateral and antero-septal walls were hypokinetic (see Supplementary material online, *Videos S1–S3*). The right ventricle (RV) was mildly dilated with a basal diameter of 4.4 cm. A coronary angiogram was performed in view of the impaired LV function, which showed normal coronary arteries. Cardiac magnetic resonance (CMR) showed a dilated LV with severely impaired function (LVEF 26%), with mild central mitral regurgitation. There was late gadolinium enhancement in the mid section of the infero-septal and antero-lateral walls, suggestive of scarring (*Figure 2*). The RV was normal in size, but its function was severely impaired.

Our patient was commenced on 12.5 mg carvedilol twice daily, sacubitril/valsartan 24/26 mg twice daily, 25 mg eplerenone once daily (OD), and 10 mg dapagliflozin OD. Oral anticoagulation was initiated for stroke prophylaxis. As our patient presented with CHB, there was a Class I indication for permanent pacing. Due to a strong suspicion of LMNA cardiomyopathy, a primary prevention ICD was recommended by the multidisciplinary team. Given that the patients underlying QRS was narrow, we elected to pace via the His bundle (HB) to preserve physiological pacing. Using a left subclavian extra-thoracic approach, an active single coil ICD lead was implanted in the right ventricular septum. A select-secure lead was used to map the location of the HB using a Medtronic C315 sheath. A clear HB signal was seen, with an H-V interval of <60 ms. Pace-mapping demonstrated selective capture of HB, but at the cost of high pacing thresholds. By positioning the lead more distally, a non-selective capture was obtained at more acceptable outputs (*Figure 3*). The paced QRS of 119 ms (*Figure 1B*) and the time to onset of global longitudinal strain (*Figure 4*) were consistent with conduction system capture, resulting in coordinated activation of the left ventricle. On discharge, our patient had a 4-month pacing check, annual clinical follow up, and 2-year TTE. A year after discharge, genetic testing confirmed mutations in the LMNA and DSP gene.

Two years after initial presentation, the patient presented to our local hospital following an appropriate ICD shock secondary to sustained ventricular tachycardia (VT). The patient was commenced on amiodarone, had the carvedilol dose up-titrated, and discharged after 72 h of monitoring. Our patient had no further episodes of VT to date, and on 3-year follow up, conduction system pacing is maintained at acceptable pacing output (see Supplementary material online, *Figure S1*). A repeat TTE showed that LV function had not deteriorated. The RV size and function had returned to normal (see Supplementary material online, *Videos S4–S6*).

Discussion

Lamin A/C cardiomyopathy should be strongly suspected in patients diagnosed with idiopathic dilated cardiomyopathy (DCM) who develop conduction abnormalities. NSVT can be prevalent in as much as 78% of patients with LMNA mutations.[5] More than 450 LMNA mutations have been identified, and mutation in the gene that codes for striated muscles results in DCM.[6] DSP gene mutations are traditionally associated with arrhythmogenic right ventricular dysplasia (ARVD).[6] However, our patient did not hit diagnostic criteria for ARVD based on clinical history, TTE or CMR. LMNA mutation carriers usually

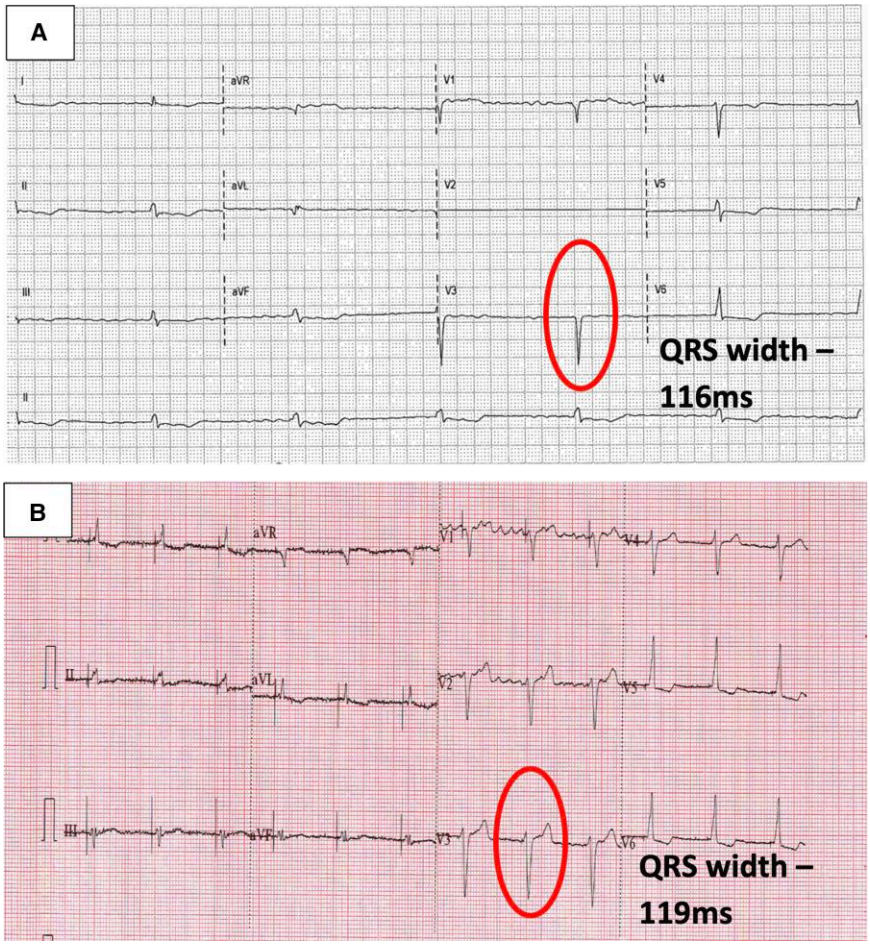

Figure 1 (*A*) Admission electrocardiogram showing evidence of junctional escape rhythm in the context of atrial fibrillation with a ventricular rate of 40 b.p.m. (*B*) Non-selective His-bundle paced rhythm with narrow QRS complexes (circle).

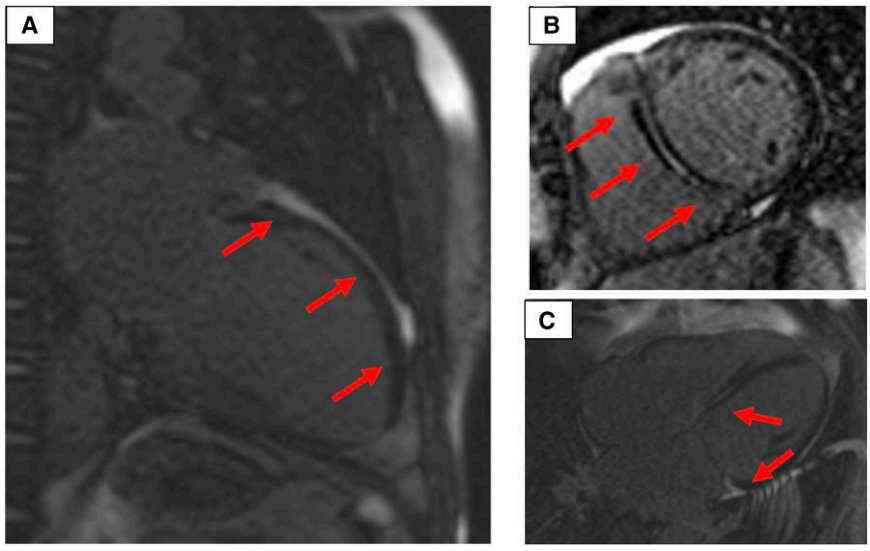

Figure 2 Cardiac magnetic resonance imaging showing evidence of late gadolinium enhancement (arrows) of the anterior, mid septum, and antero-lateral segments in the 2-chamber (*A*), short-axis (*B*), and four-chamber (*C*) views, respectively.

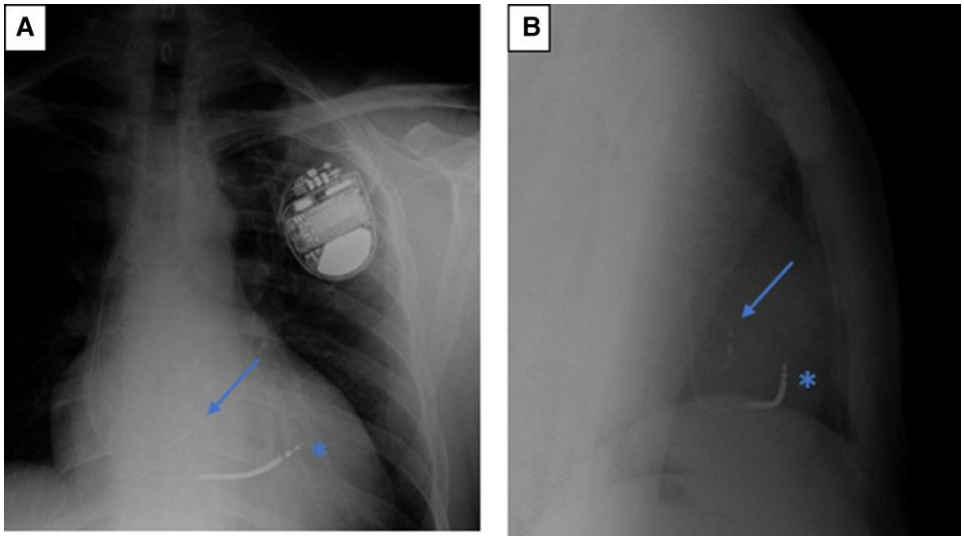

Figure 3 Antero-posterior (*A*) and lateral (*B*) plain X-ray films illustrating satisfactory position of the pacing lead in the his-bundle (arrow) and ICD lead (asterisk) in the RV outflow tract.

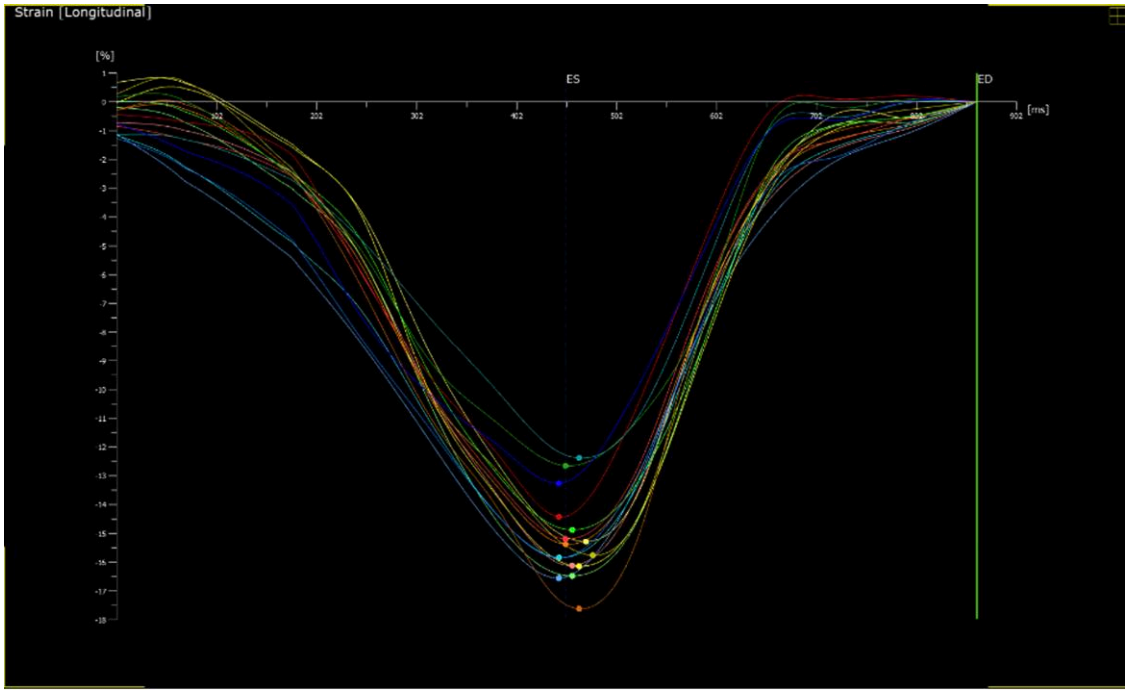

Figure 4 Graph showing the time to onset of global longitudinal strain for 16 left ventricular segments which show coordinate activation of the left ventricles during conduction system pacing.

exhibit late gadolinium enhancement in the basal- or mid-ventricular septal wall on CMR, which was the case in our patient.[7] An ICD is indicated in patients with LVEF <45% at first clinical contact, NSVT, male gender, and non-missense mutation of the LMNA gene.[2]

His-bundle pacing is an alternative approach to RVA pacing, which aims to achieve a more physiological pattern of ventricular activation.[8] Recent meta-analysis has shown that HBP does not diminish systolic function in patients with a preserved LV, and that the ejection fraction may improve up to 10% in patients with systolic dysfunction.[9] Studies have also shown that progressive accumulation of experience in HBP considerably reduces fluoroscopy time, HB capture thresholds, and reliance on back up leads.[9–11]

Presently, there is paucity of evidence in managing patients with conduction abnormalities due to LMNA cardiomyopathy. Current European guidelines recommend that patients with atrioventricular block and heart failure with reduced ejection fraction undergo a biventricular pacemaker implant. It also states that conduction system pacing can be considered as an alternative.[12] We elected to pace via the HB system, and therefore not only able to preserve physiological activation of the left ventricle, but also avoid the need for a cardiac resynchronisation therapy defibrillator, which is bulkier, more expensive, and may result in less physiological activation of the left ventricle.[13,14] There is one report in the literature which suggested that HBP failed to recruit the intrinsic conduction in patients with LMNA cardiomyopathy.[13] However, this patient had severe fibrosis in the basal interventricular septum and it is uncertain whether there was conduction system capture, as the paced QRS duration was considerably longer than the intrinsic QRS.[13]

To our knowledge, this is the longest surviving patient who had LMNA cardiomyopathy with successful conduction system pacing that had been reported in the literature. We recommend 4-month pacing checks, as there is a possibility that the conduction disease could propagate distal to current area of conduction system capture. If this becomes the case, patients may require an upgrade to a coronary sinus lead in the future.

Conclusions

In patients with LMNA associated cardiomyopathy who require permanent pacing, conduction system pacing is a feasible alternative to traditional pacing methods, and can be combined with an ICD if indicated.

Lead author biography

I am currently a cardiology registrar in training at the Grest Western Hospitals NHS trust. I graduated from Peninsula Medical School with distinction in 2015 and have worked in the Peninsula and Severn deaneries since.

Supplementary material

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

Acknowledgements

None.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

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