

Leadless atrioventricular synchronous pacing in Eisenmenger syndrome



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Introduction

Eisenmenger syndrome is at the extreme end of the phenotypic spectrum of pulmonary arterial hypertension associated with congenital heart disease. Over time, a large nonrestrictive left-to-right shunt provokes progressive pulmonary vascular disease that results in the shunt becoming bidirectional or reversing direction (ie, right-to-left). When the need for pacing arises, transvenous leads are generally considered contraindicated owing to a prohibitively high risk of paradoxical thromboembolism.^{1,2} However, epicardial lead placement also incurs substantial risk. Anesthesia induction can result in hypotension, leading to increased right-to-left shunting and desaturation. The fragile but balanced Eisenmenger physiology may collapse under the effects of fluid shifts, procedural anesthetics, or the surgery itself.³ Risk-to-benefit ratios should be thoughtfully considered and discussed within a multidisciplinary context. Herein, we present a patient with Eisenmenger syndrome and new-onset complete atrioventricular (AV) block in whom implanting a leadless pacemaker was deemed the preferred option. To our knowledge, this is the first reported case of AV synchronous leadless pacing in Eisenmenger syndrome.

Case report

A 55-year-old woman with a large (1.2 cm) unrepaired perimembranous ventricular septal defect, nonobstructive cor triatriatum sinistrum, and Eisenmenger syndrome presented with sudden worsening of shortness of breath (from NYHA class III to class IV symptoms), along with orthopnea and presyncope. Her medical history was remarkable for

KEYWORDS Atrioventricular block; Congenital heart disease; Eisenmenger syndrome; Intracardiac shunt; Leadless pacemaker; Thrombosis (Heart Rhythm Case Reports 2021;7:538–541)

Sources of funding: Dr Khairy is supported by the André Chagnon Research Chair in Electrophysiology and Congenital Heart Disease. Conflict of interest disclosures: Dr Mondésert has served as a consultant for Medtronic Inc and Abbott Medical Inc. The other authors have no relevant potential conflicts of interest to disclose. **Address reprint requests and correspondence:** Dr Paul Khairy, Montreal Heart Institute, 5000 Belanger St E., Montreal, QC, Canada, H1T 1C8. E-mail address: paul.khairy@umontreal.ca.

KEY TEACHING POINTS

- In patients with Eisenmenger syndrome who require a cardiac implantable electronic device, risk-to-benefit ratios should be thoughtfully considered by a multidisciplinary team, with procedures performed in centers with expertise in congenital heart disease.
- Transvenous leads are considered contraindicated in Eisenmenger syndrome owing to the high risk of paradoxical systemic thromboembolic complications.
- A leadless pacemaker is believed to be a less thrombogenic alternative to transvenous leads owing to the absence of foreign material within the low-flow atrial chamber and encapsulation of the device within months.
- In selected patients with Eisenmenger syndrome, a clear pacemaker indication, and a high surgical risk for an epicardial device, the leadless pacemaker may offer the least risky alternative. Long-term follow-up studies are required to assess the safety of this approach.

hypertension, dyslipidemia, and obstructive sleep apnea on continuous positive airway pressure therapy. In the outpatient setting, her oxygen saturation was 84% with a hematocrit of 0.55. Her right ventricular systolic pressure was 100 mm Hg by echocardiography, with moderate right ventricular dilation, severe hypertrophy, and preserved function, along with a normal left ventricular ejection fraction. Pharmacotherapy consisted of macitentan, ramipril, bisoprolol, furosemide, atorvastatin, and potassium supplementation.

On presentation, she was in high-grade to complete AV block (Figure 1A) with a narrow QRS complex (106 ms) and a junctional escape rate as low as 35 beats per minute (bpm). She maintained a systolic blood pressure > 100 mm

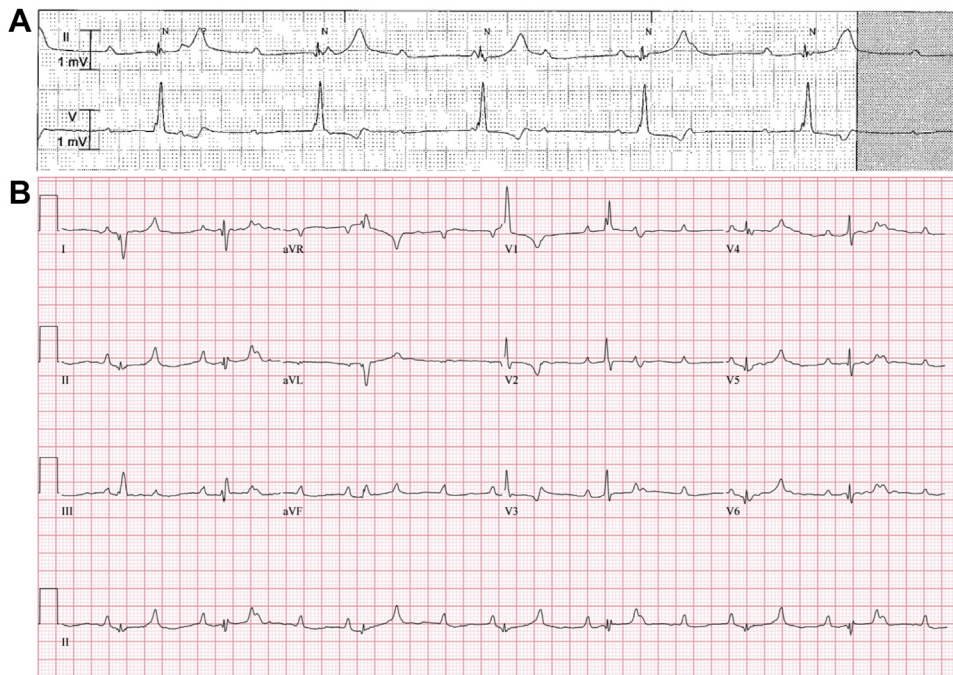


Figure 1 Electrocardiographic (ECG) tracings of atrioventricular (AV) block in an adult with Eisenmenger syndrome. **A:** The rhythm strip (leads II and V) on presentation. Complete AV block is noted with a junctional escape rhythm at 37 beats/min (bpm). **B:** A 12-lead ECG after initiation of an isoproterenol infusion. High-grade AV block is observed with a narrow QRS (106 ms) rate of approximately 45 bpm.

Hg with adequate oxygen saturation (>80%) but developed low-output heart failure with pulmonary edema, acute renal failure (decreased creatinine clearance from >60 to 31 mL/min/m²), relative anemia (hematocrit 0.39), and an NT-pro-BNP level of 7336 ng/L (baseline 269 ng/L). Bisoprolol and ramipril were discontinued. She was treated with intravenous furosemide, blood transfusions, and an isoproterenol perfusion titrated to 6 µg/min to maintain a ventricular rate of approximately 50 bpm (Figure 1B). A fluorodeoxyglucose–positron emission tomography scan was performed in the context of an unusual clinical presentation, with no prior cardiac surgery associated with a higher risk of developing AV block. It revealed focal uptake at the basal septum with an associated perfusion defect suggestive of active inflammation, with no extracardiac manifestations of sarcoidosis. A multidisciplinary team was convened to discuss the strategy for pacemaker implantation. Options considered included a transvenous device in combination with long-term anticoagulation, an epicardial system by means of a minimally invasive surgical approach, and a leadless AV synchronous pacemaker. In weighing potential risks and complications, a consensus was reached for the leadless pacemaker.

A Micra AV pacemaker (Medtronic Inc, Dublin, Ireland) was implanted under conscious sedation and local anesthetics by means of a 24F sheath introduced in the right femoral vein under ultrasonic guidance. Ventricular ectopy induced by sheath manipulation resulted in the loss of an escape rhythm, requiring a periprocedural temporary pacemaker introduced in the same vein. Several right ventricular septal sites were tested, with inadequate thresholds. The leadless pacemaker

was therefore implanted in the right ventricular apex (Figure 2). Orthogonal (right and left anterior oblique) views were used to ensure that the device did not cross the ventricular septal defect, with contrast (50:50 contrast:saline)



Figure 2 Posteroanterior chest radiograph following implantation of the leadless pacemaker. The leadless pacemaker is positioned in the right ventricular apex. Note the presence of pulmonary edema and the right-sided peripherally inserted central catheter.

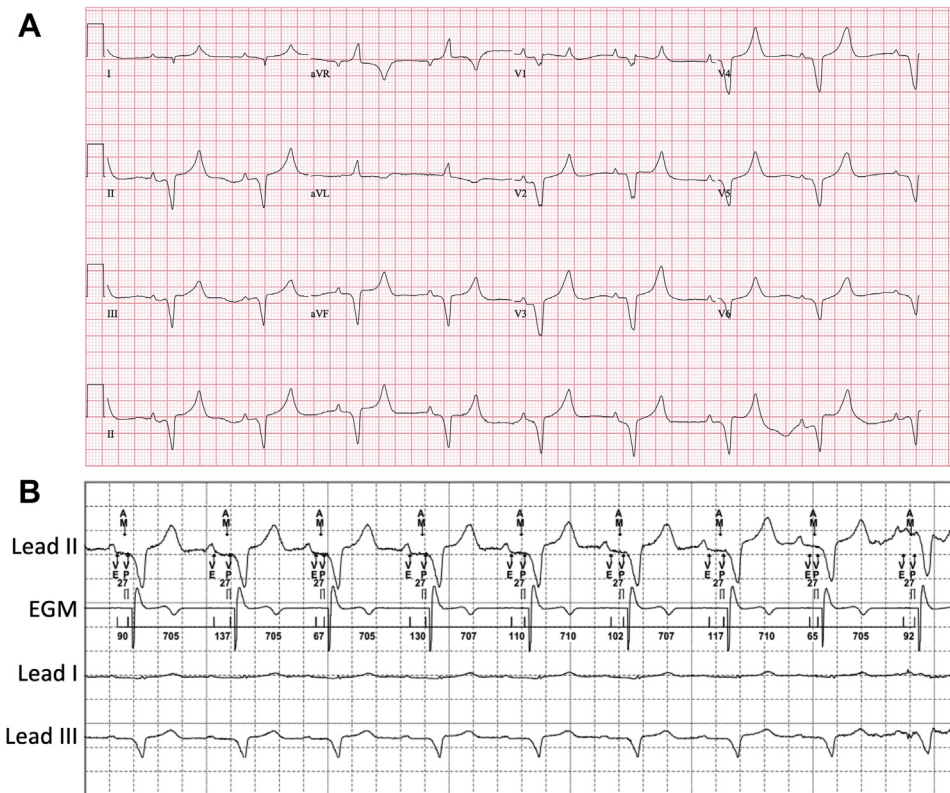


Figure 3 Atrioventricular synchronous pacing with the Micra AV leadless pacemaker (Medtronic Inc, Dublin, Ireland). **A:** The 12-lead electrocardiogram shows the left bundle branch block morphology with leadless ventricular pacing, along with 2:1 undersensing of atrial activity that prompted reprogramming of the A4 threshold. **B:** Intrinsic electrocardiographic tracings (lead II, intracardiac electrogram [EGM], and leads I and III) obtained upon device interrogation at the 3-month follow-up visit. As seen on the marker channel, the ventricular end (VE) period and atrial mechanical (AM) period are appropriately sensed following the P wave. The pacemaker spike (VP) follows after the programmed 20 ms AM-VP delay, with appropriate ventricular capture.

injected to verify the position prior to deployment. A pacing threshold of 0.38 V at a pulse width of 0.24 ms was obtained, with an impedance of 920 ohms. R waves were not measurable in the absence of an escape rhythm. Upon sheath removal, the skin was closed with a figure-of-eight suture. The procedure was hemodynamically well tolerated. The pacemaker was programmed to the VDD mode from 50 to 120 bpm.

The postoperative course was favorable. Underdetection of atrial activity (Figure 3A) prompted reprogramming (A4 threshold) to render atrial sensing more sensitive. Pulmonary edema resolved, renal function normalized, and the patient returned to her baseline clinical state. Anticoagulation with warfarin was initiated and interrupted medications were resumed. At her 3-month follow-up visit, she remained clinically stable with effective AV synchronous pacing (Figure 3B). An escape rhythm had recovered such that R waves were measured at 18.1 mV. The pacing threshold was unchanged and the estimated battery longevity was >8 years.

Discussion

Eisenmenger syndrome is a heterogeneous disorder with multiorgan involvement that afflicts approximately 5% of patients with congenital heart disease.⁴ It is associated with

the worst prognosis and poorest exercise performance even among the category of patients with cyanotic heart disease.⁵ Cardiac issues predominantly involve heart failure and arrhythmias. In a cohort of 246 adults with Eisenmenger syndrome, 5% had pacemakers for indications evenly distributed between sinus node dysfunction and AV block.⁶ An additional 1.6% had implantable cardioverter-defibrillators.

Interventions in patients with Eisenmenger syndrome should be limited to those deemed indispensable and performed in centers with expertise in congenital heart disease, including experienced anesthesiologists. Risks of complications are high and include hemodynamic instability, death, bleeding, thrombosis, and arrhythmias.³ The presence of transvenous leads in patients with intracardiac shunts confers a 2.6-fold higher risk of systemic thromboembolic complications, even after adjustment for other risk factors including older age, atrial tachyarrhythmias, and phlebotomies.¹ Among those with intracardiac shunts, patients with Eisenmenger syndrome are thought to be at highest risk for systemic emboli by virtue of right-to-left shunting, with multiple strokes reported in some.⁶ The effectiveness of anticoagulation in mitigating this risk remains unknown. As such, management guidelines recommend against implanting transvenous leads in the presence of an intracardiac shunt.²

In the absence of an implantable cardioverter-defibrillator indication, one option we considered was a minimally invasive surgical approach to implant dual-chamber epicardial leads via a subxyphoid incision using thoracoscopic tools. In small series of patients without Eisenmenger syndrome, adequate sensing and pacing values were reported using this technique.^{7,8} Although such procedures have predominantly been performed under general anesthesia, epicardial pacemaker implantation has been described in an awake patient under epidural anesthesia.⁹ Nevertheless, in patients with Eisenmenger syndrome, general anesthesia is normally preferred over epidural anesthesia. However, if the surgery permits, regional anesthesia is believed to incur lower risks than general anesthesia.³ In the case presented, the consensus was that general anesthesia would be required for an epicardial approach in light of the patient's fragile physiology with decompensated heart failure.

The leadless Micra AV pacemaker received approval from the US Food and Drug Administration and Health Canada licensing in 2020 for treatment of patients with AV block. An AV synchronous algorithm was developed to provide VDD pacing on the basis of accelerometer signals that capture distinct segments of cardiac activity in order to determine atrial contraction.¹⁰ It was deemed the preferred option for our patient on the basis of the less invasive implantation procedure and low perceived risk of thromboembolic complications. In a series of 719 patients with Micra devices followed for 6 months, only 1 (0.14%) developed pulmonary thromboemboli.¹¹ It could be hypothesized that this low risk is due to a combination of absence of foreign material within the atrium and encapsulation of the Micra device. Thrombus appears to be 5 times more likely to form on atrial compared to ventricular components of pacing leads as a result of enhanced stasis within atrial chambers.¹² Moreover, near-complete encapsulation of the nitinol retention system and body of the Micra device was reported at 4 months of follow-up,¹³ with complete coverage by fibrous tissue at 1 year.¹⁴

Although anticoagulation is not routinely recommended post implantation, we opted to prescribe short-term (4–6 months) warfarin therapy in the context of intracardiac foreign material in a patient with pulmonary hypertension and right-to-left shunting. One study reported that increased pulmonary arterial systolic pressure (PASP) was the only factor significantly associated with lead thrombosis,¹² and a PASP > 40 mm Hg is listed as a contraindication to implantation of the Nanostim leadless pacemaker (Abbott Medical Inc, Abbott Park, IL).¹⁵ Although no such contraindication was issued for the Micra device, there is limited safety data on patients with elevated PASPs and none on patients with

Eisenmenger syndrome in whom the primary concern is systemic thromboembolism.

In conclusion, there is no low-risk solution to implanting cardiac electronic devices in patients with Eisenmenger syndrome. Indications must be carefully deliberated and procedures limited to those deemed essential. As this case illustrates, when the need for pacing arises, a leadless pacemaker system may offer the least risky alternative in selected patients. The long-term safety of this approach has yet to be established and the need for, and optimal duration of, oral anticoagulation remains to be determined.

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