


# A case report of unusually long episodes of asystole in a severe COVID-19 patient treated with a leadless pacemaker

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## Background

Experience has been emerging about cardiac manifestations of COVID-19-positive patients. The full cardiac spectrum is still unknown, and management of these patients is challenging.

## Case summary

We report a COVID-19 patient who developed unusually long asystolic pauses associated with atrioventricular block (AV) block and atrial fibrillation who underwent leadless pacemaker implantation.

## Discussion

Asystole may be a manifestation of COVID-19 infection. A leadless pacemaker is a secure remedy, with limited requirements for follow-up, close interactions, and number of procedures in a COVID-19 patient.

## Keywords

Case report • COVID-19 • Asystole • Leadless pacemaker • Atrial fibrillation • Atrioventricular block

## Learning points

- COVID-19 patients can present with an acute coronary event early on in the disease. Our patient had an acute coronary event 2 days after COVID-19 was diagnosed.
- Asystole can present in severe COVID-19 patients despite preserved LV function. This can occur later on in the disease, as in our patient who experienced the first episode on day 14.
- Other concomitant phenomena, such as atrial fibrillation or AV block, may be also related to COVID-19 infection.
- A leadless pacemaker is a secure remedy, with limited requirements for follow up, close interactions, and number of repeat procedures with a COVID-19 patient.

## Introduction

COVID-19, the pandemic viral illness caused by SARS-CoV-2, continues to actively spread across the world, with an approximate case fatality rate of 1%. Even though it is mainly a respiratory illness, it causes multiorgan dysfunction, especially in severe cases.

There has been growing experience with cardiac manifestations of COVID-19 patients. Besides precipitation of acute coronary syndrome, myocarditis and resultant malignant tachyarrhythmias have been described.<sup>1</sup> Bradyarrhythmias including sinus node dysfunction and transient heart block have also been reported.<sup>2,3</sup> However, prolonged and recurrent pauses requiring pacemaker implantation has not been reported in COVID-19 patients so far. Cardiac involvement indicates a worse prognosis, and management of these patients can be challenging. We report a COVID-19 patient with unusually long asystolic pauses who underwent leadless pacemaker implantation.

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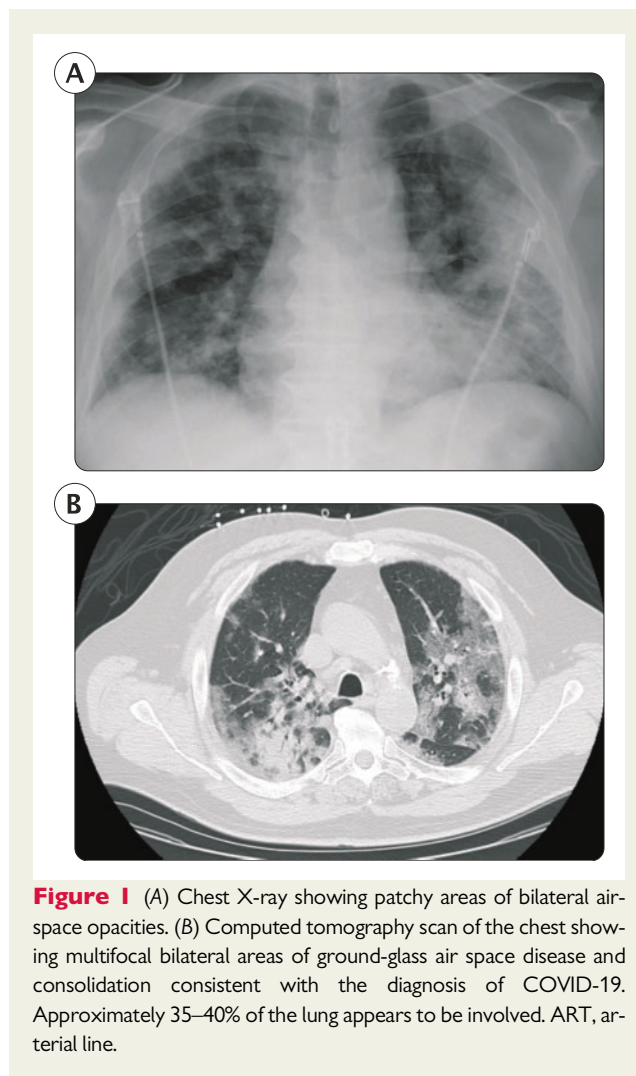
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## Timeline

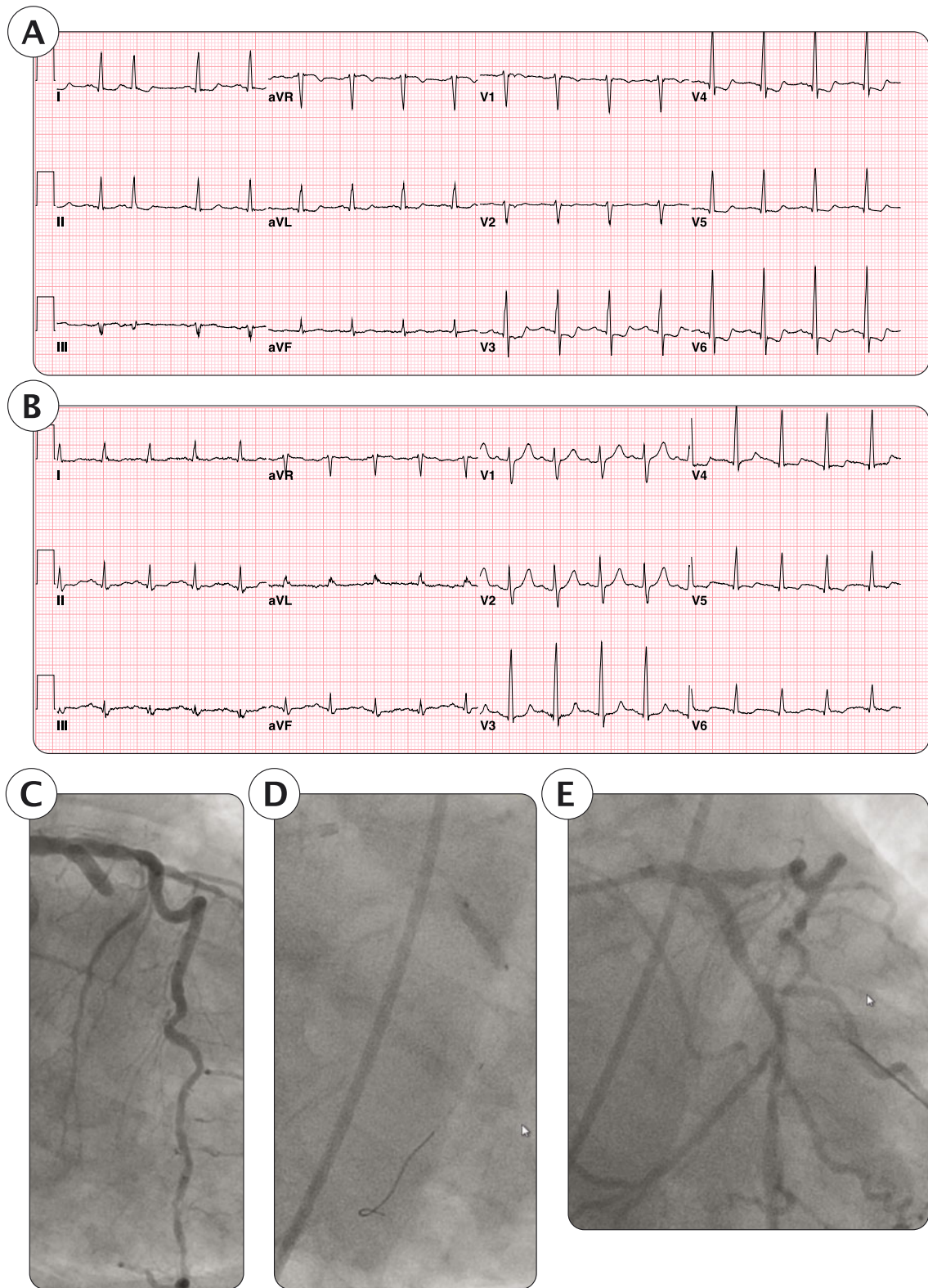
Time	Progress
Day 1	Diagnosed with COVID-19; bilateral infiltrates on chest X-ray and CT scan
Day 2	Acute ischaemia/posterior MI; PCI of Lcx and intubation
Day 5	V-V ECMO
Day 8	Decannulation from V-V ECMO
Day 14	First episode of asystole; recurrent pauses over the next 3 days
Day 17	Leadless pacemaker implantation
Day 27	Extubation
Day 50	Discharge to rehabilitation facility

## Case presentation

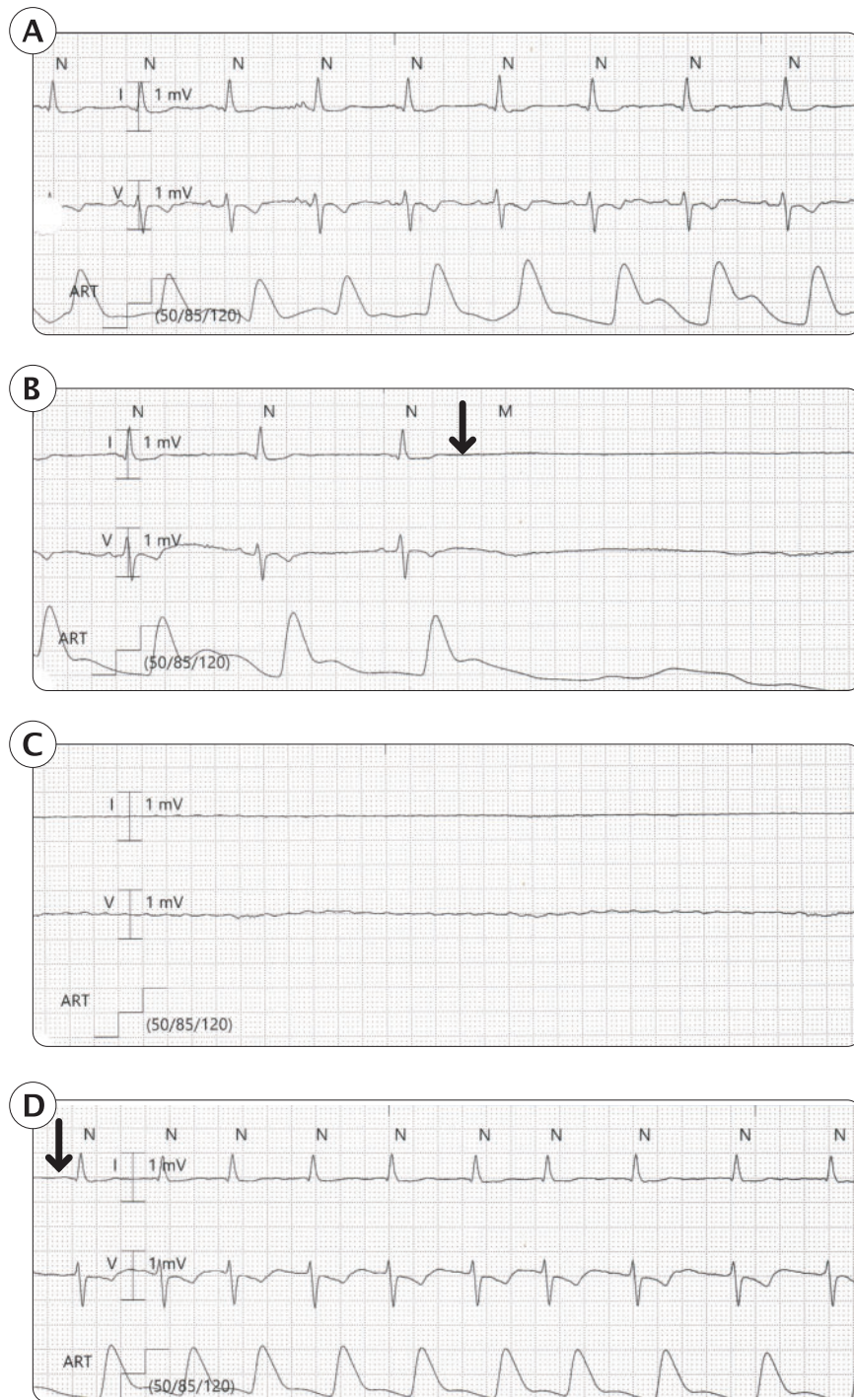
A 62-year-old white male with no significant medical history except for hypertension, presented to the emergency room of one of our community hospitals with a flu-like illness of 1 week duration and shortness of breath with hypoxia. His home medications were lisinopril 40 mg once daily and atenolol 50 mg daily. On initial presentation, his vitals were normal except for a pulse oximetry of 89% and a weight of 102 kg with body mass index (BMI) of 29.8 kg/m<sup>2</sup>. Even though he complained of low grade fever, his initial temperature was normal at 36.8°C. His cardiovascular system examination revealed a regular rhythm with normal venous pressure and heart sounds. The only positive finding in his physical examination was crackles in the back of the chest. His chest X-ray and CT scan showed multifocal bilateral infiltrates (Figure 1). Initial ECG was within normal limits, with a normal PR interval of 160 ms. He was admitted to the hospital and started treatment with supplemental oxygen via a nasal canula and the antibiotics azithromycin and ceftriaxone. COVID-19 test by polymerase chain reaction (PCR) was returned positive later that day. Two days later, he developed crushing substernal chest pain with serial ECG changes suggestive of posterior myocardial infarction. Emergency coronary angiogram revealed occlusion of a large co-dominant proximal left circumflex artery (LCx), for which he promptly underwent primary percutaneous coronary intervention (PCI) with implantation of a drug-eluting stent, Xience Alpine, 3 × 15 mm (Abbott Vascular, Santa Clara, CA, USA), with excellent angiographic results (Figure 2). Post-procedure, he was initiated on clopidogrel 75 mg/day in addition to aspirin 81 mg/day that was started previously. During the procedure, his respiratory distress worsened, requiring intubation and mechanical ventilation. He was transferred to our centre on the fifth day after the initial hospitalization because of worsening hypoxia and haemodynamic instability. Soon after arrival, he was placed on veno-venous extracorporeal membrane oxygenation (V-V ECMO). He was decannulated 3 days later while remaining on the ventilator. He was given a full 10-day course of hydroxychloroquine and also received the additional antibiotics



piperacillin/tazobactam. Serum troponin I levels peaked at 40.47 ng/mL on day 5 of the hospitalization and then down-trended to <1 ng/mL (reference <0.03 ng/mL), though not completely reaching baseline. Other pertinent laboratory data included normal renal function, normal complete blood cell count with relative lymphopenia at 380 cells/mm<sup>3</sup> and elevated lactate dehydrogenase (LDH) levels at 336 U/L (reference range 84–246 U/L) on admission. Interleukin-6 (IL-6) levels was at 14 pg/mL (reference range is <5 pg/mL) on day 3. C-reactive protein at 30.34 mg/dL (reference value <1), D-dimer levels of 33 976 ng/mL FEU (reference range <500) and ferritin levels at 1592 µg/L (reference range 20–300) were also elevated, on admission. On his 14th hospital day he had his first episode of asystole lasting 16 s. In the next 3 days, he had multiple sinus pauses without an escape rhythm, many lasting longer than 20 s (Figure 1). These episodes occurred spontaneously without any negative chronotropic medications and without events causing an increase in intrathoracic pressure such as coughing, suctioning of the endotracheal tube, changing the patient's position, etc. He had not been hypoxic or on any pressors or inotropes during this time. As expected, concomitant arterial pressure tracing also showed flatline, along with the episodes of asystole. At the end of each pause, the returning rhythm was atrial



**Figure 2** (A) Twelve-lead ECG showing acute ST-segment depressions in the precordial and lateral leads. (B) Follow-up ECG showing an increase in the R/S ratio in leads V1 and V2 suggestive of evolving posterior wall myocardial infarct. (C) Initial coronary angiogram showing acute total occlusion of the LCx artery. (D) Deployment of a drug-eluting stent in the LCx artery. (E) Final angiogram showing full patency in the LCx artery post-stent deployment. ART, arterial line.



**Figure 3** (A) Normal sinus rhythm at 83 b.p.m. preceding the pause. (B) Onset of the pause with slowing of the sinus rate for three cycles. (C) Part of the body of the pause. Duration of the pause between the arrows of 16 s. (D) Return rhythm of atrial fibrillation after the pause. ART, arterial line.

fibrillation that would spontaneously convert into normal sinus rhythm after several hours. His echocardiogram on the day when he had his first episode of asystole showed preserved left ventricular systolic function with an ejection fraction of 55–60% and posterior-lateral hypokinesia.

Initially transcutaneous pacing was attempted but was not effective even at maximum outputs. The episodes continued for the next 2 days. As these episodes occurred some time after the index myocardial infarction and without provocation, the need for a permanent pacemaker was thought to be high. Because we wanted to minimize

the number of procedures for the patient and reduce the risk of exposure for the healthcare staff during the implant and during the follow-up period, a decision to proceed with the implantation of a leadless pacemaker was made, without going through an interim temporary pacemaker.

The leadless pacemaker was inserted on the 17th hospital day after obtaining appropriate consent. Micra™ VR (Medtronic, Minneapolis MN, USA) was inserted in a standard fashion through the femoral vein (Figure 4). Our pre-established COVID-19 protocol was followed, including adequate personal protective equipment and the procedure being performed in a designated, catheterization laboratory.

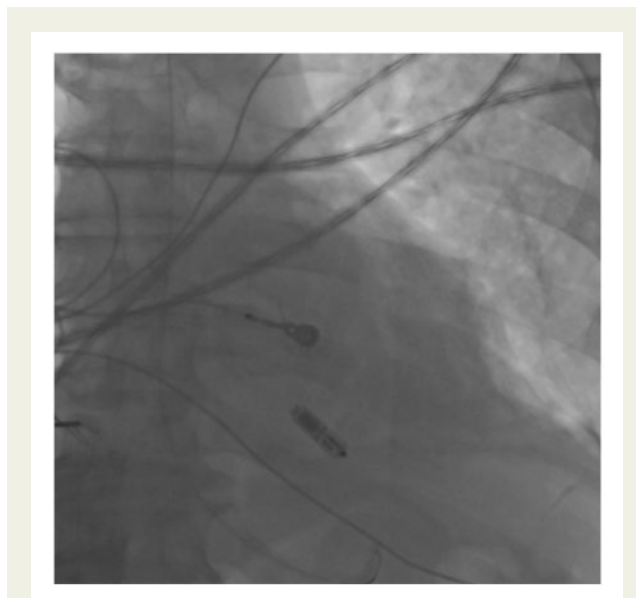
On completion of the procedure, the patient was transferred back to the COVID-19 unit, where he continued to remain on a ventilator for the next 10 days, followed by successful extubation.

The leadless pacemaker was interrogated wirelessly without added exposure risk to the staff on the day following the implantation and 5 days after the implant. Seven days post-implant the percentage of pacing was 3.4% and at 6 weeks post-implant it as 1.5%. A week after the implant, the patient underwent magnetic resonance imaging (MRI) of the brain due to mental status changes without any adverse effects on his pacemaker. He was successfully extubated 10 days after the leadless pacemaker implantation, and was eventually discharged on the 50th day of hospitalization to a rehabilitation facility, where he continues to recover gradually. His discharge medications included aspirin 81 mg/day, atorvastatin 80 mg/day, and metoprolol 12.5 mg twice per day.

## Discussion

We present a case of a severely ill COVID-19 patient who developed unusually long episodes of asystole treated with a leadless pacemaker. To our knowledge, this is the first report of prolonged episodes of asystole in a COVID-19 patient receiving leadless pacemaker implantation.

Very long asystolic pauses, lasting 20 s and longer without any escape rhythm, are unusual in hospitalized patients irrespective of their clinical status. This was especially puzzling in our patient who had no previous major comorbidities and had an apparently structurally normal heart, except for his recent acute posterior myocardial infarction, treated promptly and successfully by primary PCI to the co-dominant LCx artery. The rhythm preceding the pause was always normal sinus rhythm with rates in the 80s and the pauses were preceded with slowing of the sinus beats for 2–3 cycles. During the pauses, atrial fibrillation occurred consistently, with absence of atrioventricular (AV) conduction. The presence of concomitant sinus arrest, AV block, and atrial fibrillation, many days after successful revascularization spoke against intrinsic sinus node dysfunction and ischaemia. Heightened parasympathetic tone can result in simultaneous sinus slowing and AV block. These episodes, especially in intubated patients, have provoking factors. However, in our patient, these episodes started occurring 2 weeks after intubation without any provoking factors. Inflammation, on the other hand, has been shown to activate afferent vagus nerves.<sup>4</sup> Prostaglandin-dependent mechanisms have also been implicated in activating vagus nerve afferents by increasing levels of circulating IL-1β.<sup>5</sup> SARS-CoV-2 infection is known to provoke a



**Figure 4** The leadless pacemaker Micra™ VR (Medtronic, Minneapolis MN, USA) in its final position on the septal wall of the right ventricle.

severe immune response<sup>6</sup> thought to be responsible for many of the systemic symptoms. It is not known whether there is an excess of local or systemic adenosine release with severe COVID-19. Adenosine has been associated with simultaneous sinus bradycardia and AV block after ticagrelor administration.<sup>7</sup> All reported cases with ticagrelor administration occurred in the first few hours/days of the onset of acute coronary syndrome.<sup>8</sup> Our patient has been on clopidogrel and his presentation of bradyarrhythmia was much more dramatic than those reported with ticagrelor. Finally, the virus is known to have a direct myocardial effect, but asystole has not been reported, although recently a transient AV block was reported as well as case series of sinus node dysfunction in COVID-19 patients.<sup>2,3</sup> We did not perform an endomyocardial biopsy to positively rule out myocarditis because the patient's left ventricular systolic function was preserved.

Management of bradyarrhythmia in hospitalized patients who have a reversible or inciting cause is usually accomplished with the placement of a transvenous temporary pacemaker. In our patient, the dramatic episodes of asystole had occurred very late after revascularization and hence were unlikely to be predictably reversible. We were unclear about the aetiology and therefore the natural history of the asystole. The episodes of asystole also prevented the attempts to extubate him. The lack of negative pressure rooms created a challenge if repeated procedures were to be performed. In order to minimize the number of procedures, personnel involved, and utilization of personal protective equipment, as well as to maximize the reliability of the pacing when needed, the decision to implant a leadless pacemaker from the femoral vein was considered the best choice under the circumstances. The femoral venous route also helped to observe a safer distance from the patient's respiratory tract, operating from the groin area, in comparison with a conventional permanent pacemaker implantation.

## Conclusion

We report here a case of prolonged episodes of asystole in a patient who is COVID-19 positive. A leadless pacemaker can be used to successfully remedy this situation, with limited requirements of close interaction with the patient including during the immediate follow-up period.

## Lead author biography



Ivan Cakulev, MD, is a clinical cardiac electrophysiologist at University Hospital Cleveland and assistant professor at Case Western Reserve University. He has a very busy clinical practice performing large number of complex ablations but also device implants. He also spends significant amount of his time educating and training cardiology and cardiac electrophysiology fellows.

## Supplementary material

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

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

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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