Lazarus in asystole: a case report of autoresuscitation after prolonged cardiac arrest

David J. Sprenkeler *, Gerardus P.J. van Hout, and Steven A.J. Chamuleau

Division of Heart & Lungs, Department of Cardiology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands

Received 17 March 2019; first decision 23 April 2019; accepted 22 July 2019; online publish-ahead-of-print 7 August 2019

Background
Third-degree atrioventricular (AV) block can result in sudden cardiac death if no reliable escape rhythm is present. Here, we report a case of an 86-year-old female patient who developed a third-degree AV block leading to cardiac arrest. Surprisingly, sinus rhythm returned after 4 min of asystole, and she showed complete neurological recovery.

Case summary
Emergency services were contacted by the husband of an 86-year-old woman after she was found unconscious. Ambulance personnel diagnosed a third-degree AV block without an escape rhythm and transcutaneous pacing was started. At arrival on the emergency ward, pacing was inadequate, resulting in absence of circulation for ~10 min. After consultation with the family, the patient turned out to have signed a ‘do not resuscitate’ order. Given the impression that the considerable delay deemed favourable neurological recovery unlikely, it was decided together with the family to stop the resuscitation. Subsequently, she had an intermittent junctional escape rhythm but eventually developed a documented asystole of more than 4 min. Against all expectations, she regained sinus rhythm and fully recovered. Eventually, a pacemaker was implanted and she was discharged home without neurological sequelae of the cardiac arrest.

Discussion
Autoresuscitation, also known as the Lazarus syndrome, is the spontaneous return of circulation after cardiac arrest and is incidentally seen after failed cardiopulmonary resuscitation (CPR). Autoresuscitation in the absence of CPR is highly unusual, but could, in this case, be due to the total AV block as the cause of the cardiac arrest.

Keywords
Case report • Autoresuscitation • AV block • Asystole • Lazarus syndrome

Learning points
• Autoresuscitation, also known as the Lazarus syndrome, is a rare medical phenomenon of spontaneous return of circulation after cardiac arrest.
• In the case of atrioventricular block resulting in asystole and cardiac arrest, electrical activity can reappear, even after a long period of asystole.
• In those cases, one should be cautious of diagnosing death prematurely.

* Corresponding author. Tel: +31 6 5310 4790, Email: D.J.Sprenkeler@umcutrecht.nl
Handling Editor: Tom de Potter
Peer-reviewers: Konstantinos Iliodromitis and Dmitry Duplyakov
Compliance Editor: Amir Aziz
Supplementary Material Editor: Peregrine Green
© The Author(s) 2019. Published by Oxford University Press on behalf of the European Society of Cardiology.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
Introduction

Third-degree atrioventricular (AV) block, also known as complete heart block, is, like most severe conduction disease of the heart and can lead to sudden cardiac death if no reliable escape rhythm is present. Here, we describe a case of complete heart block without escape rhythm, resulting in prolonged cardiac arrest. Against all odds, the patient made a full neurological recovery.

Timeline

| Time       | Event                                                                 |
|------------|----------------------------------------------------------------------|
| 22:30      | Complete heart block, start of transcutaneous pacing by ambulance personnel |
| 23:20      | Presentation at emergency department, significant delay until adequate pacing |
| 23:40      | Because of poor prognosis, decided to stop pacing                      |
| 00:00–02:00| Intermittent agonal heart rhythm, <20/min and complete atrioventricular (AV) block with junctional escape rhythm of 40/min, start of palliative sedation |
| 02:07–02:11| Total AV block without escape rhythm resulting in asystole of 4 min    |
| 04:00      | Regained consciousness, midazolam infusion stopped                    |
| 06:30      | Fully awake, maximal Glasgow coma scale, no neurological sequelae of cardiac arrest |
| Day 2      | Dual-chamber pacemaker implantation                                    |
| Day 3      | Discharged home                                                        |

Case presentation

An 86-year-old woman was brought to the emergency department after she was found unresponsive by her husband. She was known with insulin-dependent type II diabetes mellitus and an anaplastic oligodendroglioma with epileptic seizures, diagnosed 1 year ago, for which she was started on levetiracetam and recently received radiotherapy.

The first cardiac rhythm recorded by the ambulance personnel was third-degree AV block in absence of an escape rhythm. Transcutaneous pacing with an external defibrillator was started, which resulted in return of circulation with a systolic blood pressure of around 90 mmHg.

Upon arrival in the hospital, however, she was accidentally disconnected from the external pacemaker, which went unnoticed until she was connected to the electrocardiogram (ECG) monitor. At that moment, the patient had complete heart block with no escape rhythm, an agonal breathing, and was peripherally cold. A second attempt of transcutaneous pacing was made, which at first had no capture, but after increasing the output of the pacemaker, circulation was restored. A point-of-care arterial blood gas revealed a pH of 7.22, a pCO₂ of 40 mmHg, a pO₂ of 136 mmHg, a bicarbonate of 16.2 mmol/L, and a base excess of -12 mmol/L. The lactate level was 11.7 mmol/L.

It then became known from the medical record that the patient had previously signed a ‘do not resuscitate’ (DNR) order. However, her wishes concerning intubation and mechanical ventilation were not further specified. Yet, due to the high amperage of the transcutaneous pacing, she was in acute distress, demanding sedation and intubation if transcutaneous pacing was to be continued.

The dilemma regarding intubation and mechanical ventilation was discussed with the family. Her husband made clear that she would not have wanted to be kept alive by mechanical support if there was no chance for a meaningful recovery. Due to the combination of a malignant brain tumour and prolonged cerebral hypoxia caused by substantial delay in adequate pacing (out-of-hospital before ambulance arrival ~10 min, in-hospital ~5 min), we considered the chances of neurological recovery highly unlikely. Therefore, in agreement with the family, it was decided to stop the transcutaneous pacing, after which an agonal heart rhythm of <20 b.p.m. was seen. The family was then given some time alone with the patient during her (presumed) final moments.

However, when the patient was reassessed 20 min later, she was breathing spontaneously, had a faint pulse and had regained a junctional escape rhythm of 50 b.p.m. Considering the poor prognosis, we decided together with the family, to admit her to the ward for palliative sedation to limit physical distress.

In the next hour, intermittent sinus bradycardia and total AV block with a nodal escape rhythm were seen. However, 1 h later, heart rate slowed down, resulting in complete heart block and asystole, which lasted for ~4 min (Figure 1). Again, an escape rhythm of around 40 b.p.m. reappeared.

Another 2 h later, the family informed the medical staff that the patient had regained consciousness, despite continuous sedation with infusion of midazolam of 1.5 mg/h. When we reassessed her, she opened her eyes spontaneously and could obey simple commands. She had a heart rate of 40 b.p.m., a blood pressure of 130/60 mmHg, a temperature of 36.7°C, and an oxygen saturation of 95% at room air. The ECG showed a third-degree AV block with a ventricular escape rhythm of 40/min with a left bundle branch block morphology (Figure 2). The midazolam infusion was stopped. One hour later, the patient was fully awake and had a maximal score on the Glasgow coma scale. In the following hours and days, no neurological sequelae of the prolonged cardiac arrest were seen. Furthermore, AV conduction recovered completely (Figure 3). Two days after the event, a permanent dual-chamber pacemaker was implanted and the patient was discharged home.

Discussion

We report a case of full neurological recovery after autoresuscitation from complete heart block without escape rhythm, resulting in documented asystole of at least 4 min. Autoresuscitation or the spontaneous return of circulation after cardiac arrest is referred to as the ‘Lazarus phenomenon’, named after the biblical figure Lazarus of Bethany, who was resurrected by Jesus Christ 4 days after his death.1 While autoresuscitation is rare medical phenomenon, increasingly more cases have been reported in recent years.2 In most cases, autoresuscitation is seen after failed cardiopulmonary resuscitation (CPR). The current literature on this phenomenon is primarily

Figure 1

Figure 2

Figure 3
Figure 1 Three snapshots from the telemetry between 2:07 and 2:10. (Above) At 2:07:13 sinus rhythm with 2:1 block evolves into a third-degree atrioventricular block without escape rhythm and subsequently asystole. (Middle) Between 2:07 and 2:10 complete asystole is seen. (Below) At 2:10:44, a premature ventricular complex occurs, after which a ventricular escape rhythm returns.

Figure 2 Complete atrioventricular block with a ventricular escape rhythm of ~40 b.p.m. with a leftward axis and left bundle branch block morphology and terminal negative T waves in V1–3.
anecdotal with only two observational studies published so far. Sheth et al.\textsuperscript{3} studied if the 2-min observation period after asystole is sufficient to declare death in patients that underwent organ donation. Of 73 patients included, no cases of autoresuscitation were seen after 2 min of asystole. In another study of 41 intensive care unit patients for whom was decided to withdraw life-sustaining therapy, Dhanani et al.\textsuperscript{4} found that circulation does not resume after 89 s of its absence. Therefore, in the presented case, the recovery of cardiac activity after 4 min of asystole in the absence of CPR is highly exceptional.

While the underlying mechanism remains unknown, some theories exist, which all involve the delayed effects of interventions during CPR. Rapid mechanical ventilation can result in hyperinflation of the lungs and positive end-expiratory pressure, causing a reduction in venous return and reduced cardiac output.\textsuperscript{5} Furthermore, because of the impaired venous return, drugs (e.g. adrenaline) administered during CPR are poorly delivered centrally. After cessation of CPR, venous return is improved, causing a delayed effect of the adrenaline.\textsuperscript{6} However, in our case, because of the DNR, no chemical resuscitation with adrenaline was performed. Nonetheless, the specific cause of cardiac arrest in this case, i.e. third-degree AV block, can be intermittent, probably due to alterations in vagal tone in combination with underlying degenerative conduction disease. This may the cause of the recurrence of an escape rhythm after the prolonged asystole.

In general, prognosis after autoresuscitation is poor. A systematic review of Ballesteros-Peña et al.\textsuperscript{7} found that 64% of all patients died prior to discharge. Even if the patient survives, the risk of neurological impairment is considerable. Therefore, the perfect neurological recovery in our case is puzzling. Ischaemic preconditioning of the brain due to intermittent cerebral perfusion is an interesting hypothesis. Similar to preconditioning of the heart, exposing the brain to short periods of ischaemia–reperfusion can protect against the debilitating effects of prolonged ischaemia.\textsuperscript{8} Thus, the intermittent recurrence of cardiac output may have saved her from substantial brain damage due to the 4-min asystole.

As Lazarus was resurrected 4 days after his death, we presented a patient who recovered completely after 4 minutes of asystole.

**Lead author biography**

David J. Sprenkeler was born on 2nd of May, 1990 in Amsterdam, the Netherlands. From 2008 to 2014, he studied Medicine at Utrecht University. During study, he discovered his fascination for Cardiology and particularly the field of cardiac arrhythmias and electrophysiology.

After obtaining his Medical degree, he started a PhD trajectory at the Department of Medical Physiology and Cardiology. He defended his thesis entitled 'Ventricular arrhythmias in the remodeled heart: focus on risk prediction and monitoring' in 2018.

Since January 2019 he is a resident in training in Cardiology in the University Medical Center Utrecht.

**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.

References
1. Bray JG. The Lazarus phenomenon revisited. Anesthesiology 1993;78:991.
2. Hornby L, Dhanani S, Shemie SD. Update of a systematic review of autoresuscitation after cardiac arrest. Crit Care Med 2018;46:e268–e272.
3. Sheth KN, Nutter T, Stein DM, Scales TM, Bernat JL. Autoresuscitation after asystole in patients being considered for organ donation. Crit Care Med 2012;40:158–161.
4. Dhanani S, Hornby L, Ward R, Baker A, Dodek P, Chamber-Evans J, Fowlser R, Friedrich JG, Gower RJ, Kutsogiannis DJ, McIntyre L, Momoli F, Morin K, Ramsay T, Salee D, Writer H, Yildirim S, Young B, Shemie S. Vital signs after cardiac arrest following withdrawal of life-sustaining therapy. Crit Care Med 2014;42:2358–2369.
5. Adhiyanam V, Adhiyanam S, Sundaram R. The Lazarus phenomenon. J R Soc Med 2007;100:552–557.
6. Sahni V. The Lazarus phenomenon. JRSM Open 2016;7:205427041665352.
7. Ballesteros-Peña S, Fernández-Aedo I, Lornio S. Spontaneous return of circulation after termination of cardiopulmonary resuscitation maneuvers: a systematic review of cases of Lazarus phenomenon. Emergencias 2014;26:307–316.
8. Sprick JD, Mallet RT, Przyklenk K, Rickards CA. Ischaemic and hypoxic conditioning: potential for protection of vital organs. Exp Physiol 2019;104:278.