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Ventricular Fibrillation Unresponsive to Standard Defibrillation Followed by Unassisted Return of Spontaneous Circulation: The Lazarus Phenomenon

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Abstract The Lazarus phenomenon or the unassisted return of spontaneous circulation (ROSC) after cessation of cardiopulmonary resuscitation (CPR) continues to be a mystery and so far there is no scientific explanation of the exact mechanism of autoresuscitation. The occurrence of this phenomenon is probably widely underreported and have been described in the medical literature at least 40 times since 1982. This paper presents an unique case of an 68-year-old man with third-degree atrioventricular (AV) block and an implanted cardiac pacemaker with refractory ventricular fibrillation (RVF) unresponsive to standard defibrillation (SD) followed by delayed or unassisted ROSC after cessation of CPR with an irregular idioventricular rhythm, as well as intermittent ventricular non-capture pacemaker stimuli. We decided to share this case via publication because this phenomenon is not well understood and there are likely many cases of unassisted ROSC after cessation of CPR that are no reported.

Keywords: *autoresuscitation, cardiopulmonary resuscitation (CPR), cardiac arrest, Lazarus phenomenon, unassisted return of spontaneous circulation, refractory ventricular fibrillation (RVF)*

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1. Introduction

Refractory ventricular fibrillation (RVF) is a life-threatening arrythmia that persists despite at least 3 single standard defibrillation (SD) attempts and administration of anti-arrhythmic medication [1]. Patients who remain in RVF have a high mortality rate and those who survive resuscitation may present post-cardiac arrest myocardial dysfunction, significant ischemic burden and poor neurologic outcomes at hospital discharge [2]. The survival rates from VF are between 21.4-29.3% vs. 5.6-8.2% in RVF [1]. Autoresuscitation was not reported in medical literature until 1982 [3]. The term Lazarus Phenomenon was first used, by the anesthesiologist Jack G. Bray, in 1993. The term originates from the Biblical story of Lazarus of Bethany, who died and was resurrected by Jesus Christ four days later [4]. The Lazarus phenomenon or autoresuscitation, was defined as an unassisted return of spontaneous circulation (ROSC), after cessation of cardiopulmonary resuscitation (CPR) [3]. The exact mechanism or causes of delayed or unassisted ROSC are not well understood. The incidence of this phenomenon is probably widely underestimated and underreported [5]. There is virtual no medical information available to clinicians and researchers describing autoresuscitation. Most of the literature available on this topic is found in the form of case reports or small retrospective literature reviews. There have been at least 40 reported cases in the medical literature of autoresuscitation since the term was described in 1982 [6-12]. This paper presents an unique case of an 68-year-old man with third-degree atrioventricular (AV) block and an implanted cardiac pacemaker with RVF unresponsive to SD followed by delayed or unassisted ROSC after cessation of CPR with an irregular idioventricular rhythm, as well as intermittent ventricular non-capture pacemaker stimuli. We decided to share this case via publication because this phenomenon is not well understood and there are likely many cases of unassisted ROSC after cessation of CPR that are no reported.

2. Case Presentation

An 68-year-old man with a significant past medical history of hypertension, coronary artery disease (CAD), third-degree atrioventricular (AV) block and an implanted cardiac pacemaker was brought to the emergency department by ambulance with a chief complaint of sudden onset of substernal chest pain, accompanied by mild shortness of breath (SOB), nausea and several episodes of exertional chest pain over the past three months. Vital signs (VS) upon initial presentation reveal a temperature of 37.2°C, a pulse rate of 67 beats/min, a respiratory rate of 18 breaths/min, oxygen saturation of

98% at room air and blood pressure of 158/94 mmHg. He had a decrescendo II/VI diastolic murmur at the left lower sternal border. No jugular venous distension (JVD) or carotid bruits were noted. Family history revealed that the patient's father suffered from hypertension and died of myocardial infarction (MI). The initial 12-lead electrocardiogram (EKG) revealed a ventricular-paced rhythm at a rate of 64 beats/min, PR interval of 184 ms, QRS duration of 104 ms and devious signs of left ventricular hypertrophy. His chest x-ray (CXR) revealed a pacemaker on the left side, upper lobe pulmonary venous congestion (PVC) and an atheromatous and tortuous thoracic aorta. His initial laboratory evaluation showed a CK-MB fraction of 1.4 ng/ml, troponin T (cTnT) of 0.182 ng/mL, and an unremarkable comprehensive metabolic panel (CMP). Recommended guidelines for the initial prompt workup and treatment of non-ST elevation myocardial infarction (NSTEMI) were followed at the emergency department before he was admitted to non-intensive telemetry monitored bed with the diagnosis of NSTEMI. The patient was subsequently referred to the cardiology department for recommendations and follow up for electrophysiology studies. The calculated GRACE 2.0 score was of 94 points for a 3 % probability of death from admission to 6 months. The second set of cardiac enzymes showed a CK-MB of 3.0 ng/mL and troponin T (cTnT) of 0.442 ng/mL. Transthoracic echocardiography (TTE) ordered as part of the admission workup was consistent with diastolic dysfunction. The TTE revealed mild concentric left ventricular hypertrophy (IVSd 1.2cm), global hypokinesis of the left ventricle and reduce myocardial contractility (dP/dt 908.4 mmHg/s). The calculated left ventricular ejection fraction (LVEF) was 45%. The next day of the admission the patient developed VF. He was immediately defibrillated at 200 J and the Advanced Cardiovascular Life Support (ACLS) algorithm was followed for VF. He underwent endotracheal intubation and received bag-valve-endotracheal tube ventilation during the resuscitation. The patient received several doses of IV epinephrine, and two doses of IV amiodarone (300 mg and then 150 mg), and twelve unsuccessful defibrillation attempts at 200 J. Unfortunately, he continued in RVF, there was no improvement despite subsequent management, ultimately no ROSC was achieved, and resuscitation was stopped after thirty-eight minutes of ACLS. Subsequently, seven minutes after the termination of resuscitation unassisted ROSC occurred. Unfortunately, ROSC was sustained for at least six minutes before the patient's rhythm was followed by asystole (Figure 1 - Figure 2). Furthermore, no rescue breaths or chest compressions were given to prevent unnecessary prolongation of life. The decision to continue CPR beyond 30 minutes was based on the refractory nature of the dysthymia to SD and the disposal of a large number of medical personnel available to sustain CPR. The decision to forego further CPR and life-prolonging therapies was based on the patient baseline status and the coronary ischemia from the outset.

Figure 1. EKG showing an irregular idioventricular rhythm (IVR) with non-capture pacemaker spikes at a rate of 30-45 beats/min followed by unassisted ROSC after cessation of cardiopulmonary resuscitation

Figure 2. EKG showing an irregular idioventricular rhythm (IVR) and non-capture pacemaker spikes after unassisted ROSC followed by asystole

Table 1. Characteristics and outcomes of patients with RVF and those with a cardiac pacemaker before unassisted ROSC occurred.

Author	Year of publication	Diagnosis	Age, y	Gender	Location	Total resusc. time [a]	Rhythm before unassisted ROSC	Cessation of CPR to unassisted ROSC [a]	Survival [b]
Gomes et al	1996	MI	66	M	IHCA/ED	30	RVF	…	Yes [d]
Powage-Delaney et al	2017	MI	66	M	OHCA/ED	45	RVF	6	Yes [c]
Kämäräinen et al	2007	…	47	M	OHCA	46	RVF	15	Yes[e]
Krarup	2010	MI	85	M	OHCA	15	RVF	5	Yes [c]
Thong	2013	Head Trauma	62	M	IHCA/ICU	40	PEA/Pacemaker	5	No
Wiese	2007	AMI	85	…	IHCA/OR	0	PEA/Pacemaker	6	Yes [f]

AMI = acute mesenteric ischemia; CPR = cardiopulmonary resuscitation; ellipses (...) = data not available; ED = emergency department; ICU = intensive care unit; IHCA = in-hospital cardiac arrest; M = male; MI = myocardial infarction; OHCA = out-of-hospital cardiac arrest; OR = operating room; PEA = pulseless electrical activity; resusc. = resuscitation; ROSC = return of spontaneous circulation; RVF = refractory ventricular fibrillation.

[a] Time from cessation of CPR to unassisted ROSC and total resuscitation time are reported in minutes.

[b] Refers to 24-hour survival.

[c] CPC ≤2 at the time of discharge.

[d] CPC 3 to 5 at the time of discharge.

[e] Died at 3 months post-discharge.

[f] Death occurred within 48-hour of onset of unassisted ROSC.

3. Discussion

There are several etiologies and pathophysiological mechanisms that have been suggested as underlying causes of autoresuscitation; however, since this is an insufficiently researched topic in medicine, the exact mechanism or etiology of delayed or unassisted ROSC are not well understood. So far the only plausible explanation is auto-PEEP and impaired venous return [6]. In most cases of RVF, myocardial ischemia remains the most likely etiology. Ischemia to the heart it associated with an increased risk of potentially fatal cardiac arrhythmias and cardiac arrest. Although, there is a whole spectrum of possible causes and risk factors that could have triggered the cardiac arrhythmia in this patient perhaps ischemia from the outset remained the most likely etiology. We decided to share this case via publication because there are likely many cases of unassisted ROSC after cessation of CPR that are no reported. There have been at least 40 reported cases of the Lazarus phenomenon in medical literature since 1982 [6,7]. The majority of cases of Lazarus phenomenon have been diagnosed as having MI or obstructive pulmonary lung disease (COPD). Most of the cases were on non-VF rhythms (asystole and pulseless electrical activity) when resuscitation was discontinued [6]. Our case is similar to previously described cases in that the patient had been diagnose with NSTEMI during hospital admission and had absent blood pressure, absent heart sound and absent pulse before unassisted ROSC occurred. Nevertheless, it is unique since there is no evidence in the medical literature of a case presenting RVF unresponsive to the best standard of care followed by delayed or unassisted ROSC after cessation of CPR with an irregular idioventricular rhythm, as well as intermittent ventricular non-capture pacemaker stimuli. The most likely explanation that triggered unassisted ROSC in this patient was the implanted cardiac pacemaker. However, this is in seemingly unlikely because his rhythm post unassisted ROSC showed an irregular idioventricular rhythm, as well as intermittent ventricular non-capture pacemaker stimuli (Figure 1-2). There are only four cases that have described unassisted ROSC followed by RVF [13,14,15,16]. All four patients survived 24-hour post-cardiac arrest. Respectively, the first died 3 months post-discharge, the second had a cerebral performance category (CPC) of 2 and was alive one year post-cardiac arrest, the third had a CPC $\geq$ 3 at hospital discharge, and the fourth was discharged 9 days after admission with full neurological recovery. Likewise, two paper have reported unassisted ROSC in patients with a cardiac pacemaker or an implantable cardioverter-defibrillator (ICD). The deaths occurred within 1 hour of onset of unassisted ROSC in one patient and the other within 2 days [17,18]. Previous literature review in this particular subject has reported that about 60% of patients with the Lazarus phenomenon died prior to discharge [6]. Furthermore, there has been reported cases that show patients who have had full neurological recovery [16,19,20]. Table 1 summarizes the characteristics and outcomes of patients with RVF and those with a cardiac pacemaker before unassisted ROSC occurred. This table serves as a quick reference of the currently available literature.

4. Conclusions

Despite several cases of delayed or unassisted ROSC being reported, the Lazarus phenomenon remains a mystery and so far there is no a scientific explanation that can be supported by the available clinical evidence. Most of the reported cases of autoresuscitation have occurred within 10 minutes following the cessation of resuscitation. For the time being, it would be wise to maintain continuous monitoring of cardiac electrical activity for at least 10 minutes, in the patients diagnosed with cardiac arrest due RVF with multiple unsuccessful SD attempts, before the diagnosing of death.

Conflict of Interests

The authors have no conflict of interests.

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