Mode of death in Shapiro syndrome: a case report

Natalia Joanna Braams *, Matthijs L. Hendriks, and Vokko P. van Halm

Department of Cardiology, Amsterdam UMC, Vrije Universiteit Amsterdam, De Boelelaan 1117, 1081HV Amsterdam, The Netherlands

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Background

Shapiro syndrome is extremely rare and is characterized by the triad of spontaneous periodic hypothermia, hyperhidrosis and agenesis of the corpus callosum, resulting in neurological and psychological disorders. The exact mechanism of this syndrome is unknown and treatment consists of controlling the periodic attacks. This case report describes a case of Shapiro syndrome presenting with ventricular fibrillation (VF) who was treated with dual chamber implantable cardioverter defibrillator (ICD) therapy.

Case summary

A 45-year-old man, suffering from Shapiro syndrome with frequent hypothermic attacks, was admitted to the emergency department with an out of hospital cardiac arrest caused by VF due to hypothermia. To prevent cardiac death during future hypothermic attacks with VF, the patient was treated with a dual chamber ICD. Within 1 month after ICD implantation the patient had two events of ventricular tachycardia/VF during hypothermia, which were both successfully terminated by an ICD shock. One year after ICD implantation the patient suffered from an uncontrolled urinary tract infection and the patient passed away. Post-mortem interrogation of the ICD did not reveal further episodes of VF and showed a higher supraventricular heartrate in the last days before his death, probably due to a sinus tachycardia driven by the infection. It was concluded that the most likely cause of death was an uncontrolled sepsis.

Discussion

The current case showed that ICD therapy can be successful in treating VF episodes in patients with unexpected periods of hypothermia.

Keywords

Shapiro syndrome • ICD • Osborn waves • Case report

Learning points

- Implantable cardioverter defibrillator therapy can be successful in treating ventricular fibrillation (VF) episodes in patients with unexpected periods of hypothermia.
- Ventricular fibrillation in patients with Shapiro syndrome can occur without QT lengthening.
- Patients with hypothermic-related VF are at higher risk of developing VF, and should be monitored carefully.

Introduction

Shapiro syndrome is extremely rare with only a few cases in world and first described in the literature in 1969. It is characterized by the triad of spontaneous periodic hypothermia, hyperhidrosis and agenesis of the corpus callosum. The accepted pathophysiological mechanism is the decrease of the ‘set point’ temperature in the hypothalamus, resulting in neurological and psychological disorders. Although the exact mechanism of this syndrome is unknown, some case reports suggest that attacks can be controlled with clonidine or...
In this report, we describe a patient with Shapiro syndrome presenting with ventricular fibrillation (VF) who was treated with dual chamber implantable cardioverter defibrillator (ICD) therapy. So far, this is the first Shapiro syndrome case describing arrhythmias during episodes of hypothermia, hyperthermia and the final episode leading up to the death of the patient.

**Timeline**

| Date       | Event Description                                                                 | Notes                                      |
|------------|-----------------------------------------------------------------------------------|--------------------------------------------|
| February 2016 | Out of hospital cardiac arrest due to ventricular fibrillation (VF) during a hypothermic attack in the context of Shapiro syndrome — dual chamber implantable cardioverter defibrillator (ICD) implantation. |                                            |
| March 2016  | Two periods of ventricular tachycardia (VT)/VF during hypothermic attack, successfully terminated by ICD shock. |                                            |
| April 2017  | Uncontrolled urinary tract infection — patient passed away. Post-mortem interrogation of ICD:  
  - No further episodes of VT/VF.  
  - Higher supraventricular heart rate last days before death; probably a sinus tachycardia in the context of the uncontrolled infection. |                                            |

**Case presentation**

A 45-year-old man was admitted to our emergency department with an out of hospital cardiac arrest caused by VF. His medical history included Shapiro syndrome with many years of recurrent hospitalizations for hypothermia as low as 32°C, often accompanied by ataxia and/or delirium. In an effort to control his hypothermic episodes he was treated with chlorpromazine.

The electrocardiogram (ECG) made by the paramedics on arrival demonstrated VF, which was successfully terminated with three external defibrillator shocks. At return of spontaneous circulation the ECG revealed a sinus bradycardia of 40/min with a normal heart axis, a first-degree AV block and Osborn waves.5,6 A study of Fleming and Muir4 concluded that the appearance of Osborn waves in hypothermic patients is a forerunner of VF, since five out of six hypothermic patients developed VF within 45 min after the appearance of Osborn waves.

Within 1 month after hospital discharge the patient experienced two episodes of ventricular tachycardia (VT)/VF. During the first episode anti-tachycardia pacing during charging was not successful and a high energy shock was delivered (Figure 3). Two weeks later a second episode of VT/VF was terminated for which two high energy shocks were necessary (Figure 4). Hypothermic attacks returned every few days and during both episodes of VT/VF the patient experienced hypothermia. As a consequence of these and former hypothermia episodes, his neurological state was severely affected resulting in being bedridden.

One year after ICD implantation the patient was admitted for a prolonged period due to recurrent episodes of ‘fever’. During the ‘fever’ his temperature was 37.9°C and assumed extremely elevated for this patient. He was diagnosed with a urinary tract infection which was treated with several antibiotics after which he was discharged. Two weeks after discharge the patient unfortunately passed away. Post-mortem interrogation of the ICD did not disclose any further ventricular arrhythmias. At the time of his death the only finding seen on the ICD was a higher supraventricular heart rate, most likely a sinus tachycardia, although a supraventricular arrhythmia could not be excluded (Figure 5). Given the history of the patient, this was attributed to a recurrent infection. Since no autopsy was performed a definitive diagnosis could not be made. It was concluded that the most likely cause of death was an uncontrolled infection.

**Discussion**

To the best of our knowledge, this is the first patient with Shapiro syndrome who was successfully treated with an ICD for recurrent VT/VF. The ICD gave us the possibility to assess the cause of death in the present patient. Although the ICD had successfully converted life-threatening arrhythmias before, the final cause of death was not VT/VF. The fact that ventricular arrhythmias are present and can successfully be treated in Shapiro syndrome was not shown before. On the other hand it could be debated that ICD therapy without treating the underlying hypothermia would be unsuccessful. With the present case we were able to show that ICD treatment in a malignant hypothermic syndrome was successful in treating the VT/VF episodes, something that was not demonstrated before.

Several things can be learned from this case. First, it seems fair to say that VT/VF in patients with Shapiro syndrome can occur without QT lengthening since no QT lengthening was observed directly after resuscitation. Furthermore, the Osborn waves observed after resuscitation reflected the hypothermic state which could be the cause of VF in this patient. Several studies showed an increased risk of VF in hypothermic patients with Osborn waves.5,6 A study of Fleming and Muir6 concluded that the appearance of Osborn waves in hypothermic patients is a forerunner of VF, since five out of six hypothermic patients developed VF within 45 min after the appearance of Osborn waves. However, other reports did not find this association.

The prevalence and amplitude of Osborn waves increase with the severity of hypothermia7 but do not increase the risk of VF.8 In contrast to the study of Fleming and Muir, several other reports have shown that the incidence of VF in hypothermic patients with Osborn waves is low, ranging from 0% to 2%.9–11 Therefore, the correlation between Osborn waves and the development of VF in hypothermic patients is not clear. However, patients with hypothermic-related Osborn waves are at higher risk of developing VF, and should be monitored...
Figure 1 (A) Electrocardiogram after resuscitation; the patient had a temperature of 28.7°C. Notice the Osborn waves (arrows), which are deflection waves in the shape of a hump formed after the QRS complex, typically seen in hypothermia. (B) Electrocardiogram during patient’s normothermic episode of 34°C, where the Osborn waves are not present.

Figure 2 Rhythm strip showing bradycardia and a 2nd degree AV block Type 2 (arrows pointing to P waves).

Figure 3 Beginning of first ventricular tachycardia/ventricular fibrillation episode. Antitachycardia pacing fails to terminate ventricular tachycardia/ventricular fibrillation. ATP, antitachycardia pacing.
In this case, despite the fact that the underlying trigger of the arrhythmias could not be treated, lengthening of life was achieved by successful ICD treatment of the VF episodes. In addition, we were able to demonstrate that the cause of death was not a malignant arrhythmia.

**Lead author biography**

Drs Braams: ‘After finishing my MD I started my PhD at the Amsterdam UMC. The main focus of my thesis is to investigate the effect of treatment of CTEPH on the right ventricle and pulmonary circulation. By using advanced imaging techniques and invasive cardiopulmonary exercise tests we aim to improve patients care’.

**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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