



Propofol Infusion Syndrome Leads to Severe Right Heart Injury and Lethal Arrhythmias

Yuan-Teng Tseng¹, Wen-Rui Hao¹, Ju-Chi Liu¹, Ming-Hsiung Hsieh^{2,3*}

¹Division of Cardiovascular Medicine, Department of Internal Medicine, Taipei Medical University–Shuang Ho Hospital, Taipei, Taiwan

²Division of Cardiovascular Medicine, Department of Internal Medicine, Taipei Medical University–Wan Fang Hospital, Taipei, Taiwan

³Institute of Clinical Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan

Received: Sep 29, 2009
Revised: Mar 30, 2010
Accepted: Apr 28, 2010

KEY WORDS:

cardiac arrest;
coved-type ST elevation;
heart failure;
propofol;
ventricular arrhythmia

Propofol-related infusion syndrome (PRIS) has a high mortality with myocardial failure and dysrhythmias. However, there is no detailed description of the serial cardiac conditions presenting during the critical and recovery periods during PRIS. We report the case of a 24-year-old man with a traumatic head injury who developed PRIS after propofol infusion. Cyanosis, hypotension, neck vein distension, cardiac arrest and ventricular tachycardia occurred. The patient survived PRIS by prompt cessation of propofol, the use of inotropic agents, and short-term hemofiltration. A timely Holter electrocardiogram (ECG) recording, serial echocardiograms and 12-lead ECGs revealed isolated right heart failure, sequential bradycardia, arrest, left bundle branch block-like ventricular tachycardia, and varied coved-type ST elevation in the right precordial leads. All these clinical abnormalities (symptoms, echocardiograms, and ECGs) subsided within a few hours after treatment. The patient was eventually discharged with clear consciousness and without any cardiopulmonary sequelae. Our cardiac survey implied that in PRIS, the right heart is severely injured, both mechanically and electrophysiologically. Injured right hearts can completely and rapidly recover if recognition and treatment are timely.

1. Introduction

Propofol-related infusion syndrome (PRIS) is a rare drug-related complication with a high mortality rate. It was first described by Parke et al in 1992¹ and designated “PRIS” by Bray in 1998.² A total of 69 PRIS cases (33 children and 36 adults) were reported in the literature from 1992 to 2007 and the overall mortality rate is 64%.³ Patients are at high risk of developing PRIS when the propofol infusion rate is higher than 4–5 mg/kg/hr and for a duration greater than 48 hours.^{3,4} The clinical features of PRIS include myocardial failure with dysrhythmias, metabolic acidosis, and rhabdomyolysis.^{5,6} Although

cardiac injury contributes to the high mortality of PRIS, there is no detailed description of the serial cardiac conditions during the critical and recovery periods. To the best of our knowledge, this report is the first description of a timely cardiac survey consisting of Holter electrocardiogram (ECG) recording, paired echocardiograms, and serial 12-lead ECGs in a patient who survived PRIS.

2. Case Report

A 24-year-old man with no significant medical history underwent urgent craniotomy for right intracranial

*Corresponding author. Division of Cardiovascular Medicine, Taipei Medical University–Wan Fang Hospital, 111, Section 3, Hsing Long Road, Taipei 116, Taiwan.
E-mail: mhhsieh@tmu.edu.tw

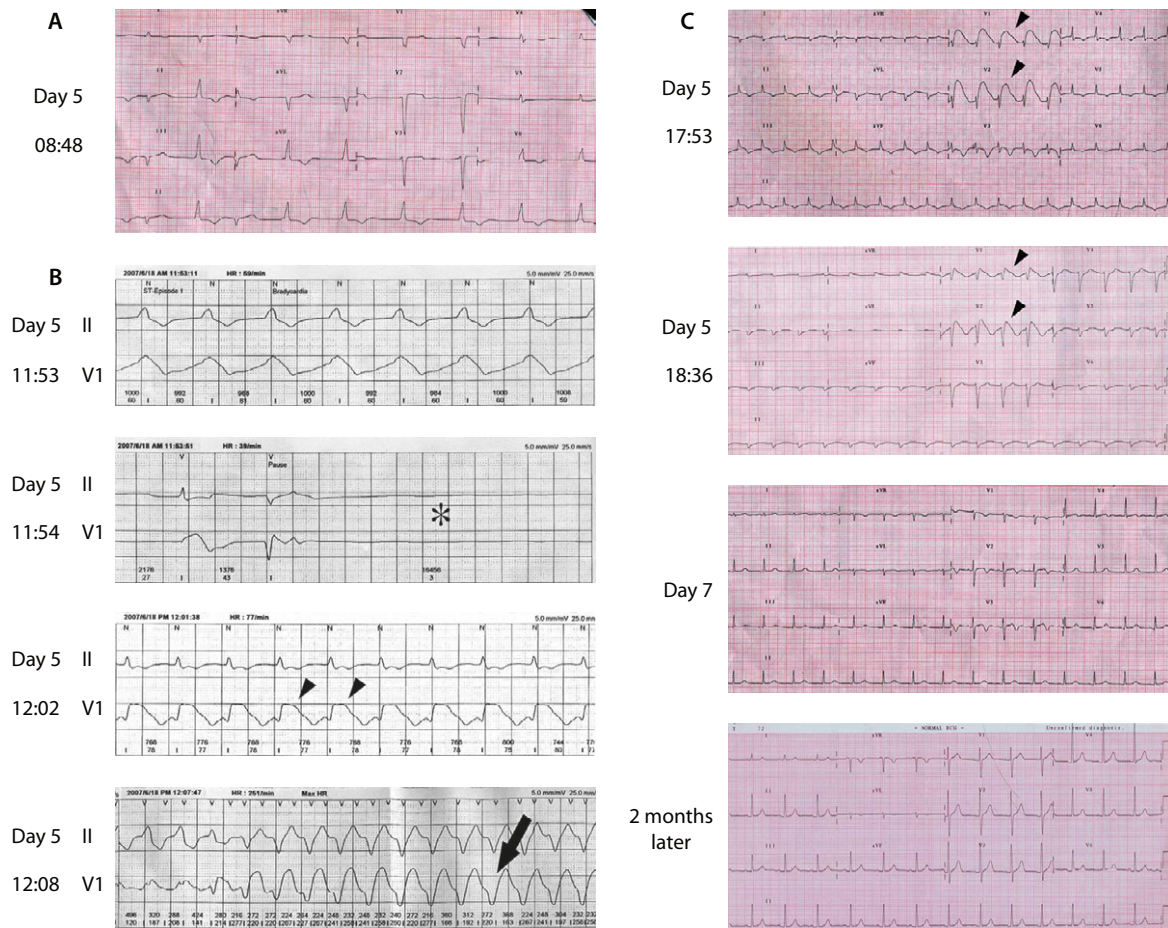


Figure 1 (A) 12-lead electrocardiogram (ECG) after an 84-hour propofol infusion. Junctional bradycardia with intraventricular conduction delay occurred and, therefore, the propofol was discontinued. (B) Holter ECG recordings during the critical period. Three hours after discontinuing propofol, cardiac arrest (asterisk, at 11:54) and a left bundle branch block-like ventricular tachycardia (arrow, at 12:08) occurred. Note the coved-type ST elevation in channel 2 (arrowheads, 12:02) preceding ventricular tachycardia. (C) 12-lead ECGs during the recovery period. Dynamic ST-T changes in leads V1, V2 and V3 occurred. Note the varied types of coved-type ST elevations in the right precordial leads (arrowheads). The ECG was completely normalized 2 months later.

hemorrhage because of a head injury. He was then admitted to the intensive care unit where propofol was infused (at a rate of 3.0–5.8 mg/kg/hr) for sedation and to maintain a low intracranial pressure. After an 84-hour infusion, bradyarrhythmias occurred (Figure 1A) and the propofol was withdrawn. No other sedative agents were given; morphine and cisatracurium besylate were given for pain control and muscle relaxation. However, a junctional rhythm at 45–55 beats/min persisted despite the use of intravenous atropine and catecholamines. Progressive neck vein distension and hypoxia developed. Emergent echocardiography revealed right heart pump failure, right-sided volume overload, and preserved left ventricular contractility (Figure 2A). Meanwhile, a Holter ECG recording was initiated. Three hours after discontinuing the propofol, bradycardia with intraventricular conduction delay progressed to cardiac arrest (Figure 1B), which was resolved after giving inotropic agents and cardiac massage. However, supraventricular tachycardia with coved-type ST elevation in the right precordial leads occurred, followed by ventricular tachycardia

(Figure 1B), which subsided after electric cardioversion. Laboratory examination revealed metabolic acidosis (pH, 7.24; base excess, –15), hyperkalemia (K, 7.7 mmol/L), hepatic failure (alanine aminotransferase, 1379 U/L; total bilirubin, 5.4 mg/dL), and marked muscle damage (creatinine phosphokinase, 79,188 U/L) (Table 1). Serial data of the serum levels of triglyceride were within normal limits and the color of the patient's urine was dark brown. PRIS was diagnosed, and continuous venovenous hemofiltration was initiated. In the following few hours, the neck vein distension, hypoxia and hypotension all resolved and, therefore, the inotropic agents were discontinued. Follow-up echocardiography, 3 hours after the first echocardiography, disclosed the recovery of right ventricular contractility without any volume overload (Figure 2B). During the recovery period, serial 12-lead ECGs revealed dynamic ST-T changes in the right precordial leads, including varied coved-type ST elevations in V1–3 (Figure 1C). No cardiac arrest or ventricular arrhythmias recurred. The continuous venovenous hemofiltration lasted for a total of 7 hours, and no further

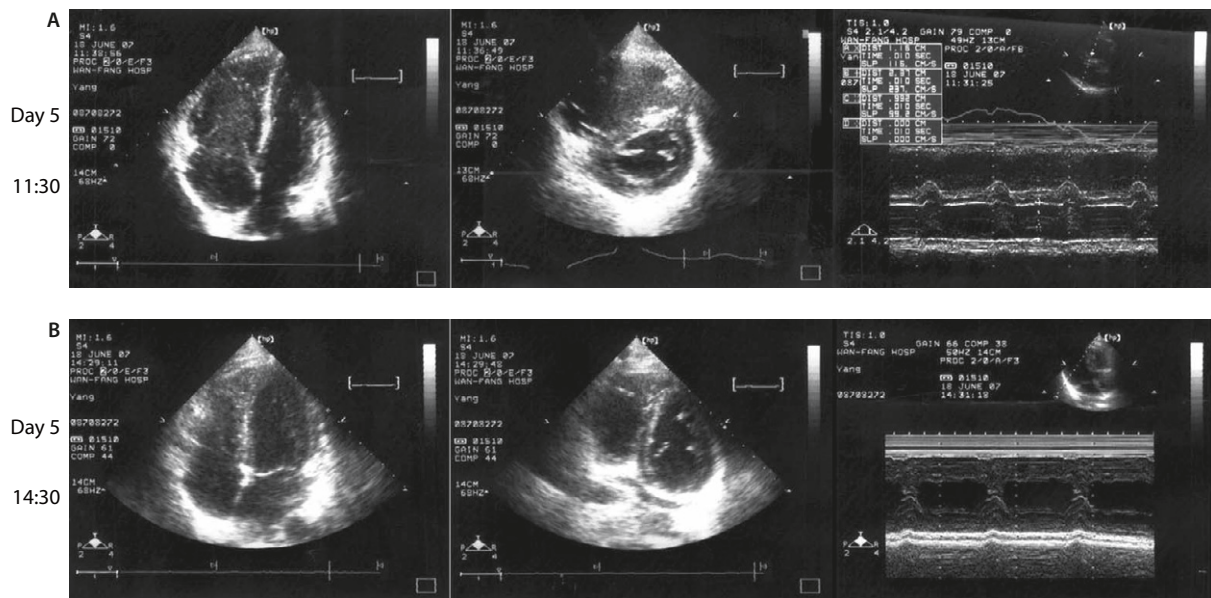


Figure 2 Transthoracic echocardiograms taken during the: (A) critical period; and (B) recovery period. (A) A few minutes prior to the lethal arrhythmia, right heart failure was identified. Left panel: dilated right atrium and right ventricle with stasis of the infused fluid (hyperechoic particles); middle and right panels: flattened septal wall (D sign) during diastole in the short-axis view and paradoxical septal wall motion in the M-mode indicating marked right ventricle volume overload. (B) Three hours later, the right heart failure had completely recovered.

Table 1 Results of the laboratory examination on day 5

	pH/BE	Creatinine (mg/dL)	Potassium (mmol/L)	CPK/CK-MB (U/L)	Tn-I (ng/mL)	AST/ALT (U/L)	Bilirubin total/ direct (mg/dL)
Day 5 morning (during bradycardia)	–	1.7	4.2	48,221/418	0.17	–	–
Day 5 noon (after arrest & VT)	7.24/–15	–	7.7	–	–	639/129	5.4/3.8
Day 5 evening (recovery period)	7.35/–4	2.4	5.1	79,188/458	1.2	2584/1379	4.2/2.5

VT=ventricular tachycardia; BE=base excess; CPK=creatine phosphokinase; CK-MB=MB fraction of creatine phosphokinase; Tn-I=troponin-I; AST=aspartate aminotransferase; ALT=alanine aminotransferase.

metabolic acidosis occurred. The patient recovered well and was eventually discharged 3 months later, after a rehabilitation program for his left hemiparesis. There were no significant cardiovascular or pulmonary sequelae. Follow-up 12-lead ECGs showed that the ECG had recovered to a normal pattern (Figure 1C). To exclude the possibility of any underlying Brugada syndrome, genetic analysis was performed, which showed that there were no *SCN5A* gene mutations. However, a flecainide provocation test was not performed.

3. Discussion

The mechanism of PRIS is thought to be direct mitochondrial respiratory chain inhibition by propofol or its metabolites.^{4,7,8} However, it is unknown whether impaired mitochondrial fatty acid metabolism plays a role.⁹ Propofol uncouples oxidative phosphorylation

and energy production in mitochondria, impairs oxygen utilization and inhibits electron flow along the mitochondrial electron transport chain. It antagonizes beta-adrenoceptor binding and inhibits cardiac L-type calcium currents, leading to diminished cardiac contractility.^{8,9} Treatment strategies include early recognition of PRIS, prompt cessation of propofol, administering inotropic agents, and hemodialysis or hemofiltration.⁴

Among previously reported PRIS patients, six PRIS adults have had an echocardiogram.^{5,10,11} Three of these patients exhibited left ventricular dysfunction, one had a large right ventricle, one had global hypokinesia (unreported which ventricle or whether it was both ventricles), and one had normal results. These findings are discrepant and the details of each echocardiogram were not reported. Our timely 3-hour-interval echocardiograms in both the critical and recovery periods disclosed transient severe right heart failure (right ventricle pump failure with a marked dilated right atrium and ventricle).

Right heart injury may also correlate with coved-type ST elevation in the right precordial leads and lethal arrhythmias.

With regard to dysrhythmias observed in the 36 previously reported PRIS adults, 53% had tachyarrhythmias, 22% had asystole, and 22% had bradycardia.³ Our Holter ECG recording showed all these lethal arrhythmias in sequence, and the lethal ventricular tachycardia had a left bundle branch block-like morphology (Figure 1B). In one case series, six PRIS patients who developed a Brugada-like ECG pattern (coved-type ST elevation in leads V1–3) died within hours because of a ventricular arrhythmic storm.⁷ The authors concluded that the unique ECG pattern in PRIS patients predicts an imminent cardiac death. Our patient had a Brugada-like coved-type ST elevation, not only during the critical period, but also during the recovery period, and various types of the coved-type ST elevation were recorded (Figure 1C). In our patient, the absence of *SCN5A* gene mutations may exclude any underlying Brugada syndrome. Although there is some similarity between PRIS and Brugada syndromes (coved-type ST elevation preceding ventricular tachycardia), it remains inconclusive as to whether they have the same arrhythmogenesis (e.g., right ventricle transmural dispersion of the repolarization, which creates a vulnerable window during which extrasystole can induce ventricular tachycardia).^{7,9,12} Nevertheless, in PRIS, the repolarization abnormalities observed in the right precordial leads and left bundle branch block-like ventricular tachycardia suggest an electrophysiological disturbance of the right heart.

According to our findings from serial echocardiograms, ECGs and Holter recordings, we believe that severe right heart injury, both mechanical and electrophysiological, is of crucial concern in PRIS. Injured right hearts can completely and rapidly recover if recognition and treatment are timely.

Acknowledgments

We thank Professor Lin-Ping Lai for his help with the *SCN5A* gene analysis.

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