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Recovery Following Propofol Associated Brugada Electrocardiogram

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Keywords

Brugada; propofol; sudden death

Introduction

Brugada Syndrome is a genetic disorder associated with an increased risk of sudden cardiac death that has typical electrocardiographic (ECG) patterns. Recently, there have been reports of Brugada ECG patterns seen in critically ill patients who received propofol 1, and this pattern was associated with a very high imminent mortality. We report a case in which a critically ill patient developed a Brugada ECG pattern following high dose propofol infusion. Once the ECG pattern was recognized, the propofol was discontinued and the ECG pattern resolved, and the patient was discharged home with no arrhythmic sequelae.

Case Presentation

A previously healthy 21 year old male was found unresponsive on his couch by his father early one morning after taking alprazolam 9 mg and tramadol 1000 mg orally the evening before. He was taken to a nearby emergency room where he was intubated and started on intravenous propofol 25 mcg/kg/min for sedation and dopamine 10 mcg/kg/min due to hypotension. He was transferred to the ICU of our academic medical center while still under sedation. An electrocardiogram on arrival (2 hours after initial presentation) showed an RSR' pattern with mild ST elevation in V1-V2 (Figure 1). The patient was initially hypothermic (temperature of 33°C) with a mixed acidosis (pH=7.14) and a potassium of 5.4 mEq/L. In addition, he had acute renal failure (creatinine = 2.34 mg/dl), which was thought to be due to rhabdomyolysis (CPK=3269 U/L) from his prolonged immobility post-overdose and exacerbated by use of propofol for sedation. Fourteen hours later, the patient developed a pronounced Type I Brugada pattern on his electrocardiogram with coved type ST segment elevations in V1-V2 (Figure 2). At this time he remained on propofol and dopamine, but his core temperature and potassium had normalized. Due to the ST elevations in the anteroseptal leads and troponin-I elevation of 2.82 ng/mL (normal < 0.1), the patient was sent for cardiac catheterization. Coronary angiography revealed no obstructive coronary disease. The propofol was stopped and the patient was rapidly extubated. His next electrocardiogram, 24 hours after propofol sedation was stopped, showed resolution of the Brugada pattern (Figure

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Conflicts of Interest: None

3). The patient had no prior history of syncope and there was no family history of syncope or sudden death in members of his immediate family. However, given the type I Brugada pattern on his earlier EKG, the patient was taken to the cardiac electrophysiology laboratory. A procainamide challenge could not reproduce the earlier ST elevation over the right precordial leads, and programmed electrical stimulation of the ventricle could not induce any ventricular arrhythmias. A cardiac magnetic resonance imaging study showed normal LV and RV function with no structural abnormalities.

Discussion

The Brugada Syndrome is associated with a high risk of sudden cardiac death due to ventricular tachyarrhythmia 2. The molecular pathophysiology centers around two theories: 1) the repolarization disorder theory espouses phase 2 reentry coupled with an ill-timed extrasystole and 2) the depolarization theory which relies on delayed conduction in the right ventricular outflow tract creating a closed-loop of conduction between the this region and the rest of the right ventricle 3. The Brugada syndrome is diagnosed in the setting of a typical ECG pattern combined with at least 1 of the following clinical features: documented ventricular fibrillation or polymorphic ventricular tachycardia (VT), family history of sudden cardiac death at <45 years of age, coved-type ECGs in family members, inducible VT with programmed electrical stimulation, syncope, or nocturnal agonal respirations. Our patient did not display any of the clinical features diagnostic of Brugada Syndrome and thus was diagnosed with an induced Brugada-type ECG. The Brugada electrocardiographic pattern is much more common than the Brugada Syndrome 2. There are a number of factors that can induce a Brugada-type ECG pattern including hypothermia 4 and hyperthermia 5, hyperkalemia, and drugs 6 including class I antiarrhythmic drugs, tricyclic antidepressants and propofol. Our patient was hypothermic and had a mild hyperkalemia on presentation, but both of these perturbations had resolved prior to the development of the Type I Brugada pattern. In the case of propofol, a syndrome has been described that is characterized by rhabdomyolysis, hyperkalemia, cardiac failure and sudden death. The term *Propofol infusion syndrome* (PRIS) has been coined to encompass this clinical entity 7. Brugada-type ECG changes have been described in the setting of propofol use, and have been linked to a poor prognosis 1:7:8. Vernooy et al reported 7 patients with severe head injuries and PRIS, 6 of whom died of electrical storm within hours of developing a Brugada electrocardiographic pattern. In a series published by Junttila et al, 7 patients were identified to have developed the Brugada ECG pattern during propofol infusion 8. Five of the seven developed sudden cardiac death, one had ventricular tachycardia but survived, and one patient had no clinical consequences.

The mechanism of the PRIS-related Brugada-type ECG and malignant arrhythmias is not clear. Propofol has been shown to block sodium channels in skeletal muscle sarcolemma 9, and patch clamp data from Saint et al suggests that this is also the case for whole-cell rat cardiac sodium channels 10. However, when a canine myocardial wedge preparation was perfused with propofol, ST segment elevation was not observed 1. A common clinical feature observed in the available published case series is high infusion doses of propofol, such that some authors have put forward recommendations that propofol infusions be limited to 4-5 mg/kg/hr 7. However, our patient received an infusion rate of 1.5 mg/kg/hr which is well below this threshold.

Genetic susceptibility to PRIS is not well defined. In the series by Junttila et al, genetic analysis for the SCN5A mutation was only available for 1 of the 7 patients found to have a propofol induced Brugada ECG (and that patient was negative for a SCN5A mutation) 8. Deficiency in the medium-chain acyl-coenzyme A dehydrogenase (MCADD) can present a clinical picture similar to PRIS and may provide a model for future study of the genetic

susceptibility to propofol infusion syndrome 7. Genetic analysis in our patient has been planned for the outpatient setting, but he has not returned for his follow-up appointments.

In the case we have presented, the electrocardiogram reverted to normal after cessation of propofol. The temporal association of propofol infusion and the appearance of the Brugada-type ECG suggests, but does not prove, causality. A re-challenge with propofol to prove the hypothesis of causality was not clinically indicated and did not meet local ethical standards. We did perform provocative testing using a procainamide infusion challenge to bring out the Brugada pattern, and programmed electrical stimulation to gain risk stratification data for planning of future management, and both tests were negative. Ajmaline may be more potent at inducing ST segment elevation in susceptible individuals than procainamide 11, but this is not available for clinical use in the United States of America. Given the absence of clinical events and the negative electrophysiological study, our patient did not receive an implantable defibrillator.

Conclusions

We present a case of a Brugada-type ECG following propofol infusion in which the electrocardiographic signs were recognized, prompting cessation of propofol. Previously published case series have indicated that a Brugada-type ECG in the setting of PRIS is a harbinger of death by cardiac arrhythmias. Although limits to propofol infusion rates have been proposed to avoid this, our patient developed this pattern following an infusion rate (1.5 mg/kg/hr) that is well below the thresholds proposed in the literature (4 to 5 mg/kg/hr). Unlike most other cases reported in the literature, the ECG pattern was promptly recognized, the propofol was discontinued and the patient recovered and was safely discharged. Awareness of this complication is encouraged for physicians who use propofol for sedation and anesthesia.

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Figure 1.

Electrocardiogram on transfer to our tertiary care intensive care unit 2 hours after initial presentation following the overdose. Sinus tachycardia is present with diffuse ST segment elevation with a rSr' pattern in V1-V2. He was on a propofol infusion for sedation and agitation.

Figure 2.

Electrocardiogram 13.5 hours after the initial electrocardiogram. The patient developed a pronounced Type I Brugada pattern with coved ST segment elevation in V1 and V2.

Figure 3.

Electrocardiogram 2 days later. The propofol had been discontinued. The ST segment elevation resolved, leaving only a rS' pattern similar to the initial electrocardiogram.