Published in final edited form as:

J Electrocardiol. 2014 ; 47(1): 80–83. doi:10.1016/j.jelectrocard.2013.07.014.

Catastrophic neurologic syndrome with dramatic ECG changes[☆]

Zachary D. Goldberger, MD, MS^{a,b}, Claire J. Creutzfeldt, MD^{a,c}, and Ary L. Goldberger, MD^{d,*}

^aUniversity of Washington School of Medicine, Harborview Medical Center, Seattle 98104, WA

^bDepartment of Internal Medicine, Division of Cardiology, Seattle 98104, WA

^cDepartment of Neurology, Seattle 98104, WA

^dDivision of Interdisciplinary Medicine and Biotechnology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston 02215, MA

Abstract

Cerebrogenic ECG abnormalities, especially prominent T wave inversions and prolongation of the QT(U) interval, are well-described. Brady- and tachyarrhythmias, including polymorphic VT, have been also described in the setting of neurologic injury. We report an unusual case of a 22-year-old man who presented with idiopathic acute encephalopathy. His hospital course was complicated by persistent fevers, along with refractory seizures treated with propofol. Serial ECG findings included marked ventricular repolarization prolongation with bursts of torsade de pointes, diffuse ST elevations simulating extensive myocardial ischemia or infarction, as well as a Brugada-like pattern. To our knowledge, this case is the first reported with the combination of such findings in a patient with a catastrophic neurologic syndrome.

Keywords

Brugada pattern; Electrocardiogram; Polymorphic ventricular tachycardia; Propofol toxicity; Pseudo-infarct pattern; QT prolongation; Torsade de pointes

Introduction

We report an unusual case of a young adult patient who presented with seizures, associated with an acute, idiopathic encephalopathic process. Treatment included propofol, a potentially cardiotoxic anesthetic. Serial electrocardiograms (ECGs) demonstrated the appearance of a markedly QT(U) interval, polymorphic ventricular tachycardia (VT), bradyarrhythmias, a Brugada-like pattern, as well as more diffuse ST elevations. This case has important basic and clinical implications because it highlights the heterogeneity of major ECG abnormalities that can occur in the context of severe intracranial disease, including

[☆]Disclosures: None.

© 2014 Elsevier Inc. All rights reserved.

*Corresponding author. Harborview Medical Center, 325 9th Avenue, Box 359748, Seattle 98104, WA., zgoldber@uw.edu.

those mimicking acute myocardial infarction and those predisposing to potentially fatal arrhythmias.

Case presentation

A 22-year-old previously healthy man was brought to the emergency department with acute confusion and seizures. He was intubated and transferred to the ICU, with a Glasgow Coma Score of 3. His core temperature was 37.0 °C, heart rate 84 beats per minute, with normal arterial blood gasses (on assisted mechanical ventilation at 12/min, with 5 mmHg of positive end-expiratory pressure, breathing 30% inspired oxygen). His physical examination showed no meningismus or rash. He had intact cranial nerves and no focal findings. Initial laboratory tests were remarkable for a normal metabolic panel and complete blood count. His creatine kinase (CK) was 1,807 units/L (normal 30–285), with normal CK-MB and troponin levels. A chest x-ray revealed no evidence of pneumonia, pulmonary edema, cardiomegaly or other acute process. Computed tomography and magnetic resonance imaging of the brain were unremarkable. A lumbar puncture showed a high opening pressure (34 mmHg; normal 15) and an elevated white blood cell count (16 cells/ μ L; normal 5), consistent with a central nervous system inflammatory process. Initial electrocardiogram (ECG) is shown in Fig. 1.

Continuous electroencephalographic (EEG) monitoring showed non-convulsive status epilepticus. His seizures were refractory to therapeutic doses of phenytoin and levetiracetam. Therefore, propofol was initiated and titrated to suppress the ictal EEG bursts. Viral serologies were negative.

Subsequent ECGs, obtained 3 days after admission, are shown below (Figs. 2 and 3). While initially afebrile, he developed intermittent fevers, with a maximum core temperature of 38.9 °C, and broad-spectrum antibiotic therapy with vancomycin and cefipime was initiated. Of note, in the 16 hour window between these 2 ECGs, there was no increase in core temperature, no new administered medications (nor cessation of previous ones), and his electrolytes were grossly unchanged. A repeat chest x-ray revealed the interval development of pulmonary edema, and bilateral pleural effusions. A transthoracic echocardiogram revealed normal left ventricular size and function, with moderate to severe right ventricular (RV) dilation and dysfunction. A right heart catheterization, performed to further evaluate the unexpected RV dysfunction seen on echocardiography, revealed an elevated mean pulmonary artery pressure of 31 mmHg (normal 9–16), with a mildly elevated pulmonary vascular resistance of 133 dyne/sec/cm⁻⁵ (normal 44–90).

The patient was maintained on a propofol infusion of 6 mg/kg/h. By hospital day 8, his propofol drip was discontinued and replaced by pentobarbital. He had no further recorded tachyarrhythmias, or Brugada-type pattern, and his QTc remained within normal limits.

He remained in critical condition, intubated with a tracheotomy tube, with intermittent seizures despite antiepileptic and barbiturate therapy.

Discussion

This case is remarkable for the heterogeneity of the ECG findings and their rapid evolution, including: marked ventricular repolarization prolongation with bursts of torsade de pointes, diffuse ST elevations simulating extensive myocardial infarction (MI) or ischemia, associated with a junctional bradycardia, and a Brugada-like pattern. To our knowledge, this case is the first reported with the combination of such findings in a patient with a catastrophic neurologic syndrome. The cause of these changes may be related to a number of different mechanisms and etiologies.

Cerebrogenic ECG abnormalities, including T wave inversions (or tall, positive T waves), QTc prolongation and a variety of arrhythmias were first recognized over 60 years ago,¹ with the most dramatic findings reported in patients with intracranial bleeds. Prolongation of the QT interval, often with prominent U waves, is well-documented with cerebrovascular accident, especially subarachnoid hemorrhage.^{2,3} The prolonged QT(U) increases risk for torsade de pointes tachycardia.

Supraventricular and ventricular brady- and tachyarrhythmias, and specifically polymorphic ventricular tachycardia (VT), have also been reported with intracranial disease.^{4,5} The basic mechanisms may be related to alterations in autonomic tone modulation associated at least in part with compression of the brain. Increased vagal nerve activity may occur from stimulation of parasympathetic foci in the region of the hypothalamus and of medullary vagal nuclei.⁶ In addition, intracranial injury can induce heightened sympathetic tone, sometimes resulting in diencephalic seizures (so-called “sympathetic storms”), which are associated with profound dysregulation of hemodynamic and thermal control due to direct toxic effects of catecholamines on the already damaged central nervous system.^{7–9} ECG abnormalities, including prolonged QT(U) intervals and deep T wave inversions (or tall, positive T waves) in patients with certain central neurologic injuries, are not due to myocardial ischemia, but appear to be related to effects of excessive sympathetic stimulation.¹⁰

The classic Brugada pattern, marked by coved, down-sloping ST elevations in the right precordial leads, is also a risk factor for sudden death due to ventricular arrhythmia. The electrophysiologic mechanism responsible is incompletely understood.¹¹ The appearance of Brugada-type patterns has been associated with a variety of agents with sodium-channel blocking effects,¹² especially Class I_C anti-arrhythmic agents). Lithium, tricyclic antidepressants, and cocaine have also been associated with the “unmasking” of Brugada-type patterns.¹³ Moreover, fever, present in this case, can induce this pattern in susceptible individuals, possibly due to premature inactivation of sodium channels.

Propofol (2,6-diisopropylphenol) is a commonly used centrally-acting anesthetic. Toxicity (so-called propofol-related infusion syndrome, manifested by heart failure, rhabdomyolysis, severe metabolic acidosis, and renal failure), is usually seen in patients undergoing long-term (>48 h) sedation at higher doses (>4 mg/kg/h).¹⁴ The risk of sudden death with propofol is well-described, and is heightened in patients with head injury and in those with more sustained drug exposure. Of note, sodium channel blockade from propofol has been

demonstrated in vitro.^{15,16} Furthermore, the development of the full-blown Brugada syndrome with polymorphic ventricular arrhythmias, has been associated with propofol.¹⁷ The cardiotoxicity may be multi-factorial, due to effects on cardiac muscle cells and ion channels, including oxidative uncoupling and impaired mitochondrial respiration contributing to impaired myocardial contractility.¹⁷

Central nervous system catastrophes have also been associated with so-called acute stress-induced cardiomyopathy (also termed left ventricular apical ballooning syndrome or takotsubo cardiomyopathy), with ECG changes that may exactly mimic those of acute ST elevation MI due to epicardial coronary occlusion.¹⁸ The acute stress cardiomyopathy syndrome, associated with left ventricular dysfunction (which was not noted in this case) has been ascribed to catecholamine excess, inducing direct ventricular dysfunction or possible coronary vasospasm. Of interest, right ventricular dilatation and dysfunction, documented by this patient's echocardiogram, have also been described with propofol cardiotoxicity.¹⁹

In summary, this case illustrates of how acute, severe intracranial pathology, in concert with a potentially cardio-toxic anesthetic, can produce dramatic, serial ECG changes and predispose a previously healthy patient to a potentially lethal ventricular tachyarrhythmia. The case calls attention to the wide range of electrophysiologic and structural heart changes that can occur as a consequence of intracranial processes and with associated drug therapy.

Acknowledgments

The support of the National Institutes of Health (R01-GM104987) and the G. Harold and Leila Y. Mathers Charitable Foundation is gratefully acknowledged.

References

1. Byer E, Ashman R, Toth LA. Electrocardiograms with large, upright t waves and long q-t intervals. *Am Heart J.* 1947; 33:796. [PubMed: 20242366]
2. Oppenheimer SM, Cechetto DF, Hachinski VC. Cerebrogenic cardiac arrhythmias. Cerebral electrocardiographic influences and their role in sudden death. *Arch Neurol.* 1990; 47:513. [PubMed: 2185720]
3. Saritemur M, Akoz A, Kalkan K, Emet M. Intracranial hemorrhage with electrocardiographic abnormalities and troponin elevation. *Am J Emerg Med.* 2013; 31:271.e275–277. [PubMed: 22809772]
4. Davis TP, Alexander J, Lesch M. Electrocardiographic changes associated with acute cerebrovascular disease: A clinical review. *Prog Cardiovasc Dis.* 1993; 36:245. [PubMed: 8234777]
5. Huemer M, Boldt LH, Wutzler A, Parwani A, Rolf S, Blaschke D, Haverkamp W. Polymorphic ventricular tachycardia in a patient with herpes encephalitis. *J Clin Neurosci.* 2012; 19:483. [PubMed: 22284924]
6. Larson GM, Koch S, O'Dorisio TM, Osadchey B, McGraw P, Richardson JD. Gastric response to severe head injury. *Am J Surg.* 1984; 147:1:97. [PubMed: 6691557]
7. Rossitch E, Bullard DE. The autonomic dysfunction syndrome: aetiology and treatment. *Br J Neurosurg.* 1988; 2:471. [PubMed: 3077053]
8. Boeve BF, Wijdicks EFM, Benarroch EE, Schmidt KD. Paroxysmal sympathetic storms "diencephalic seizures" after diffuse axonal head injury. *Mayo Clin Proc.* 1998; 73:148. [PubMed: 9472998]
9. Thorley RR, Wertsch JJ, Klingbeil GE. Acute hypothalamic instability in traumatic brain injury: a case report. *Arch Phys Med Rehabil.* 2001; 82:2:246. [PubMed: 11239318]

10. Samuels MA. The brain-heart connection. *Circulation*. 2007; 116:77. [PubMed: 17606855]
11. Wilde AAM, Postema PG, Di Diego JM, Viskin S, Morita H, Fish JM, Antzelevitch C. The pathophysiological mechanism underlying Brugada syndrome: depolarization versus repolarization. *J Mol Cell Cardiol*. 2010; 49:543. [PubMed: 20659475]
12. Postema PG, Wolpert C, Amin AS, et al. Drugs and Brugada syndrome patients: review of the literature and an up-to-date website. *Heart Rhythm*. 2009; 6:1335. www.brugadadrugs.org. [PubMed: 19716089]
13. Darbar D, Yang T, Churchwell K, Wilde AA, Roden DM. Unmasking of brugada syndrome by lithium. *Circulation*. 2005; 112:1527. [PubMed: 16144991]
14. Annecke T, Conzen P, Ney L. Propofol-related infusion syndrome induced by “moderate dosage” in a patient with severe head trauma. *J Clin Anesth*. 2012; 24:51. [PubMed: 22284319]
15. Haeseler G, Karst M, Foadi N, et al. High-affinity blockade of voltage-operated skeletal muscle and neuronal sodium channels by halogenated propofol analogues. *Br J Pharmacol*. 2008; 1552:265. [PubMed: 18574460]
16. Rehberg B, Duch DS. Suppression of central nervous system sodium channels by propofol. *Anesthesiology*. 1999; 912:512. [PubMed: 10443615]
17. Vernooy K, Delhaas T, Cremer OL, et al. Electrocardiographic changes predicting sudden death in propofol-related infusion syndrome. *Heart Rhythm*. 2006; 3:131. [PubMed: 16443524]
18. Wittstein IS. Stress cardiomyopathy: a syndrome of catecholamine-mediated myocardial stunning? *Cell Mol Neurobiol*. 2012; 32:847. [PubMed: 22297544]
19. Martin C, Perrin G, Saux P, Papazian L, Albanese J, Gouin F. Right ventricular end-systolic pressure-volume relation during propofol infusion. *Acta Anaesthesiol Scand*. 1994; 38:223. [PubMed: 8023660]
20. Nademanee K, Veerakul G, Chandanamattha P, et al. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. *Circulation*. 2011; 123:1270. [PubMed: 21403098]

Fig. 1.

Baseline ECG shows sinus rhythm at about 84 bpm with a normal rate-corrected QT (QTc) interval of 442 ms (Hodges formula), with non-specific T wave inversions in the inferolateral leads. The borderline rightward QRS axis may be a normal variant. Color illustration online.

Fig. 2.

Junctional bradycardia at 57 bpm, with broad, deep QT(U) complexes in the anterior-lateral and inferior leads (as shown above, present in leads II and V5). The QTc is markedly prolonged at 623 ms. After the second QRS complex, a burst of torsade de pointes ventricular tachycardia occurs with characteristic “twisting of the points” morphology best seen in the rhythm strips. The non-sustained torsade de pointes episode terminates with a fusion complex (arrow), before the junctional rhythm resumes at a rate of 65 bpm with a markedly prolonged QTc of 749 ms. Artifact simulating pacemaker activity is noted at the end of the tracing. Color illustration online.

Fig. 3.

ECG taken about 16 hours later after the previous tracing demonstrates a junctional escape-capture bigeminal rhythm. Marked ST elevations consistent with a current of injury pattern are seen in the anterior-lateral and inferior leads, and are most evident in the second beat of these couplets. Note that the second beat in the couplets shows a pseudo-right bundle branch block pattern, with an apparent R-prime wave followed by downsloping (“coved”) ST-segment elevations in V1–V3 (V1 shown above) with negative T-waves, characteristic of a Brugada-type pattern (arrowheads). The enhanced repolarization abnormalities in the second of the R–R (i.e., short) cycle beats may be related to their more abbreviated action potential durations or due to rate dependent conduction slowing.²⁰ Color illustration online.